Title

Polymorphisms of the Hypoxia Inducible Factor 1 and microRNA Related Genes and the Susceptibility and Survival of Lung Cancer and Upper Aero-Digestive Tract Cancers

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Polymorphisms of the Hypoxia Inducible Factor 1 and microRNA Related Genes and the Susceptibility and Survival of Lung Cancer and Upper Aero-Digestive Tract Cancers

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Epidemiology

by

Ying Yang

2014

ABSTRACT OF THE DISSERTATION

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by

Ying Yang

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2014

Professor Zuo-Feng Zhang, Chair

Background: Hypoxia inducible factor 1(HIF-1) and microRNAs (miRNAs) regulate transcriptional activities and contribute in several biological processes such as oxygen homeostasis, cell growth, progression and apoptosis that are important in lung and upper aero-digestive tract (UADT) cancer etiology and outcomes. Nonetheless, there are few published studies of the relationship between HIF-1 and miRNA gene polymorphisms and susceptibility and survival of lung cancer or UADT cancers. **Methods:** 1,212 cancer patients (611 lung, 303 oral, 100 pharyngeal, 90 laryngeal, and 108 esophageal) and 1040 population controls were included and the cases were followed for a median duration of 11 years. We genotyped 18 single

nucleotide polymorphisms (SNPs) using Fluidigm Dynamic 96.96 Array Assay--two from HIF-1, seven from the miRNA biogenesis pathway, two from hypoxia regulated miRNAs and seven from miRNA target genes--and investigated their associations with lung and UADT cancer risk with logistic regression and survival using Cox regression. We explored interactions between selected SNPs and established environmental risk factors. A semi-Bayesian shrinkage approach was used to reduce the potential false positive findings caused by multiple comparisons and small sample sizes. **Results:** The minor allele carriers CT+TT (vs. CC) of *RAN* rs14035 was associated with lung cancer development (posterior aOR=1.28, 95% posterior limits=1.00, 1.63), especially with non-small cell lung cancer (NSCLC); and associated with esophageal squamous carcinoma (SQC) susceptibility (posterior aOR=1.81, 95% posterior limits=1.07, 3.07). It was inversely associated with NSCLC death (posterior aHR=0.74, 95% posterior limits=0.59, 0.93). The minor allele carriers AC+CC (vs. AA) of *XPO5* rs11077 presented inverse association with UADT cancer risk (posterior aOR=0.75, 95% posterior limits=0.58, 0.96), especially with UADT SQC and oral and oropharyngeal SQC; and its minor homozygote CC (vs. AA+AC) was inversely related to lung cancer mortality (posterior aHR=0.67, 95% posterior limits=0.51, 0.89), which was pronounced in NSCLC. The minor allele carriers CG+GG (vs. CC) of *GEMIN4* rs2740348 were inversely related to UADT SQC susceptibility (posterior aOR=0.75, 95% posterior limits=0.57, 1.00) and associated with increased mortality of lung cancer (posterior aHR=1.28, 95% posterior limits =1.01, 1.62). In the Caucasian-only population, we repeatedly observed the inverse association between *XPO5* rs11077 CC (vs. AA+AC) and lung cancer mortality; and the association between *GEMIN4* rs2740348 CG+GG (vs. CC) and lung cancer death. **Conclusion:** Our findings suggested that single nucleotide polymorphisms (SNPs) of

miRNA processing and maturation relevant genes played an important role in cancer development and progression; due to the population heterogeneity, their influence in the cancer pathophysiology need further investigations.

The dissertation of Ying Yang is approved.

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2014

DEDICATION

I dedicate my dissertation work to my parents who give me encouragement, supports and all their love.

I also dedicate this dissertation and give thanks to my friends and colleagues for being there for me throughout the process.

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Introduction

I. Lung and upper aero-digestive tract cancers

Lung cancer and upper aero-digestive tract (UADT) cancers are common cancers that account for serious morbidity and mortality. There are two major pathology types of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The NSCLC can be further divided into 3 subtypes: squamous cell carcinoma (SQC), adenocarcinoma (ADC) and large cell carcinoma (LCC) [1, 2]. Lung cancer ranks third in incidence and first in mortality of cancers in the United States (U.S.) [3]. The estimated new cases and deaths from lung cancer in 2014 are 224,210 and 159,260 and the overall 5-year survival of lung cancer was 16.8% in the U.S. [4, 5]. UADT cancers comprise the cancers of the airway and upper digestive tracts, specifically, oral cavity, pharynx, larynx and esophagus, which are contiguous and commonly exposed to toxic substances inhaled and sometimes swallowed. SQC and ADC are major pathology types of UADT caners [6]. For UADT cancers in 2014, it has been estimated that 42,440 new cases and 8,390 deaths of cancers of the oral cavity and pharynx; 12,630 new cases and 3,610 deaths of larynx cancer; and 18,170 new cases and 15,450 deaths of esophageal cancer would occur. The overall 5-year survival was 62.7% for cancers of the oral cavity and pharynx, 60.0% for larynx cancer and 17.5% for esophagus cancer in the U.S. [4, 5].

Cigarette smoking is a well-established risk factor of lung and UADT cancers [7, 8]; and alcohol beverage consumption is equally important as smoking in UADT cancer development [9]. Somatic mutations such as *TP53* gene mutation are also crucial in both lung and UADT cancer development [10]. As to the prognosis, age, stage, histology and treatment are identified to be related to cancer survival [11].

In the recent decade, energy metabolism and microRNA (miRNA) have attracted more attention in the fields of cancer development, progression and prognosis research.

II. Hypoxia inducible factor 1 and cancer

Energy metabolism, composing of glucose metabolism and oxygen homeostasis, has been established as a new hallmark of cancer [12]. The hypoxia inducible factor 1 (HIF-1), a member of hypoxia inducible factors which include HIF-1, HIF-2 and HIF-3, is a key transcript mediator to adapt to hypoxia and maintain oxygen homeostasis [13]. HIF-1 is a heterodimer constituted of HIF-1α and HIF-1β units, of which HIF-1β is non-hypoxia regulated and constantly expressed and HIF-1α is the oxygen-regulating factor that controls HIF-1 activity [14, 15]. HIF-1α is destructed by an ubiquitin-dependent proteasome system under normoxia; while low oxygen interrupts this process and HIF-1α escapes from demolition and combines with HIF-1β to form the heterodimer; then the complex enters into the nucleus and combines with the hypoxia response element of target DNAs, which control cascade pathways and restore the oxygen supply [16, 17]. More than 60 target genes are regulated by HIF-1 and they not only function in metabolic adaptation to hypoxia and stimulation of angiogenesis but also promote cell proliferation and survival [18, 19]. HIF-1 is entangled with cancer by various means. First, tumor development and progression can be dominated by energy metabolism activities. In order to adapt to the rapid growth, tumor vascularization rises to guarantee oxygen delivery; and cancer cells switch to anaerobic metabolism instead of oxidative metabolism, which is known as the Warburg's effect. The Warburg's effect refers to cancer cells feeding on glucose and producing lactic acid even under normoxia. This unique feature of cancer cells is conceived to confer cell growth advantage in the tumor microenvironment [20-23]. Second, cancer cells interrupt the

balance between pro and anti-apoptosis to get survival benefit under poor environmental conditions [24, 25]. Taking mutated *TP53* cells as an example, HIF-1α could increase the stability of the wild tumor suppressor *TP53* that induces cell death via proapoptotic factors such as BCL-2-associated X protein or the discharge of cytochrome c from mitochondria under the physiology status; however, it could not interact with mutated *TP53* and the programmed cell death is disturbed [19, 26, 27]. Third, overexpression of HIF-1α is associated with the accumulation of common genetic alterations in cancer cells, which suggest that HIF-1α might provide selective advantages for the cells with carcinogenesis mutations [24, 28, 29]. In summary, due to the unique metabolism characteristics of cancer cells, the critical role of HIF-1 in energy metabolism, and the contribution of productions of HIF-1 target genes making to carcinogenesis and the selective advantage HIF-1 conferring to malignant transformed cells, it is reasonable to consider that HIF-1 is important in cancer pathophysiology.

Epidemiology studies on various cancer sites have focused on two non-synonymous single nucleotide polymorphisms (SNPs) of *HIF-1*, rs11549465 and rs11549467, and reported positive relationship with cancer development; some are about other polymorphisms of *HIF-1* gene and have not reached consistent results [30-41]. However, most studies suffered from small sample size due to stratifications; and lacked the interaction assessments between environmental factors and the inherited factors.

III. microRNA and cancer

MicroRNA (miRNA) has been another hotspot in cancer research in recent years. Most miRNAs reside within intergenic or intronic regions of other genes. They are non-coding, single stranded RNAs of ~22 nucleotides and negatively regulate their target mRNAs at the post-transcriptional

level [42-46]. The biogenesis of a miRNA is a two-step procedure and takes place in both nucleus and cytoplasm. In nucleus, a large precursor RNA known as a pri-miRNA is transcribed by the RNA polymerase II. The pri-miRNA is processed by the RNase III enzyme, Drosha, into a ~70-nucleotide pre-miRNA. The pre-miRNA is exported from the nucleus to the cytoplasm by the RAN GTP-dependent transporter exportin 5 (XPO5). In cytoplasm, the pre-miRNA is further processed into a double-stranded RNA of ~22 nucleotides—miRNA: miRNA* duplex by another RNase III enzyme, Dicer. Finally, one strand of the duplex is incorporated into the RNA induced silencing complex (RISC) that is composed of the Argonaute proteins, Gemin3 and Gemin4 and others; and the target mRNA will be degraded or repressed for the translation depending on the degree of the complementarity of the miRNA to its target sequences [43, 46-58].

So far, miRNAs have been identified to regulate one third of human mRNA expression, and impact various genetic pathways including carcinogenesis-related pathways; thus it is possible that the disrupted function of miRNAs may contribute to diverse diseases, including cancer [47, 59-64]. Also, miRNAs themselves can be oncogenic or tumor suppressing [47, 65-67]. Studies have shown that the global repression of miRNA maturation is a common phenomenon observed in human tumors [68-70]. The altered functions of proteins involved in miRNA biogenesis machinery such as slicing pre-RNAs or constructing the RISC can cause the dysregulation of miRNAs and contribute to cancer development, progression and prognosis [47, 71]. For example, the reduced Dicer expression is in proportion to let-7 down-regulation and associated with poor prognosis of lung cancer [72].

In summary, variation of miRNA processing genes may result in the dysregulation of mature miRNAs, miRNAs themselves may function as oncogenes or tumor suppress genes; and related

miRNA target genes may be involved in cell proliferation, differentiation and apoptosis; thus, it is conceivable that deviant allele frequency of sequence variations from miRNAs, their biogenesis machinery, and their regulating downstream genes might contribute to cancer risk, prognosis and survival by biological mechanisms at different levels, for example, through the transcription of primary transcripts, or through the evolution of pri-miRNAs and pre-miRNAs, or by miRNA-mRNA interactions [73, 74]. Epidemiology studies on miRNA related SNPs and cancer susceptibility and prognosis are inconsistent due to the heterogeneity of cancer types, study design and sample size, and genetic backgrounds of different populations. Approximately twenty epidemiologic studies of miRNA have been conducted, but results are conflicting; even fewer studies have focused on lung- and UADT cancers [75-96].

IV. HIF-1 and miRNA in cancer

Recent work has illustrated that most transcription factors harbor a miRNA component and shed light on the mechanism in the context of hypoxia adaption [97]. A new concept known as hypoxia-regulated miRNAs (HRMs) has been proposed referring to miRNAs that are consistently induced in response to low oxygen at several time points in at least two lines of cancer cells, for example, miR-20, miR-23, and miR-26, miR27 and miR155 and let-7 family are all identified as HRMs [98-101]. HRMs provide another connection between tumor specific stress and gene expression controls, and HIF-1 as a master transcript factor in response to hypoxia is established to play a critical regulatory role for at least some HRMs, the exact mechanism of which is still under investigation [74, 97]. There are few epidemiologic studies on the relationship between the polymorphisms of this specific group of miRNAs and cancer.

Nevertheless, their importance should be attached to, considering the role energy metabolism, tumor microenvironment and miRNA playing in cancer.

V. miR-SNP

miR-SNPs are a group of SNPs that are located in miRNAs, binding sites of miRNA downstream genes or the constituents of the miRNA biogenesis machinery, and might affect miRNA functions [102].

For decades, researchers have devoted to explore both environment and genetic factors contributing to lung and UADT cancer growth and progression, and their achievements have greatly helped prevent cancer development and achieve better prognosis; however, despite advances in understanding the pathogenesis of lung and UADT cancers, improvements in surgical procedures and the introduction of newer treatment regimens, lung and UADT cancers are still at the top of the list of cancer incidence and mortality; and survival, especially for lung and esophageal cancers, has not been improved much [4].

Gaps in literature

A brief summary of current epidemiology publications on the association between *HIF-1* related genetic polymorphisms as well as miR-SNPs and lung and UADT cancer susceptibility and survival is presented in Table 1[78, 81, 94, 103-127].

Table 1. Current epidemiology publications on *HIF-1* SNPs and mi-SNPs in lung and UADT cancers

SNP	Lung cancer susceptibility	UADT cancer Susceptibility	Lung cancer Survival	UADT cancer survival

HIF-1α	Three studies on two non-synonymous SNPs (rs11549465&rs11549467)	Six studies in various cancers (oral, esophageal, head and neck) on two non-synonymous SNPs (rs11549465&rs11549467)	None	None
miR-SNP	Five studies in the Chinese; One in the Caucasians; One in the Koreans	Various cancers (oral, esophageal, head and neck) Eight studies in the Chinese; Four in the Caucasians	Six in the Chinese; One in the Caucasians; One in the Koreans; One in the Spanish	One in the Chinese

Taking miR-SNPs as an example shown in Table 2 [78, 81, 94, 104-127], due to the heterogeneity of study design, dissimilar genetic backgrounds of different populations, and the diverse SNP selections, the conclusions of existing studies are incompatible.

Table 2. Previous studies on miR-SNPs in lung and UADT cancers

Published year	Cancer	Sample Size	Gene	SNP	Population	Risk	Prognosis	Notes
2008	Esophageal	346/346	miRNA processing	41 SNPs	White	Yes		
2008	NSCLC	893	miR-196a2	rs11614913	Chinese		Yes	
2009	Lung	1058/1035	miR-196a2	rs11614913	Chinese	Yes		
2010	Lung	1984/2073 (165 ADC, 125 SQC)	RNA mediated interference machinery	12 SNPs	Caucasians	Yes	Yes	
2010	Lung	652/652	miRNA processing	24 SNPs	Koreans	Yes		
2010	Esophageal SQC	444/468	miR-146a	rs2910164	Chinese	Yes		
2010	HNC SQC	1109/1130	Pre-miRNA	4 SNPs	Caucasians	Yes		
2011	NSCLC	175	miR-SNP	11 SNPs	Caucasian		Yes	recurrence
2011	SCLC	666/758	MYCL1	rs3134615	Chinese	Yes		
2011	HNC SQC	1077/1073	miR-184	rs8126	Caucasians	Yes		
2012	HNC	397/900	miRNA processing	3 SNPs	Chinese	Yes		
2012	Esophageal SQC	537/608	RAP1A (miR-196a)	rs6573	Chinese	Yes	Yes	metastasis
2012	NSCLC	442	miR-196a2	rs11614913	Chinese		Yes	treatment
2012	NSCLC	388	miRNA	5 SNPs	Korean		Yes	recurrence
2012	Oral	40/40	miR-146a	rs2910165	Chinese	Yes		

Published year	Cancer	Sample Size	Gene	SNP	Population	Risk	Prognosis	Notes
2013	Lung	2332/2457	CD133	rs2240688	Chinese	Yes	Yes	
2013	Nasopharyngeal	837	miR-608	rs4919510	Chinese		Yes	recurrence
2013	NSCLC	576	pre-miR-27a	rs895819	Chinese		Yes	
2013	NSCLC	116	XPO5	rs11077	Chinese		Yes	
2013	NSCLC (early stage)	535	miR-SNP	240 SNPs	Caucasians		Yes	recurrence
2013	SCLC	42	XPO5	rs11077	Chinese		Yes	
2013	Esophageal SQC	380/380	miR-196a2	rs11614913	Chinese	Yes		
2013	HNC	1066/1074	CASP3 (miR-885-5p)	rs1049253	Caucasians	Yes		
2013	Lung	600/600	BIRC5(miR-335)	rs2239680	Chinese	Yes		
2013	Nasopharyngeal	158/242	miR-149	rs2292832	Chinese	Yes		
2013	Nasopharyngeal	167/171	miR-151bingding site	rs3218073/rs7201	Chinese	Yes		
2013	NSCLC	120/164	miR-502 binding site	rs16917496	Chinese	Yes		

Our study was the first to investigate the relationships between *HIF-1A* gene polymorphisms and lung- and UADT-cancer survival, and the first to explore the environment-gene interactions; we also initially constructed polygenic risk scores based on functionally closed pathways in lung and UADT cancers.

Hypotheses and specific aims

I. Specific aim and hypothesis 1

The first specific aim is to estimate the associations between selected SNPs and the susceptibility of lung cancer and UADT cancers. The underlining hypothesis is that SNPs of the genes involved in HIF-1, miRNA processing genes and HRMs and their target genes might be associated with susceptibility of lung cancer and UADT cancers. Those genes may play an important role in carcinogenesis: variations of those genes may affect the transcription or translation activities and consequently change the function of protein products; in turn they might contribute to tumorigenesis and alter the susceptibility of lung cancer and UADT cancers.

II. Specific aim and hypothesis 2

The second specific aim is to estimate the associations between selected SNPs and survival of lung cancer and UADT cancers. The underlining hypothesis is that SNPs of the genes involved in HIF-1, miRNA processing genes and HRMs and their target genes might affect lung and UADT cancer survival. Due to the important role of those genes playing in cancer progression, SNPs may affect the transcription or translation activities of genes and consequently change the function of protein products; in turn they might contribute to cancer growth, progression and apoptosis and influence the prognosis of lung cancer and UADT cancers.

III. Specific aim and hypothesis 3

The third specific aim is to explore the interactions of selected SNPs and established environmental risk factors, including cigarette smoking of lung and UADT cancers and alcohol drinking of UADT cancers as to cancer risks. The underlining hypothesis is that there might be potential interactions between genetic variations and tobacco smoking in lung cancer and UADT cancer development (or interactions with alcohol drinking in UADT cancers). Both environmental factors and genetic factors may be associated with cancer initiation and development through a complex interactive network such as DNA repair and inflammation reactions[128], thus it is reasonable to assume that they would influence each other's effects to some extent.

IV. Specific aim and hypothesis 4

The fourth specific aim is to explore the interactions of selected SNPs and established environmental factors, including cigarette smoking of lung and UADT cancers and alcohol drinking of UADT cancers as to cancer survival. The underlining hypothesis is that there might be potential interactions between genetic variations and tobacco smoking in lung cancer and UADT cancer cases (or interactions with alcohol drinking in UADT cancer cases). Both environmental factors and genetic factors might impact cancer apoptosis and progression through a complex interactive network such as c-Myc or KRAS pathways [129], thus it is reasonable to assume that they would influence each other's effects to some extent.

Methods

I. Study population

We conducted a population-based observational study. The source population was residents in Los Angeles County (LAC) from 1999 to 2004. The study population was chosen based on the following criteria,

(a) they were residents of LAC at the time of recruitment (for controls) or diagnosis (for cases);

(b) were ages 18 to 65 years during the study period; and

(c) were able to speak either English or Spanish or had a translator available on site.

Cases were pathologically confirmed new incidences of lung cancer or UADT cancers, including oral cancers, pharyngeal cancer, laryngeal cancer and esophageal cancer, all of which were identified by the rapid ascertainment system of the LAC Cancer Registry under the Cancer Surveillance Program at the University of Southern California (USC). Recurrent cancer cases were excluded from our study. Population-based controls that were lung cancer and UADT cancer free were identified through a formal algorithm from a census within the neighborhood of each individual case. Cases and controls were initially matched by age decade, gender, and neighborhood.

Recruitment rates among eligible cases were 39%, 54%, 45%, 42% and 35% for lung, oral, pharyngeal, laryngeal and esophageal cancer, respectively, and 72% for controls. The reasons for nonparticipation in cases included:

(i) the patients died before being contacted with (25% for lung) (10% for UADT);

(ii) the patients could not be reached due to incorrect addresses (14% for lung) (18% for UADT);

(iii) the patients were too ill to get interviewed (5% for lung) (4% for UADT);

(iv) the patients were not willing to participate the study (16% for lung) (21% for UADT); and

(v) the physicians refused our requests to contact their patients (1% for lung).

The reasons for nonparticipation in controls were:

(i) the controls could not be contact with due to incorrect addresses (8%); and

(ii) the controls were not willing to participate the study (19%).

A total of 1,212 cases were recruited in our study. There were 611 lung cancer cases, including 95 (16%) lung squamous carcinomas (SQC), 297 (49%) lung adenocarcinomas (ADC), 115 (19%) large cell carcinomas (LCC), 75 (12%) small cell carcinomas (SCC) and 29 (5%) others. There were 335 oral and oropharyngeal cancers, 90 laryngeal cancers and 40 other head and neck sites, of which 465 (94%) were SQC and 28 (6%) were other histology types. 108 esophageal cancer cases including 32 (30%) SQC, 74 (69%) ADC and 2 (2%) others were also counted in. A total of 1040 population controls were comprised in our study.

II. Data collection

Participants were interviewed from 1999 to 2004. Trained interviewers used study specific standardized questionnaires to collect general information. The questionnaires included demographic characteristics--age, gender, ethnicity, and education; detailed behavioral factors--diet (modified short national cancer institute health habits and history questionnaire) such as fruit, vegetable or meat intake; drug abuse; cigarette smoking and alcohol drinking; and occupational and environmental exposure history such as environmental smoke, employment history in chemical plants or mining industry; selected clinical features such as chronic diseases and family history of cancer. The lifetime accumulated history of tobacco smoking and alcohol

drinking was recorded, which provided information on age of onset, duration of exposures, intensity of exposures, and years of quitting before diagnoses for cases or interviews for controls. For the data analysis purpose, cigarette smoking was measured in pack-years. One pack-year of cigarette use is equivalent to smoking one pack of cigarettes per day for one year (i.e., 1 pack year is the total of 365 packs or 7,300 cigarettes a year); smoking was also measured as never vs. ever smoking, and never smokers were those smoking less than 100 cigarettes lifetime; otherwise were ever smokers. Similarly, alcohol drinking was measured by the average number of drinks (including wine, beer or liquor) consumed per day; and was also assessed as never vs. ever drinking. Alcohol drinkers were those who drank one alcoholic drink per month for a period of at least six months; otherwise were nondrinkers. The personal interview took 40 minutes to 1 hour. For 89% of cases, interviews were conducted within 6 months after diagnoses.

At the end of interviews, buccal cells were collected for DNA analysis by the method of brushing of buccal mucosa and rinsing with mouthwash. The rates for interviewed participants providing buccal cells were 89% for controls and 89%, 68%, 88%, and 90% for lung, oropharyngeal, laryngeal and esophageal cancer cases, respectively. All specimens were transported and stored at -70°C freezers in the Molecular Epidemiology Laboratory, Fielding School of Public Health, University of California at Los Angeles (UCLA).

The vital status was checked through the Social Security Death Index. The survival time was calculated as the interval between the date of diagnosis and the date of death or the date of the last follow-up that was July 13th, 2012, if still alive.

III. SNP selection

Based on biological function importance and previous literature, we identified SNPs of gene *HIF1A*, which plays a critical role in hypoxia microenvironment, carcinogenesis and cell survival; of HRMs, which are regulated by HIF-1 and believed to contribute in cancer development and survival; of genes regulating miRNA processing and maturation, taking the complicate and crucial function of miRNAs presenting in cancer into account; and target genes regulated by HRMs and involved in cancer pathophysiology. We mostly focused on coding non-synonymous SNPs, SNPs located in regions regulating gene transcriptions, such as promoter areas and SNPs of which minor allele frequency value (MAF) ≥ 5% in the Caucasians. All SNPs were determined from the National Center for Biotechnology Information SNP database[130]. The candidate SNPs are shown in Table 3.

Table 3. Candidate SNPs of HIF-1 and HRM related genes and pathways

Gene	Description	Chromosome	SNP	Minor Allele	MAF (%)	Function
HIF1A	HIF-1 pathway	14	rs2057482	T	10	3' UTR
HIF1A	HIF-1 pathway	14	rs2301113	C	17	intron
RAN	miRNA processing and maturation	12	rs14035	T	30	Near Gene-3
XPO5	miRNA processing and maturation	6	rs11077	C	42	3' UTR
DICER1	miRNA processing and maturation	14	rs3742330	G	8	3' UTR
AGO2	miRNA processing and maturation	8	rs4961280	A	13	Near Gene-5
GEMIN3	miRNA processing and maturation	1	rs197412	C	42	missense
GEMIN4	miRNA processing and maturation	17	rs7813	A	49	missense
GEMIN4	miRNA processing and maturation	17	rs2740348	G	18	missense
MIR-26A1	miRNA coding	3	rs7372209	T	26	Within miRNA
MIR-27	miRNA coding	19	rs895819	C	30	Within miRNA
DOCK4	Within a miR-20/miR-106 binding site	7	rs3801790	G	30	3' UTR

Gene	Description	Chromosome	SNP	Minor Allele	MAF (%)	Function
IL6R	Within a miR-23 binding site	1	rs4072391	T	21	3' UTR
CXCL12	Within a miR-23a/b binding site	10	rs1804429	C	6	3' UTR
TAB3	Within a miR-23 binding site	X	rs3816757	C	20	3' UTR
CDK6	Within a miR-26 binding site	7	rs42031	T	22	3' UTR
TP53INP1	Within a miR-155 binding site	8	rs896849	C	10	3' UTR
E2F2	Within a Let-7 binding site	1	rs2075993	A	47	3' UTR

DNA samples were isolated by the method of modified phenol-chloroform and assayed for purity and concentration by spectrometry [131]. Samples were first held at 92°C for 10 minutes; then underwent 60 thermocycles of denaturing at 92°C for 15 seconds; finally were annealed at 62°C for 80 seconds. SNP genotyping was performed by a customized Fluidigm Dynamic 96.96 Array™ Assay (Fluidigm, South San Francisco, CA) at the UCLA Genotyping and Sequencing Core. The assays were based on allele-specific PCR SNP detection chemistry with Dynamic Array™ integrated fluidic circuits (IFCs). The SNP type assay employed tagged, allele specific PCR primers and a common reverse primer. A universal probe set was used in every reaction producing uniform fluorescence and Fluidigm provided locus-specific primer sequences that allowed one to confirm target locations. We also performed replicate quality control with about 5% of the samples.

SNPs were finalized in our analysis based on the following criteria:

(i) Hardy-Weinberg equilibrium (HWE) p-value > Bonferroni-adjusted p-value 0.0028;

(ii) genotyping call rate ≥ 95% and

(iii) the pairwise linkage disequilibrium (LD) $r^2 < 0.8$.

Table 4 presented the HWE p-value of each SNP in our study.

Table 4. HWE p-values of SNPs

Gene	Description	SNP	HWE p-value in controls	HWE p-value in the Caucasian controls
HIF1A	HIF-1 pathway	rs2057482	0.6122	0.3053
HIF1A	HIF-1 pathway	rs2301113	<0.0001	0.2889
RAN	miRNA processing and maturation	rs14035	0.1189	0.5488

Gene	Description	SNP	HWE p-value in controls	HWE p-value in the Caucasian controls
XPO5	miRNA processing and maturation	rs11077	0.0680	0.0111
DICER1	miRNA processing and maturation	rs3742330	0.7597	1.0000
AGO2	miRNA processing and maturation	rs4961280	0.0654	0.3435
GEMIN3	miRNA processing and maturation	rs197412	0.2538	0.4806
GEMIN4	miRNA processing and maturation	rs7813	0.0976	0.6602
GEMIN4	miRNA processing and maturation	rs2740348	0.5535	0.6619
MIR-26A1	miRNA coding	rs7372209	0.9340	0.8253
MIR-27	miRNA coding	rs895819	0.2846	0.0326
DOCK4	Within a miR-20/miR-106 binding	rs3801790	0.7781	0.3486
IL6R	Within a miR-23 binding site	rs4072391	0.0402	0.8880
CXCL12	Within a miR-23a/b binding site	rs1804429	1.0000	1.0000
TAB3	Within a miR-23 binding site	rs3816757	<0.0001	<0.0001
CDK6	Within a miR-26 binding site	rs42031	0.3771	0.7956
TP53INP1	Within a miR-155 binding site	rs896849	0.0603	0.0554
E2F2	Within a Let-7 binding site	rs2075993	1.0000	0.0567

TAB3 rs3816757 was excluded from further analysis due to the violation of the HWE. Although *HIF1A* rs2301113 violated the HWE in the overall population ($p<0.0001$), but the HWE still held in the Caucasians ($p=0.2889$), we decided to keep it in our analysis.

IV. Statistical analysis

For the analyses of associations between genetic variations and cancer susceptibility, unconditional logistic regression models were used to determine crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs). The reason for unconditional logistic regression models was to increase precision and power over standard matched analyses, as inclusion of the matching covariates-age and gender-allowed the comparison of the cases of each cancer type with all controls. We listed detailed information on logistic regression models as the following:

i) Independent variables: 1) lung cancer development; 2) NSCLC development; 3) SCLC development; 4) lung ADC development; 5) lung SQC development; 6) lung LCC development; 7) UADT cancer development; 8) UADT SQC development; 9) oral and oropharyngeal SQC development; 10) laryngeal SQC development; 11) esophageal SQC development； 12) esophageal ADC development. (categorical; case=1, control=0).

ii) Dependent variables: identified SNPs in genotype model (categorical; wild homozygote=0, heterozygote=1, variant homozygote=2), log-additive model (continuous; wild homozygote=0, heterozygote=1, variant homozygote=2). SNPs were further analyzed in dominant model (categorical; minor allele carries=1 vs. wild homozygote=0) or recessive model (categorical; minor homozygote=1 vs. wild homozygote and heterozygote=0).

iii) Covariates: age (continuous); gender (categorical; male=0; female=1); ethnicity (categorical; Caucasian=0, Hispanic=1, African American=2, Asian=3, other=4); education level (categorical; 0-12 years of education (high school) =0, 13-16 years of education (college) =1, more than 16 years of education (beyond college)=2); packyears (continuous); and alcoholic drinks per day (continuous).

As to the adjusted estimations of cancer risk, age, gender, ethnicity and education and cigarette smoking were included in lung cancer susceptibility analysis; in addition to those variables, alcohol drinking was included in UADT cancer susceptibility analysis.

For the survival analysis, only cases were counted in. The survival time was calculated as the interval between the date of diagnosis and the date of death or the date of the last follow-up that was July 13th, 2012, if still alive. The median follow-up time was 11.1 years in all cases, and 11.5 years in lung cancer cases and 10.8 years in UADT cancer cases, respectively. Semi-parametric Cox proportional hazards models were used to obtain crude and adjusted hazard ratios (HRs) and corresponding 95% CIs. Proportional hazard assumptions were checked in each model [132] and no noteworthy violations were detected, so we proceeded to the analysis. We listed detailed information on Semi-parametric Cox proportional hazards models as the following:

i) Independent variables: 1) lung cancer survival; 2) NSCLC survival; 3) SCLC survival; 4) lung ADC survival; 5) lung SQC survival; 6) lung LCC survival; 7) UADT cancer survival; 8) UADT SQC survival; 9) oral and oropharyngeal SQC survival; 10) laryngeal SQC survival; 11) esophageal SQC survival； 12) esophageal ADC survival. (death=1, censored=0, categorical; survival days, continuous).

ii) Dependent variables: identified SNPs in genotype model (categorical; wild homozygote=0, heterozygote=1, variant homozygote=2), log-additive model (continuous; wild homozygote=0, heterozygote=1, variant homozygote=2). SNPs were further analyzed in dominant model (categorical; minor allele carries=1 vs. wild homozygote=0) or recessive model (categorical; minor homozygote=1 vs. wild homozygote and heterozygote=0).

iii) Covariates: age (continuous); gender (categorical; male=0; female=1); ethnicity (categorical; Caucasian=0, Hispanic=1, African American=2, Asian=3, other=4); education level (categorical; 0-12 years of education=0, 13-16 years of education=1, more than 16 years of education=2); packyears (continuous); alcoholic drinks per day (continuous); pathology types (categorical; for lung cancer: SQC=1, ADC=2, LCC=3, SCLC=4, other=5; for UADT cancers: SQC=1, ADC=2, other=3); and cell differential grades (categorical; well differentiated=0, moderately differentiated=1, poorly differentiated=2, undifferentiated=3, undetermined=4).

In terms of adjusted estimations of survival analysis, age, gender, ethnicity and education, and cigarette smoking, cell differential grades and pathology types including SQC, ADC, LCC and SCC and others were adjusted in lung cancer models; while age, gender, ethnicity and education, and cigarette smoking, alcohol drinking, cell differential grades and pathology types including SQC, ADC and others were adjusted in UADT cancer models.

For both the case control study and the survival analysis, we first analyzed SNP genotypes as continuous and dummy variables. These results were used to determine the propriety of use of a dominant or a recessive model. However, to facilitate the presentation of our results, we analyzed and presented all models of all eligible SNPs.

We explored multiplicative interactions with adding a product term of two main variables in addition to main variables, and potential confounding factors in the model. For example, for SNP-smoking multiplicative interactions, a SNP was in its dominant or recessive model (categorical; reference=0, comparison=1), and smoking was categorized as ever smoking and never smoking (categorical; nonsmokers=0, smokers=1); these two dichotomous variables, together with their product term and other covariates were put in the statistical models. The

scenario of alcohol drinking was similar; thus alcohol drinking was categorized as ever drinking and never drinking (categorical; nondrinkers=0, drinkers=1).

We also explored additive interactions between environmental factors, say, smoking and alcohol drinking, and selected SNPs that were associated with lung- or UADT cancer development after semi-Bayesian shrinkage with adjustment for covariates. We referred to methods proposed by Tyler J. VanderWeele et al., Mirjam J. Knol et al. and David B. Richardsonet et al. [133-135]. For the additive interactions, the genotypes were categorized as binary and the category associated with the lowest gene-environment joint effect was as the reference group. We applied inverse probability treatment weighting approach and bootstrap to construct profile-likelihood confident limits.

In addition, we used all SNPs of miRNA processing and maturation to construct a polygenic risk score [136-138] and estimated the associations between the score and lung- or UADT cancer development and survival. Compared to the wild homozygote group, the heterozygote was considered as having one risk score, and the variant homozygote was taken as getting two risk scores. The total score was calculated by adding all scores together and was evaluated both as continuous variables and as their quartiles in controls; or quartiles in all patients for survival analyses. We also drew Receiver Operating Characteristic (ROC) curves for polygenic risk scores for lung cancer and UADT cancers, respectively.

We performed semi-Bayesian shrinkage approaches to address potential false positive findings caused by multiple comparisons or small sample size [139, 140]. Referring to the distribution of the available genome wide study results, existing biological mechanism evidence and limited previous epidemiology studies; also taking the exploration feature of our study into account, we

applied a Normal coefficient prior with mean 0 and variance 0.125 (corresponding to OR/HR = 1.00, 95% prior limits = 0.50, 2.00, after exponentiation) for the shrinkage.

Due to nonparticipation, unwilling to answer questionnaires or provide buccal cells, and genotyping, there was missing in our database; however, since imputation of SNPs was problematic, we restrained all analyses in complete data only.

We conducted a sensitivity analysis in the Caucasians to estimate the potential impacts of mixed ethnicities to our study.

All statistical analyses and ROC curves were done with SAS v9.3 software (SAS Institute Inc., Cary, NC). We constructed Kaplan-Meier curves for each SNP; and we also built forest plots on major findings to visualize our results with R 2.15.1 (The R Foundation for Statistical Computing).

The study was approved by the institutional review boards of UCLA and USC. Informed consents were obtained from all participants.

Results

I. Specific aim 1. Cancer susceptibility analyses using a case control study design

(i) Demographics

Table 1.1.1 showed the demographic distributions of LA study. The proportion of males among UADT cancer cases (76%) was higher than that among controls (60%); and lung cancer cases had fewer males (50%) than controls. The average cigarette consumption among smokers (mean ± standard deviation) was 38.2±22.4 pack-years in lung cancer cases; 32.3±23.2 pack-years in UADT cancer cases and 17.6±17.9 in controls. A higher proportion of alcohol drinkers was

found among UADT cancer cases than that among controls (80% vs. 75%); and the proportion of alcohol drinkers who drank 2 or more drinks per day in UADT cancer cases was higher than that in controls (42% vs. 18%). The prevalence of ever alcohol drinking was slightly lower among lung cancer cases (72%) than among controls.

(ii) Lung cancer susceptibility

Table 1.1.2 to table 1.1.4 showed the main associations between identified SNPs and lung cancer development; also with the risk of pathology-stratified subtypes of lung cancer. Table 1.1.5 to table 1.1.10 presented the posterior results after semi-Bayesian shrinkage approach based on the initial findings from table 1.1.2 to table 1.1.4. Both crude and adjusted results were presented and as to the latter, adjusted covariates included age, gender, and ethnicity, education level, and tobacco smoking as pack-years. Table 1.1.11 showed the multiplicative interactions of each SNP and cigarette smoking in lung cancer and table 1.1.12 were results of semi-Bayesian shrinkage for multiplicative interactions.

1) Gene *HIF1A*

The TT (vs. CC) genotype of rs2057482 of *HIF1A* was associated with lung cancer (aOR=2.32, 95% CI=1.15, 4.71). The association was also observed in NSCLC (aOR=2.40, 95% CI=1.17, 4.91) but not in SCLC. Further stratified on NSCLC, similar associations persisted in ADC (aOR=2.34, 95% CI=1.06, 5.16). If we stratified by tobacco smoking status, in the recessive model, the association of TT (vs. CC+CT) genotype of rs2057482 with lung cancer was only observed in nonsmokers (aOR=9.60, 95% CI=3.10, 29.74) but not in smokers (aOR=1.10, 95% CI=0.48, 2.54). The adjusted p-value of the SNP-smoking product term was 0.01 and the posterior p-value was 0.27. All adjusted associations were pulled towards the null after semi-

Bayesian shrinkage. Similarly, the association between CC (vs. AA+AC) genotype of another *HIF1A* SNP, rs2301113, and lung cancer was observed in nonsmokers (aOR=3.04, 95% CI=1.34, 6.86) but not in smokers (aOR=0.80, 95% CI=0.49, 1.31); and the adjusted p-value of the SNP-smoking product term was 0.08.

2) miRNA biogenesis machinery

The minor allele carriers CT+TT (vs. CC) of rs14035 of *RAN* was related to lung cancer in the adjusted model (aOR=1.32, 95% CI=1.02, 1.72). Similar associations were observed in NSCLC (aOR=1.35, 95% CI=1.03, 1.77), and LCL (aOR=1.80, 95% CI=1.08, 3.01). After semi-Bayesian shrinkage, the associations remained in lung cancer (posterior aOR=1.28, 95% CI=1.00, 1.63) and NSCLC (posterior aOR=1.30, 95% CI=1.01, 1.67).

In the recessive model, the CC (vs. AA+AC) genotype of rs11077 of *XPO5* was associated with lung cancer (aOR=1.46, 95% CI=1.03, 2.07), SCLC (aOR=2.61, 95% CI=1.27, 5.35), SQC (aOR=2.20, 95% CI=1.21, 4.32) and ADC (aOR=1.53, 95% CI=1.01, 2.31). However, all associations were weakened and contained the null after semi-Bayesian shrinkage. When stratified on tobacco smoking status, in the recessive model, the CC (vs. AA+AC) genotype was related to lung cancer in nonsmokers (aOR=1.98, 95% CI=1.01, 3.86), but not in smokers (aOR=1.39, 95% CI=0.92, 2.10); and the adjusted p-value for the heterogeneity was 0.74.

The minor allele carriers TC+CC (vs. TT) of rs197412 of *GEMIN3* showed inverse relationship with SCLC (aOR=0.48, 95% CI=0.27, 0.86) which was pulled towards the null after semi-Bayesian shrinkage (posterior aOR=0.65, 95% posterior limits=0.41, 1.03). When stratified by tobacco smoking status, the association was observed in nonsmokers only (aOR=0.58, 95%

CI=0.34, 0.97), but not in smokers (aOR=1.14, 95% CI=0.81, 1.60), and the p-value for the smoking-SNP product term was 0.09.

The SNP rs2740348 of *GEMIN4*, in its dominant model (CG+GG vs. CC), showed an inverse relationship with lung cancer development in nonsmokers only (aOR=0.53, 95% CI=0.29, 0.95), but not in smokers (aOR=0.89, 95% CI=0.62, 1.27); and the adjusted p-value for the heterogeneity was 0.30.

Table 3.1.1 presented the associations between the polygenic risk score of all seven SNPs of miRNA biogenesis machinery and lung cancer susceptibility, after adjusting for covariates. No non-null associations were observed.

3) HRMs

The TT (vs. CC) genotype of rs7372209 of *MIR26-1A* was associated with lung cancer (aOR=1.62, 95% CI=1.00, 2.62) and of ADC (aOR=1.98, 95% CI=1.15, 3.42) after adjusting for covariates. The associations were weakened and included the null after semi-Bayesian shrinkage. When stratified by tobacco smoking status, the minor allele carriers CT+TT (vs. CC) was associated with lung cancer only among smokers (aOR=1.39, 95% CI=1.01, 1.93), but not among nonsmokers (aOR=0.79, 95% CI=0.47, 1.32), and the adjusted p-value for the heterogeneity was 0.34.

(iii)UADT cancer susceptibility

Tables 1.2.1 to 1.2.3 presented main associations of selected SNPs with UADT cancers and the corresponding histology and site stratified results. Tables 1.2.4 to 1.2.9 presented the posterior results of semi-Bayesian shrinkage based on the previous positive findings from tables 1.2.1 to 1.2.3. Both crude and adjusted results were presented and as to the latter, adjusted covariates

included age, gender, and ethnicity, education level and tobacco smoking as pack-years, and alcohol drinking as alcoholic drinks per day. Table 1.2.10 presented the multiplicative interactions between selected SNPs and cigarette smoking in UADT cancers and table 1.2.11 was the semi-Bayesian shrinkage posterior results of multiplicative interactions. Table 1.2.12 presented the multiplicative interactions of selected SNPs and alcohol drinking in UADT cancers and table 1.2.13 was the corresponding posterior results of semi-Bayesian shrinkage.

1) Gene *HIF1A*

We observed divergent association between *HIF1A* rs2301113 and UADT cancers stratified by alcohol drinking status. The minor allele carriers AC+CC (vs. AA) of *HIF1A* rs2301113 showed reverse associations in nondrinkers (aOR=0.50, 95% CI=0.28, 0.91) in comparison with alcohol drinkers (aOR=1.28, 95% CI=0.95, 1.72); the adjusted p-value of the product term was 0.02 but the posterior adjusted p-value was 0.07 after semi-Bayesian shrinkage.

2) miRNA biogenesis machinery

The minor allele carriers CT+TT (vs. CC) of rs14035 of *RAN* were associated with esophageal SQC (aOR=4.07, 95% CI=1.74, 9.55), and after Semi-Bayesian shrinkage (posterior aOR=1.81, 95% posterior limits=1.07, 3.07).

The minor allele carriers AC+CC (vs. AA) of rs11077 of *XPO5* was inversely related to UADT cancers (aOR=0.72, 95% CI=0.55, 0.93). The associations were also observed in SQC (aOR=0.71, 95% CI=0.53, 0.95), and oral and oropharyngeal SQC (aOR=0.70, 95% CI=0.50, 0.97). After semi-Bayesian shrinkage, the associations of the minor allele carriers AC+CC (vs. AA) of rs11077 remained in UADT cancers (posterior aOR=0.75, 95% posterior limits=0.58, 0.96), SQC (posterior aOR=0.75, 95% posterior limits=0.57, 0.97) and oral and oropharyngeal

cancer (posterior aOR=0.75, 95% posterior limits=0.55, 1.00). This AC+CC (vs. AA) genotype was associated with UADT cancers in smokers (aOR=0.58, 95% CI=0.41, 0.81) but not in nonsmokers (aOR=1.02, 95% CI=0.66, 1.56); the p-value for the heterogeneity was 0.04; and the posterior adjusted p-value was 0.11. Also we found the association of the minor allele carriers with UADT cancers in alcohol drinkers (aOR=0.71, 95% CI=0.53, 0.97) but not in nondrinkers (aOR=0.74, 95% CI=0.42, 1.31) and the adjusted p-value for the heterogeneity was 0.87.

In the dominant model, the minor allele carriers of rs2740348 CG+GG (vs. CC) of *GEMIN4* were inversely related to cancer susceptibility in UADT SQC (aOR=0.71, 95% CI=0.53, 0.97) and laryngeal cancer (aOR=0.51, 95% CI=0.26, 1.00); and the association persisted in UADT SQC after semi-Bayesian shrinkage (posterior aOR=0.75, 95% posterior limits=0.57, 1.00).

Table 3.2.1 presented the association between the polygenic risk score of all seven SNPs of miRNA biogenesis machinery and UADT cancer susceptibility, after adjusting for covariates. Neither the quartiles nor the continuous analysis showed associations with UADT cancer risk.

3) HRM target genes

The minor allele carriers TC+CC (vs. TT) of rs896849 of *TP53INP1* presented associations with UADT cancers (aOR=1.36, 95% CI=1.04, 1.78) and UADT SQC (aOR=1.35, 95% CI=1.01, 1.79). The association was still away from the null after semi-Bayesian shrinkage in the dominant model in UADT cancers (posterior aOR=1.31, 95% posterior limits=1.02, 1.68), and borderline in UADT SQC (posterior aOR=1.29, 95% posterior limits=0.99, 1.68).The association was observed in nonsmokers (aOR=1.78, 95% CI=1.16, 2.72) only, vs. smokers (aOR=1.18, 95% CI=0.83,1.66); and the adjusted p-value for the SNP-smoking product term was 0.17. Similarly, in nondrinkers, the minor allele carriers TC+CC (vs. TT) of rs896848 was related to UADT

cancer development (aOR=1.99, 95% CI=1.12, 3.56), vs. drinkers (aOR=1.24, 95% CI=0.92, 1.54); the p-value for the heterogeneity was 0.10.

In the dominant model, the minor allele carriers GA+AA (vs. GG) of *E2F2* rs2075993 showed inverse association only in smokers (aOR=0.69, 95% CI=0.48, 0.99) but not in nonsmokers (aOR=1.52, 95% CI=0.96, 2.42), and p-value for the SNP-smoking product term was 0.01. The posterior adjusted p-value was borderline 0.05.

II. Specific aim 2. Cancer survival analyses using a follow-up study design

(i) Demographics

Table 2.1.1 showed the demographic characteristics of lung cancer and UADT cancer patients by their vital status, separately. The median survival time of lung cancer was 2.5 years and the median survival time of UADT cancers was 9.4 years. For lung cancer, the proportion of deaths was higher in the age group 55 or older (72%), comparing to those younger than 55 years of age (62%). It was higher in the males (71%) than in the females (62%). Among different morphological types, SCLC was associated with the highest mortality (80%), and lung SQC, the lowest (56%). Mortality increased with cell differentiation, varying from 54% to 74%. More deaths occurred in smokers than in nonsmokers (69% vs. 55%), and the proportion increased slightly with increasing number of pack-years.

For UADT cancers, the mortality was higher in the patients aged 55 years or older (47%) than in the younger patients (35%-39%); and higher in esophageal adenocarcinomas (57%) than other morphological types (37%-39%). Higher proportion of deaths was observed among smokers

than among nonsmokers (46% vs. 29%); also more in alcohol drinkers than in non-alcohol drinkers (42% vs. 38%).

(ii) Lung cancer survival

Kaplan-Meier curves of survival probabilities of lung cancer by genetic variants of each SNP were shown in figure 1.1 to figure 1.17.

Table 2.1.2 to table 2.1.4 presented survival analysis in lung cancer, stratified by histological types. Table 2.1.5 to table 2.1.10 presented the results of semi-Bayesian shrinkage based on the initial positive findings from table 2.1.2 to table 2.1.4. Both crude and adjusted results were presented and as to the latter, adjusted covariates included age, gender, and ethnicity, education level and tobacco smoking as pack-years, histological types including SQC, ADC, LCL, SCLC and other, and cell differential grades.

1) miRNA biogenesis machinery

The minor allele carriers CT+TT (vs. CC) of rs14035 of *RAN* were related to decreased NSCLC death (aHR=0.71, 95% CI=0.56, 0.91) and ADC death (aHR=0.70, 95% CI=0.51, 0.98). The associations were still non-null after semi-Bayesian shrinkage in NSCLC (posterior aHR=0.74, 95% posterior limits =0.59, 0.93).

The CC (vs. AA+AC) genotype of rs11077 of *XPO5* was inversely related to lung cancer death in the recessive model (aHR=0.62, 95% CI=0.46, 0.85); and the similar associations were also observed in NSCLC (aHR=0.63, 95% CI=0.45, 0.88), ADC (CC. vs. AA: aHR=0.57, 95% CI=0.35, 0.94) and SQC (aHR=0.37, 95% CI=0.15, 0.94). The associations persisted after semi-Bayesian shrinkage in lung cancer (posterior aHR=0.67, 95% posterior limits=0.51, 0.89) and NSCLC (posterior aHR=0.68, 95% posterior limits=0.51, 0.92).

The minor allele carriers CG+GG (vs. CC) of rs2740348 of *GEMIN4* were associated with lung cancer death (aHR=1.32, 95% CI=1.03, 1.69) and SCLC death (aHR=2.60, 95% CI=1.31, 5.16). After semi-Bayesian shrinkage, the association could still be observed in lung cancer (posterior aHR=1.28, 95% posterior limits =1.01, 1.62).

Table 4.1.1 presented the associations between the polygenic risk score of all seven SNPs of miRNA biogenesis machinery and lung cancer mortality, after adjusting for covariates. No non-null relationships were found.

(iii) UADT cancer survival

Kaplan-Meier curves of survival probabilities of UADT cancers by genetic variants of each SNP were shown in figure 2.1 to figure 2.17.

Table 2.2.1 to table 2.2.3 presented survival analysis in UADT cancers, stratified by histological types and cancer sites. Table 2.2.4 to table 2.2.8 presented the results of semi-Bayesian shrinkage based on the initial positive findings from table 2.2.1 to table 2.2.3. Both crude and adjusted results were presented and as to the latter, adjusted covariates included age, gender, and ethnicity, education level, and tobacco smoking as pack-years, alcohol drinking as alcoholic drinks per day, and histological types including SQC, ADC and others, and cell differential grades.

1) miRNA biogenesis machinery

Table 4.2.1 presented the associations between the polygenic risk score of all seven SNPs of miRNA biogenesis machinery and UADT cancer mortality, after adjusting for covariates. No non-null associations were observed.

We constructed ROC curves for polygenic risk scores for lung cancer (figure 3.1) and UADT cancers (figure 3.2), separately; but the areas under the curve (AUC) were only around 0.5.

Figure 4.1.1 to figure 4.2.1 were forest plots illustrating our major results. Lung cancer, NSCLC and ADC showed similar shapes, in terms of susceptibility or survival, respectively; however, the associations between SNPs and cancer development were different from the relations between those SNPs and cancer death. Also, UADT cancers and UADT SQC presented alike shapes. In figure 4.1.4, E2F2 rs2075993 showed divergent relations in smokers vs. nonsmokers in UADT cancers. In figure 4.1.5, *HIF1A* rs2301113 showed diverse associations among drinkers as compared to nondrinkers in UADT cancers.

III. Sensitivity analysis

In the Caucasian-only population, the CC (vs. TT+TC) variant of *GEMIN3* rs197412 was inversely associated with lung cancer (aOR=0.53, 95% CI=0.31, 0.90). The minor allele carriers CT+TT (vs. CC) of miR-26a1 rs7372209 was related to lung cancer (aOR=1.75, 95% CI=1.23, 2.49) (shown in table 1.1.2) and the association was non-null after semi-Bayesian shrinkage (posterior aOR=1.56, 95% posterior limits=1.14, 2.14) (seen in table 1.1.5b).

In table 2.1.2, for lung cancer mortality, the CC (vs. AA+AC) variant of *XPO5* rs11077 was inversely related to lung cancer death (aHR=0.60, 95% CI=0.40, 0.90); the AA (vs. CC+CT) variant of *AGO2* rs4961280 was related to increased lung cancer death (aHR=2.13, 95% CI=1.02, 4.44); and the minor allele carriers CG+GG (vs. CC) of *GEMIN4* rs2740348 was related to lung cancer mortality (aHR=1.66, 95% CI=1.21, 2.28). Also, the minor allele carriers TG+GG (vs. TT) of *CXCL12* rs1804429 was associated with lung cancer death (aHR=2.12, 95% CI=1.27, 3.56); and the CC (vs. AA+AC) variant of *HIF1A* rs2301113 was related with lung cancer death (aHR=1.84, 95% CI=1.15, 2.94). After semi-Bayesian shrinkage, except for *AGO2*

rs4961280, all other associations were still non-null (*XPO5* rs11077 CC vs. AA+AC: posterior aHR=0.68, 95% posterior limits=0.49, 0.96; *GEMIN4* rs2740348 CG+GG vs. CC: posterior aHR=1.52, 95% posterior limits=1.14, 2.03; *CXCL12* rs1804429 TG+GG vs. TT: posterior aHR=1.60, 95% posterior limits=1.03, 2.48; *HIF1A* rs2301113 CC vs. AA+AC: posterior aHR=1.51, 95% posterior limits=1.00, 2.26).

Discussion

(i) Gene *HIF1A*

The TT (vs. CC) genotype of rs2057482 of *HIF1A* was associated with lung cancer (aOR=2.32, 95% CI=1.15, 4.71) and the associations were also found in NSCLC and ADC. In terms of multiplicative interactions, in lung cancer, in the recessive model, the association of TT (vs. CC+CT) genotype of rs2057482 was observed only in nonsmokers (aOR=9.60, 95% CI=3.10, 29.74) but not in smokers (aOR=1.10, 95% CI=0.48, 2.54) and the adjusted p-value of the SNP-smoking product term was 0.01 and the posterior p-value with semi-Bayesian shrinkage was 0.27. The association of CC (vs. AA+AC) genotype of rs2301113 with lung cancer was observed among nonsmokers (aOR=3.04, 95% CI=1.34, 6.86) but not among smokers (aOR=0.80, 95% CI=0.49, 1.31); and the adjusted p-value of the heterogeneity was 0.08. In addition, in UADT cancers, the minor allele carriers AC+CC (vs. AA) of rs2301113 was associated with UADT cancers in nondrinkers with adjusted OR of 0.50 (95% CI=0.28, 0.91); while among alcohol drinkers, the adjusted OR was 1.28 (95% CI=0.95, 1.72); the adjusted p-value of the product term was 0.02 but the posterior adjusted p-value was 0.07 after semi-Bayesian shrinkage.

Previous studies in the Chinese population did find any associations between rs2057482 and prostate cancer and renal cell carcinoma [96, 141]. Another study showed that rs2057482 is related to increased susceptibility of rectal cancer [37]. There was a lack of epidemiology studies on rs2301113.

HIF1A rs2057482 is at the 3'-UTR of the gene [142]. It might impact *HIF1A* expression by influencing its messenger RNA stability. In silico studies showed that rs2057482 creates several new miRNA biding sites such as miR-196a-5p, miR-196b-5p and miR-921 [143], thus it might change gene transcriptional and translational efficiency and bring up the possibility of carcinogenesis. *HIF1A* rs2301113 is localized at the intron of the gene [144]. There were very few studies on this SNP. The intron position of rs2301113 might imply that the association of the SNP with lung/UADT cancers and its interactions with environment factors were due to linkage disequilibrium (LD) with other not yet discovered functional variant(s) rather than a direct effect of rs230113; or it was also probable that there were other concealed roles of rs2301113 that needed to be explored further.

HIF-1 is a basic-helix-loop-helix-PAS heterodimer and a master transcript factor adapting to hypoxia and restoring oxygen homeostasis [14]. HIF-1 involves in tumorigenesis by regulating more than 60 genes, such as vascular endothelial growth factor, nitric oxide synthases 2 and N-myc downregulated gene 1, which function in multiple physiology processes including angiogenesis, anaerobic metabolism, proliferation and apoptosis [25, 145-148]; and also by linking to the Warburg effect [149]. HIF-1α is a subunit of HIF-1 and is the specific compartment to response to low oxygen, compared with its counterpart H1F-1β [14, 150]. Overexpression of HIF-1α is in favor of carcinogenesis genetic mutations such as *TP53* of which the accumulation

stimulates cancer development and progression [24]. It was reported that overexpression of HIF-1α is detected in many cancer tissues including lung cancer and UADT cancers but not in the adjacent normal tissues [151-157]. Therefore, it was conceived that the TT (vs. CC) genotype of rs2057482 and the CC (vs. AA) genotype of rs2301113 might enhance overexpression of *HIF1A*, increase cell proliferation and activate cancer development.

The UADT-cancer associations were only observed among drinkers and multiplicative interactions between genetic variations of rs2301113 and alcohol drinking was probable. Studies showed that ethanol administration is related to the decreased retinoic acid level; and the depletion of retinoic acid causes decreased expression of mitogen-activated protein kinase (MAPK) and increased expression of phosphorylated JNK; then followed by functional downregulation of retinoic acid receptors (RARs) and overexpression of the AP1 (JUN and FOS) transcriptional complex, resulting in cell hyperproliferation and suppression of apoptosis [158-161]. It was reported that hypoxia could induce RAR-related orphan receptor α (RORα) expression, which is physically linked with HIF-1α via DNA binding domain, increases RORα-mediated stabilization of HIF-1α and promotes HIF-1α transcriptional function[162]. Although the exact mechanism was still unknown, retinoic acid and RARs might connect drinking with HIF-1α and be involved in their interactions. Inflammation might be another explanation for our findings. Alcohol consumption would generate pro-inflammatory molecules, such as NF-κB, which contributes to UADT cancer etiology through different machineries [163-166]. HIF-1α could be stimulated by pro-inflammation cytokines such as tumor necrosis factor α and IL-1β through NF-κB pathway [167-170]. Thus, in inflammation induced carcinogenesis, NF-κB as a

central factor might mediate the modifications of drinking on the association between *HIF1A* rs2301113 and UADT cancers.

(ii) miRNA biogenesis machinery

1) Gene *RAN*

The minor allele carriers CT+TT (vs. CC) of rs14035 of *RAN* were associated with the development of lung cancer (aOR=1.28, 95% CI=1.00, 1.63) and NSCLC. This minor allele carriers were also found associated with esophageal SQC (posterior aOR=1.81, 95% posterior limits=1.07, 3.07). Meanwhile, the CT+TT (vs. CC) of rs14035 presented the preventive association against NSCLC death (posterior aHR=0.74, 95% posterior limits =0.59, 0.93). One study of oral premalignant lesions [76] and another of lung cancer in Korean population [77] did not find any relationships between rs14035 and either disease; while a study of esophageal cancer showed a positive association [78], which was consistent with our findings. In terms of cancer mortality, one study of NSCLC in the Spanish showed no association with cancer death [94] and a study of colorectal cancer prognosis showed that rs14035 is associated with cancer recurrences but not with overall survival [79].

RAN rs14035 is localized near gene-3 [171]. Ran is a component of Ran guanosine triphosphate (RanGTP), which binds to the export receptor exportin 5 and mediates the export of pre-miRNA from nucleus to cytoplasm; the disturbance of RanGTP would reduce the transportation of pre-miRNA [53]. Studies found that Ran is overexpressed in several cancer cell lines including lung cancer, indicating its involvement in malignant transformation [172, 173]. It is suggested that the reduction of miRNA biogenesis gene expression results in global decrease of mature miRNA and stimulating tumorigenesis [174]. Except for pre-miRNA carriage, there are several other

potential functions of Ran. For example, cell mitosis relies on Ran signaling in most malignant cells but not in normal ones [173]. Ran could repress apoptosis by suppressing the pro-apoptotic function of Bcl-2-associated X protein (Bax) that is a member of the Bcl-2 family and inhibiting the c-Jun N-terminal kinases (JNKs) activity [175]. Thus, it was likely that the minor allele carriers CT and TT (vs. CC) of rs14035 reduced the expression of *RAN*, restricted miRNA maturation and induced cancer development; however, the decreased expression of Ran might activate Bax and JNKs that cause cell death, repress cancer cell mitosis and eventually improve survival.

2) Gene *XPO5*

In the dominant model, the minor allele carriers AC+CC (vs. AA) of rs11077 of *XPO5* were inversely related to lung cancer (posterior cOR=0.78, 95% posterior limits=0.62, 0.97) and UADT cancers (posterior aOR=0.75, 95% posterior limits=0.58, 0.96). The associations were observed in several subtypes of UADT cancers as well, including UADT SQC and oral and oropharyngeal SQC. These minor allele carriers AC+CC (vs. AA) were inversely associated with UADT cancers in smokers (aOR=0.58, 95% CI=0.41, 0.81) but not in nonsmokers (aOR=1.02, 95% CI=0.66, 1.56); the p-value for the product term was 0.04; and the posterior adjusted p-value was 0.11. In addition, in the recessive model, the CC (vs. AA and AC) genotype of rs11077 was inversely related to lung cancer death (posterior aHR=0.67, 95% posterior limits=0.51, 0.89) and NSCLC death.

A study of lung cancer in Korean population did not observe an association between rs11077 and lung cancer [77]. Another study found that rs11077 is positively associated with esophageal cancer [78]. For the prognosis, one study in European population found that the wild genotype of

rs11077 is associated with NSCLC recurrence [94]. Another study of colorectal cancer reported that rs11077 presents inverse relationship with cancer death [79]. Three studies in the Chinese population reported that rs11077 is reversely related to cancer death including SCLC [176], advanced NSCLC [118] and liver cancer [177]. Our study found that *XPO5* rs11077 presented constantly reverse associations with both cancer susceptibility and cancer death.

The SNP rs11077 is at 3'-UTR of the miRNA nuclear export gene *XPO5* [178]. Under physiology conditions, for the proper control of cell cycle, XPO5 is induced during the cycle entry by a PI3K-dependent post-transcriptional mechanism and causes a global raise of miRNAs; suppression of XPO5 impedes the global miRNA increase and results in delayed G1/S transition and hindered cell proliferation [179]. Studies demonstrated that the inactivation mutation of *XPO5* traps pre-miRNAs in the nucleus of cancer cells with microsatellite instability, causes the decrease of the mature miRNAs in the cytoplasm and promotes tumorigenesis; while the reintroduction of wild-type *XPO5* could initiate the transportation, up-regulate the miRNA level and suppress cancer growth [180]. *XPO5* rs11077 creates a new binding site for miR-8087 [143]. However, due to a lack of *in vitro* and *in vivo* mechanism studies, we could only assume that this SNP might suppress the inactivation of *XPO5* under any circumstance, sustain the mature miRNA level, and present tumor suppression functions.

3) Gene *GEMIN4*

We explored two SNPs, rs7813 and rs2740348 of *GEMIN4.* The variant allele carriers CG+GG (vs. CC) of rs2740348 of *GEMIN4* were inversely related to UADT SQC susceptibility (posterior aOR=0.75, 95% posterior limits=0.57, 1.00). In terms of survival, these minor allele carriers

CG+GG (vs. CC) of rs2740348 were related to increased mortality of lung cancer (posterior aHR=1.28, 95% posterior limits =1.01, 1.62) but not with UADT cancer deaths.

Studies on various cancers in different populations reported contradicted results. One study in the Korean population showed that neither rs7813 nor rs2740348 is related to lung cancer risk [77], and another one on esophageal cancer showed no association of either SNP [78]. One study on bladder cancer suggested that *GEMIN4* haplotypes including rs7813 and rs2740348 are related to increased risk [87]; while the others on renal cell carcinoma [90], malignant peripheral nerve sheath tumor [84] and breast cancer [85] showed decreased risk associated with both SNPs. A study on ovarian cancer also found decreased risk associated with rs7813 [91]. At last, a study in the Chinese on prostate cancer showed that rs7813 is related to increased risk and rs2740348 is related to decreased risk [89]. Our study did not find any associations between rs7813 and lung- or UADT cancer development, but seconded the inverse association between rs2740348 and cancer susceptibility in UADT SQC. Studies also showed that rs7813 and rs2740348 are associated with colorectal cancer recurrence but not the overall survival and the findings are not confirmed in their pooled data [79].

Both rs7813 and rs2740348 locate at *GEMIN4* exons and are nonsynonymous SNPs; rs7813 causes Arg to Cys residue change [181] and rs2740348 causes Gln to Glu residue change [182]. An *in vitro* study in hepatocellular carcinoma showed that the minor allele of *GEMIN4* rs7813 inhibits cell growth comparing to the wild type [183]. This finding was not supported by our results of rs7813, probably due to the different biological behaviors of different cancers. The function of rs2740348 or the effects of these two SNPs in lung cancer or UADT cancer cells were still unclear and needed further investigations.

Gemin4 is first found in the survival of motor neurons complex; it is expresses in both cytoplasm and nucleotide and directly interacts with Gemin3 [184]. Later it is identified that together with Gemin3 and the Argonaute family, Gemin4 comprises of a 15S ribonucleoprotein complex--miRNA-induced silencing complex (miRISC) and acts at the final stage of miRNA maturation and function [185, 186]. There was a lack of biological mechanism studies of the direct effects of Gemin4 in cancer development and survival. Taking the general believe that the curbed function of miRNA biogenesis genes increases cancer susceptibility into account [174], it was reasonable to postulate that neither of these two SNPs repressed *GEMIN4* expression.

Moreover, rs2740348 that was inversely related to UADT SQC development was associated with increased deaths of lung cancer, especially SCLC. To some extent, it verified the heterogeneity of cancers and implicated potential multiple pathways intricate in *GEMIN4* functions.

SNPs that influence the expression of proteins involved in miRNA processing and maturation might change the miRNAome of the cell and result in loss or gain of miRNA function [187]. In our study, we reported that three out of the total of seven SNPs of miRNA biogenesis machinery were associated with cancer development and survival; this finding supported previous conclusions that genetic polymorphisms of miRNA processing and maturation may influence miRNA expression, contribute to tumorigenesis and cancer progression; eventually affect clinical outcomes [68, 83]. In *vitro* and in *vivo* evidence showed that the defective miRNA biogenesis would repress mature miRNA globally, and the overall repression of miRNAs promotes malignant cell transformation in multiple types of cancers and increase cancer cell motility through the deregulation of target genes [174, 180]. It was rational to presume that SNPs in this region might change functions of the productions of miRNA biogenesis genes, affect the affinity

of miRNAs, alter mature miRNA levels in the cytoplasm and deregulate their downstream genes; subsequently cause tumor growth or metastasis [83]. However, we also found that several miRNA biogenesis relevant genetic variants were associated with reduced cancer risk and mortality, indicating other impacts of these genes in carcinogenesis, which might be different from global miRNA repression; also, rising the necessity of further investigations in this class of genes.

(iii)HRMs

We did not find any associations between SNPs of miRNAs and either cancer susceptibility or survival, which was consistent with previous findings that despite of secondary structure alterations caused by sequence variants in miRNA-containing genomic regions, miRNA maturation is not interrupted and their function is not disturbed [188]. Saunders et al. identified 65 SNPs in 474 pre-miRNAs and found that few of these SNPs possess frequency data, which implies that they are of little importance to population genetics [189]. Considering all evidences above, it was reasonable to conceive that because of evolutionary conservation of pre-miRNA sequences by natural selection, genetic variants in this regions were rare and unlikely to have pathophysiological function impacts [190].

(iv) HRM downstream genes

1) Gene *TP53INP1*

The minor allele carriers TC+CC (vs. TT) of *TP53INP1* rs896849 were associated with UADT cancers (posterior aOR=1.31, 95% posterior limits=1.02, 1.68). Similar associations were seen in NSCLC, lung SQC, UADT SQC and lung ADC.

A study in the German population did not find any association between this SNP and breast

cancer [75].

The SNP rs896849 is at the 3'-UTR region of tumor protein 53-induced nuclear protein 1 (*TP53INP1*) [191]. *TP53INP1* is one of *TP53* downstream genes. P-53, the product of the well-established tumor suppressor gene *TP53*, regulates cell cycles and apoptosis and protects cells from gene mutations [192]. TP53INP1 is widely expressed in various tissues and critical in both p-53 mediated [193, 194] and p-53 independent [195] cell cycle suppression, growth inhibitions and apoptosis pathways. *TP53INP1* that is considered as a tumor suppressor gene is downregulated in numerous cancers and its knocking-out contributes to carcinogenesis [196-199]. Several miRNAs such as miR-93, miR-130b and miR-17~92 family, miR-155 and miR-125b are reported to down regulate *TP53INP* expression in multiple cancer cells [197, 199-203], therefore, rs896849 that is at 3'-UTR of the gene might enhance the interactions between *TP53INP1* and its regulatory miRNAs; also, rs896849 creates several new miRNA binding sites including miR-3136, miR-4280 and miR-586 [143], which might suppress *TP53INP1* expression; eventually cause cancer development.

2) Gene *E2F2*

The association between *E2F2* rs2075993 and UADT cancers was modified by tobacco smoking. In the dominant model, the minor allele carriers GA+AA (vs. GG) of *E2F2* rs2075993 showed inverse association only in smokers (aOR=0.69, 95% CI=0.48, 0.99) but not in nonsmokers (aOR=1.52, 95% CI=0.96, 2.42), and p-value for the SNP-smoking product term was 0.01. The posterior adjusted p-value was borderline 0.05.

There were no epidemiology studies on the interactions between rs2075993 and tobacco smoking on the risk of UADT cancers. The SNP rs20759893 is localized at 3'-UTR of *E2F2* [204] and

creates several new miRNA binding sites such as miR-3937 and miR-663a [143]. E2F2 is a member of the E2F family, which is involved in cell cycle G1/S transition and cell cycle control. It is regulated by Myc and functions in the DNA replication initiation and cell growth regulation pathway Rb-E2F [205-208]. E2F2 is overexpressed in cancers and presents proliferation-promoting effects in both *in vitro* and *in vivo* studies [207, 209, 210]. The E2F family proteins and miRNAs act together as a negative feedback loop [211]. Taking E2F2 as an example, it directly binds to the promoter of the miR-17~92 cluster and activates its transcription, in turn, the miR-17~92 cluster suppress E2F2 translation by binding its 3'-UTR [212, 213].

In the other hand, nicotine could urge E2F2 binding to proliferative promoters and launching cells into S phase [214]. Thus, rs2075993 might modify the affinity of E2F2 induced by cigarette smoking, restrain E2F2 regulated proliferation and suppress cancer development. Also, nicotine might enhance the miRNA and E2F2 binding, especially for the new binding miRNAs, boost the negative feedback loop and disrupt E2F2 expression and carcinogenesis in smokers. Also, the findings that the inverse association between the E2F2 genetic variation and UADT cancer susceptibility was only among smokers but not among nonsmokers indicated that etiology of cancer might different in non-smokers from smokers.

From forest plots, we found that in terms of cancer susceptibility or survival, respectively, the forests of lung cancer, NSCLC and ADC were alike; however, with the same set of SNPs and cancers, the forest of cancer development was different from that of cancer death, indicating dissimilar mechanisms of cancer initiation and progression; also, it implied that gene polymorphisms might contribute to various pathways and present assorted functions. UADT cancers and UADT SQC presented analogous forest shapes as well. Thus, this might suggest that

most of our findings were driven by subtypes with larger sample size, and further studies with higher power to detect an association in other histology subtypes were essential. We also observed that E2F2 rs2075993 showed divergent associations with UDAT cancers in smokers vs. nonsmokers, and that *HIF1A* rs2301113 showed diverse associations among drinkers vs. nondrinkers in UADT cancers, which helped visualize our table presentations.

In our study, we found that for some polymorphisms, only the heterozygotes presented associations. There were still no solid rationalizations for such findings, and several possibilities were proposed for explanations [215, 216]. For example, in a technical sense, it might be due to genotyping errors and need further repeated genotyping; the high risk related variant homozygotes might drop out due to high cancer mortalities. It was also probable that the heterozygote performs the maximum function that would be weakened by either of the homozygotes. This hypothesis needed to be conscientious tested in comprehensive genetic and molecular mechanism studies. Finally and the most likely, we did not have enough sample size to detect the effect of the low penetrance variant homozygote [215, 216].

We also conducted a sensitivity analysis in the Caucasians. Similar to the findings in the overall population, we still observed that the CC (vs. AA+AC) variant of *XPO5* rs11077 was inversely related to lung cancer death (posterior aHR=0.68, 95% posterior limits=0.49, 0.96) and the minor allele carriers CG+GG (vs. CC) of *GEMIN4* rs2740348 was associated with lung cancer mortality (posterior aHR=1.52, 95% posterior limits=1.14, 2.03); however, other findings could not be repeated in the Caucasian-only population. On the other hand, there were several additional results. The minor allele carriers CT+TT (vs. CC) of miR-26a1 rs7372209 was related to lung cancer development (posterior OR=1.56, 95% posterior limits=1.14, 2.14); the minor

allele carriers TG+GG (vs. TT) of *CXCL12* rs1804429 was associated with lung cancer death (posterior aHR=1.60, 95% posterior limits=1.03, 2.48) and the CC (vs. AA+AC) variant of *HIF1A* rs2301113 was associated with lung cancer death (posterior aHR=1.51, 95% posterior limits=1.00, 2.26).

The sensitivity analysis made our findings open to discussion. It was probable that the power of the ethnicity specific analysis was not large enough to detect the associations; however, it was also possible that our results generated in all participants were biased by the heterogeneous population. We presented the SNP frequencies by race in controls in supplementary table 1 and all chi-square p-values were less than 0.05, which might indicate that the race mixture should be aware of.

After semi-Bayesian shrinkage and adjusting for covariates, SNPs that were associated with lung- or UADT cancer development or survival were checked with GWAS findings (shown in the following table) to rule potential linkage disequilibrium, using SNAP [217]. We did not find any linkage disequilibrium between our identified SNPs and SNPs identified by GWAS.

	Our study		GWAS	
Chromosome	Gene	SNP	Reported Gene(s)	SNPs
3	MIR26-A1	rs7372209	TP63	rs10937405[218, 219]
			TP63	rs4488809[220, 221]
			NR	rs1530057[222]
			IL1RAP	rs7626795[223]
6	XPO5	rs11077	BTNL2	rs3817963[218]
			BAT3, APOM	rs3117582[222, 224, 225]
			TRNAA-UGC	rs4324798[224]
			ROS1, DCBLD1	rs9387478[220]
			HLA class II	rs2395185, rs28366298[220]
10	CXCL12	rs1804429	VTI1A	rs7086803[220]
			NR	rs1926203[222]
12	RAN	rs14035	RAD52	rs10849605[226]
			ALDH2	rs4767364[227]
17	GEMIN4	rs2740348	BPTF	rs7216064[218, 220]

Limitations and strengths

There were several limitations in our study. The tag-SNP selection might overlook critical functional SNPs and the partial gene coverage might worsen the issue; however, since most of the tag-SNPs determined in our analysis were function relevant, such as coding nonsynonymous proteins, localized at 3'-UTR and influencing transcription and with a minor allele frequency no less than 5% in the Caucasians, which increased the chance of identifying pertinent markers at the population level and helped raise the power of our study and enabled the analyses of interactions. It should be noted that this selection strategy also confined our ability to detect important associations with rarer genotypes - we might be at risk of missing high risk SNPs that are most likely to have much lower MAFs. There might be recall bias due to questionnaires, especially taking that the interviews were given after diagnoses into account; thus, smoking/drinking status might be exaggerated in cases. If a SNP was positively related with smoking, we would underestimate its association with cancer. It was less likely that our study was vulnerable to measurement errors from genotyping or disease diagnosis since we applied state of the art genotyping techniques and repeated 5% of samples for quality control; and the cancers were confirmed by pathology diagnoses. However, it was still possible that measurement errors come from confounders such as tobacco smoking and alcohol drinking assessments; and the direction or magnitude of the bias was hard to predict. The recruitment rates were relatively low in our study. Nonparticipation of eligible cancer cases due to early death or sickness, especially for lung and esophageal cancers with poor prognoses, might be in favor of less severe patients included in the study and made the SNP-outcome associations underestimated. The potential selection bias limited our ability to generalize our findings to all lung or UADT cancer

patients. However, by employing the semi-Bayesian shrinkage approach with a null prior, the estimated associations were conservative and the validity of our results would be reliable. The small number of certain cancers or histological subtypes also limited the power and precision for estimating the effects of low-penetrance SNPs. Another drawback in the survival analysis was that there was no tumor-node-metastasis (TNM) cancer staging information in our database. Although we used the cell differentiation grades as a proxy, it could not fully substitute and might introduce measurement errors. Most of SNPs in our study lacked related information on the functionality and most miRNA binding sites mentioned above were only in silico speculations, so the explanation should be circumspect. Finally, the involved biological mechanisms and pathways were still not fully investigated and understood. Various mechanisms were proposed by different researchers and rarely replicated by independent laboratories, which prevented definite explanations for our findings.

Further studies are warranted to replicate these SNPs in independent populations, and more detailed functional assays are necessary to explore the mechanism basis for the detected associations between the genetic polymorphisms and cancer development, progression and survival.

Public health implications

The SNPs identified by our study might be useful to assess cancer susceptibility for primary and secondary prevention and to predict prognosis for individually tailored treatment decision making and tertiary prevention. Theoretically, the repressed gene products can be replaced by chemically synthesized mimics while overexpressed gene products can be targeted by

antagonists, which can infer future clinical applications. Also, illustration of biological mechanism of SNPs related to decreased cancer susceptibility and death might contribute to future cancer prevention and treatment.

Conclusions

We found that genetic polymorphisms in miRNA processing and maturation pathways were associated with cancer development and prognosis, especially *RAN*, *XPO5* and *GEMIN4*. We speculated that except for the global influence on miRNA functions, there might be other potential pathways involved in the carcinogenesis and progression process of cancer. However, due to the population heterogeneity, their influences in the cancer pathophysiology need further investigations.

Section I

Table 1.1.1 Demographic characteristics in LA study

	Lung cancer (N=611) (%)	UADT cancer (N=601) (%)	Control (N=1040) (%)
Age (years of age)	52.2±5.4	50.4±7.6	49.9±7.3
<45	61(10)	109(18)	222(21)
45-54	301(49)	267(44)	499(48)
>= 55	249(41)	225(37)	319(31)
Missing	0(0)	0(0)	0(0)
Gender			
Male	303(50)	454(76)	623(60)
Female	308(50)	147(24)	417(40)
Missing	0(0)	0(0)	0(0)
Ethnicity			
Caucasian	359(59)	341(57)	634(61)
Hispanic	70(11)	109(18)	204(20)
Black	96(16)	69(12)	102(10)
Asian	70(11)	64(11)	62(6)
Other	15(2)	16(3)	37(4)
Missing	1(0)	2(0)	1(0)
Education (years)	13.2±3.4	13.1±3.7	14.4±3.6
Education group (years)			
0-12	265(43)	273(45)	300(29)
13-16	275(45)	259(43)	481(46)
>16	71(12)	69(11)	258(25)
Missing	0(0)	0(0)	1(0)
Tobacco Smoking (pack-years)	38.2±22.4	32.3±23.2	17.6±17.9
Tobacco Smoking status			
Never	110(18)	182(30)	491(47)
Former	390(64)	338(56)	371(36)
Current	111(18)	81(13)	178(17)
Missing	0(0)	0(0)	0(0)

	Lung cancer (N=611) (%)	UADT cancer (N=601) (%)	Control (N=1040) (%)
Ever smoking (pack-years)			
More than 0-less than 20	98(20)	145(35)	353(64)
20- less than 40	201(40)	146(35)	132(24)
40 and up	202(40)	128(31)	63(12)
Alcohol drinking (drink/day)	2.2±4.4	3.2±5.0	1.3±2.2
Alcohol drinking status			
Ever	440(72)	482(80)	776(75)
Never	170(28)	117(20)	264(25)
Missing	1(0)	2(0)	0(0)
Ever Drinking (drink/day)			
More than 0-less than 2	302(69)	279(58)	635(82)
2 and more	138(31)	203(42)	137(18)

Table 1.1.2 Crude and adjusted associations between selected SNPs and lung cancer, both in the overall population and in the Caucasians only

SNP	Overall			Caucasians only		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	193/305	1.00	1.00	104/192	1.00	1.00
AC	231/479	***0.76(0.60,0.97)***	0.76(0.56,1.03)	154/308	0.92(0.68,1.26)	0.83(0.57,1.23)
CC	106/146	1.15(0.84,1.56)	1.23(0.83,1.83)	54/78	1.28(0.84,1.95)	1.41(0.83,2.39)
Missing	81/110			47/56		
Log-additive		1.01(0.87,1.18)	1.05(0.86,1.28)		1.09(0.88,1.33)	1.10(0.85,1.43)
Dominant	337/625	0.85(0.68,1.07)	0.86(0.64,1.14)	208/386	0.99(0.74,1.33)	0.94(0.65,1.35)
Recessive	106/146	***1.34(1.02,1.77)***	***1.46(1.03,2.07)***	54/78	1.34(0.92,1.96)	1.57(0.97,2.53)
RAN rs14035						
CC	244/463	1.00	1.00	146/271	1.00	1.00
CT	233/366	1.21(0.96,1.51)	***1.44(1.09,1.90)***	135/251	1.00(0.75,1.33)	0.97(0.67,1.39)
TT	48/92	0.99(0.68,1.45)	0.92(0.58,1.46)	25/51	0.91(0.54,1.53)	0.90(0.48,1.70)
Missing	86/119			53/61		
Log-additive		1.07(0.91,1.26)	1.11(0.91,1.35)		0.97(0.78,1.21)	0.96(0.73,1.25)
Dominant	281/458	1.16(0.94,1.44)	***1.32(1.02,1.72)***	160/302	0.98(0.74,1.30)	0.96(0.68,1.35)
Recessive	48/92	0.91(0.63,1.31)	0.78(0.50,1.21)	25/51	0.91(0.55,1.50)	0.91(0.49,1.68)
DICER1 rs3742330						
AA	422/717	1.00	1.00	261/466	1.00	1.00
AG	99/200	0.84(0.64,1.10)	0.83(0.60,1.15)	52/106	0.88(0.61,1.26)	0.85(0.55,1.33)
GG	13/12	1.84(0.83,4.07)	1.87(0.75,4.70)	1/5	0.36(0.04,3.07)	0.23(0.02,3.01)
Missing	77/111			45/57		
Log-additive		0.97(0.77,1.22)	0.97(0.73,1.28)		0.84(0.59,1.18)	0.80(0.52,1.22)
Dominant	112/212	0.90(0.69,1.16)	0.88(0.64,1.21)	53/111	0.85(0.59,1.22)	0.82(0.53,1.28)
Recessive	13/12	1.91(0.86,4.21)	2.00(0.81,4.98)	1/5	0.37(0.04,3.14)	0.24(0.02,3.11)
AGO2 rs4961280						
CC	365/594	1.00	1.00	199/379	1.00	1.00
CA	141/279	0.82(0.65,1.05)	0.91(0.68,1.22)	93/169	1.05(0.77,1.42)	1.09(0.75,1.60)

SNP	Overall			Caucasians only		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	15/47	***0.52(0.29,0.94)***	0.80(0.40,1.60)	10/24	0.79(0.37,1.69)	1.11(0.43,2.82)
Missing	90/120			57/62		
Log-additive		***0.78(0.64,0.95)***	0.91(0.71,1.15)		0.98(0.77,1.26)	1.08(0.79,1.47)
Dominant	156/326	***0.78(0.62,0.98)***	0.90(0.68,1.19)	103/193	1.02(0.76,1.36)	1.09(0.76,1.58)
Recessive	15/47	***0.55(0.31,1.00)***	0.83(0.42,1.64)	10/24	0.78(0.37,1.66)	1.07(0.43,2.71)
GEMIN3 rs197412						
TT	175/307	1.00	1.00	117/220	1.00	1.00
TC	252/434	1.02(0.80,1.30)	1.03(0.76,1.38)	160/263	1.14(0.85,1.54)	1.23(0.85,1.80)
CC	101/180	0.98(0.73,1.34)	0.76(0.52,1.12)	34/89	0.72(0.46,1.13)	0.59(0.33,1.05)
Missing	83/119			48/62		
Log-additive		1.00(0.86,1.16)	0.89(0.74,1.08)		0.92(0.75,1.13)	0.88(0.68,1.13)
Dominant	353/614	1.01(0.80,1.27)	0.95(0.72,1.26)	194/352	1.04(0.78,1.38)	1.05(0.74,1.51)
Recessive	101/180	0.97(0.74,1.28)	0.75(0.53,1.06)	34/89	0.67(0.44,1.02)	***0.53(0.31,0.90)***
GEMIN4 rs7813						
CC	242/378	1.00	1.00	113/202	1.00	1.00
CT	201/400	***0.79(0.62,0.99)***	0.91(0.68,1.21)	137/270	0.91(0.67,1.24)	0.86(0.58,1.26)
TT	71/134	0.83(0.60,1.15)	0.88(0.59,1.33)	49/97	0.90(0.60,1.37)	0.80(0.47,1.35)
Missing	97/128			60/65		
Log-additive		0.88(0.75,1.02)	0.93(0.77,1.13)		0.94(0.77,1.15)	0.89(0.69,1.14)
Dominant	272/534	***0.80(0.64,0.99)***	0.90(0.69,1.18)	186/367	0.91(0.68,1.21)	0.84(0.59,1.21)
Recessive	71/134	0.93(0.68,1.27)	0.93(0.63,1.36)	49/97	0.95(0.65,1.39)	0.87(0.54,1.41)
GEMIN4 rs2740348						
CC	382/640	1.00	1.00	214/390	1.00	1.00
CG	122/250	0.82(0.64,1.05)	0.80(0.59,1.10)	80/166	0.88(0.64,1.20)	0.77(0.52,1.16)
GG	12/28	0.72(0.36,1.43)	0.50(0.22,1.18)	8/15	0.97(0.41,2.33)	0.43(0.15,1.29)
Missing	95/122			57/63		
Log-additive		0.83(0.67,1.02)	0.77(0.59,1.00)		0.91(0.70,1.19)	0.73(0.52,1.03)
Dominant	134/278	0.81(0.63,1.03)	0.77(0.57,1.04)	88/181	0.89(0.65,1.20)	0.73(0.50,1.08)
Recessive	12/28	0.76(0.38,1.50)	0.53(0.23,1.25)	8/15	1.01(0.42,2.41)	0.47(0.16,1.38)
miRNA downstream						
CDK6 rs42031						

SNP	Overall			Caucasians only		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	380/656	1.00	1.00	202/371	1.00	1.00
AT	127/241	0.91(0.71,1.17)	1.11(0.81,1.51)	89/180	0.91(0.67,1.23)	1.04(0.71,1.52)
TT	16/27	1.02(0.54,1.92)	0.78(0.35,1.75)	13/23	1.04(0.51,2.09)	0.55(0.22,1.37)
Missing	88/116			55/60		
Log-additive		0.95(0.77,1.16)	1.02(0.79,1.32)		0.95(0.74,1.22)	0.90(0.66,1.23)
Dominant	143/268	0.92(0.73,1.17)	1.07(0.80,1.44)	102/203	0.92(0.69,1.24)	0.96(0.67,1.39)
Recessive	16/27	1.05(0.56,1.97)	0.76(0.34,1.69)	13/23	1.07(0.53,2.15)	0.54(0.22,1.34)
TP53INP1 rs896849						
TT	346/666	1.00	1.00	217/418	1.00	1.00
TC	160/232	***1.33(1.05,1.69)***	1.15(0.85,1.55)	89/139	1.23(0.90,1.69)	1.08(0.73,1.61)
CC	27/31	1.68(0.99,2.85)	1.47(0.75,2.86)	4/20	0.39(0.13,1.14)	0.54(0.16,1.82)
Missing	78/111			49/57		
Log-additive		***1.31(1.09,1.59)***	1.18(0.92,1.50)		1.01(0.77,1.32)	0.96(0.69,1.34)
Dominant	187/263	***1.37(1.09,1.72)***	1.18(0.89,1.58)	93/159	1.13(0.83,1.53)	1.02(0.70,1.50)
Recessive	27/31	1.55(0.91,2.62)	1.38(0.72,2.67)	4/20	0.36(0.12,1.07)	0.52(0.16,1.77)
CXCL12 rs1804429						
TT	485/858	1.00	1.00	289/548	1.00	1.00
TG	44/73	1.07(0.72,1.58)	1.11(0.69,1.77)	20/32	1.19(0.67,2.11)	1.39(0.69,2.80)
GG	3/1	5.31(0.55,51.16)	1.98(0.17,22.79)	1/0	-	-
Missing	79/108			49/54		
Log-additive		1.17(0.82,1.68)	1.14(0.74,1.77)		1.29(0.75,2.24)	1.45(0.74,2.84)
Dominant	47/74	1.12(0.77,1.65)	1.13(0.71,1.80)	21/32	1.24(0.70,2.20)	1.43(0.72,2.85)
Recessive	3/1	5.28(0.55,50.88)	1.96(0.17,22.52)	1/0	-	-
E2F2 rs2075993						
GG	184/291	1.00	1.00	78/142	1.00	1.00
GA	230/455	0.80(0.63,1.02)	0.83(0.61,1.13)	150/311	0.88(0.63,1.23)	0.80(0.52,1.22)
AA	117/179	1.03(0.77,1.39)	1.16(0.80,1.69)	84/123	1.24(0.84,1.84)	1.21(0.74,1.98)
Missing	80/115			47/58		
Log-additive		0.99(0.85,1.15)	1.05(0.87,1.27)		1.11(0.91,1.36)	1.10(0.86,1.41)
Dominant	347/634	0.87(0.69,1.09)	0.91(0.68,1.22)	234/434	0.98(0.71,1.35)	0.91(0.61,1.36)
Recessive	117/179	1.18(0.91,1.53)	1.31(0.95,1.81)	84/123	1.36(0.99,1.87)	1.41(0.94,2.10)

SNP	Overall			Caucasians only		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
DOCK4 rs3801790						
AA	233/376	1.00	1.00	145/253	1.00	1.00
AG	237/427	0.90(0.71,1.13)	1.02(0.77,1.34)	134/266	0.88(0.66,1.18)	0.94(0.65,1.35)
GG	62/126	0.79(0.56,1.12)	0.91(0.60,1.39)	30/58	0.90(0.56,1.47)	1.04(0.57,1.89)
Missing	79/111			50/57		
Log-additive		0.89(0.76,1.04)	0.97(0.80,1.18)		0.92(0.75,1.14)	0.99(0.76,1.29)
Dominant	299/553	0.87(0.70,1.08)	0.99(0.76,1.29)	164/324	0.88(0.67,1.17)	0.96(0.67,1.35)
Recessive	62/126	0.41(0.61,1.16)	0.90(0.61,1.34)	30/58	0.96(0.61,1.53)	1.07(0.60,1.90)
IL6R rs4072391						
CC	334/593	1.00	1.00	204/377	1.00	1.00
CT	175/279	1.11(0.88,1.40)	1.10(0.83,1.47)	96/177	1.00(0.74,1.35)	1.14(0.78,1.67)
TT	20/49	0.73(0.42,1.24)	0.66(0.35,1.24)	9/19	0.88(0.39,1.97)	0.75(0.28,2.01)
Missing	82/119			50/61		
Log-additive		0.99(0.82,1.19)	0.96(0.77,1.20)		0.98(0.76,1.26)	1.03(0.75,1.41)
Dominant	195/328	1.06(0.85,1.32)	1.03(0.79,1.35)	105/196	0.99(0.74,1.33)	1.10(0.76,1.58)
Recessive	20/49	0.70(0.41,1.19)	0.63(0.34,1.19)	9/19	0.87(0.39,1.96)	0.72(0.27,1.91)
HIF1A						
HIF1A rs2057482						
CC	354/672	1.00	1.00	215/428	1.00	1.00
CT	150/234	1.22(0.96,1.55)	1.09(0.81,1.48)	83/135	1.22(0.89,1.68)	1.38(0.93,2.07)
TT	26/23	***2.15(1.21,3.82)***	***2.32(1.15,4.71)***	12/15	1.59(0.73,3.46)	2.18(0.84,5.66)
Missing	81/111			49/56		
Log-additive		***1.31(1.08,1.59)***	1.25(0.98,1.59)		1.24(0.96,1.61)	***1.42(1.03,1.97)***
Dominant	176/257	***1.30(1.03,1.64)***	1.19(0.90,1.59)	95/150	1.26(0.93,1.71)	1.46(0.99,2.15)
Recessive	26/23	***2.03(1.15,3.60)***	***2.26(1.12,4.55)***	12/15	1.51(0.70,3.27)	2.00(0.78,5.15)
HIF1A rs2301113						
AA	238/467	1.00	1.00	161/325	1.00	1.00
AC	190/310	1.20(0.95,1.53)	1.12(0.83,1.50)	112/186	1.22(0.90,1.64)	1.34(0.92,1.96)
CC	82/100	***1.61(1.16,2.24)***	1.17(0.74,1.83)	26/34	1.54(0.90,2.66)	1.89(0.96,3.73)
Missing	101/163			60/89		
Log-additive		***1.25(1.07,1.46)***	1.09(0.89,1.34)		1.23(0.98,1.54)	***1.36(1.03,1.80)***

SNP	Cases/Controls	Overall Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Caucasians only Crude OR (95% CI)	Adjusted* OR (95% CI)
Dominant	272/410	***1.30(1.05,1.62)***	1.13(0.85,1.49)	138/220	1.27(0.95,1.68)	1.42(0.99,2.03)
Recessive	82/100	***1.49(1.09,2.04)***	1.10(0.72,1.68)	26/34	1.43(0.84,2.44)	1.68(0.87,3.25)
miRNAs						
MIR-26A1 rs7372209						
CC	287/494	1.00	1.00	141/322	1.00	1.00
CT	197/366	0.93(0.74,1.16)	1.15(0.86,1.52)	139/219	***1.45(1.08,1.94)***	***1.73(1.20,2.50)***
TT	47/66	1.23(0.82,1.83)	***1.62(1.00,2.62)***	29/35	***1.89(1.11,3.22)***	1.88(0.99,3.59)
Missing	80/114			50/58		
Log-additive		1.03(0.87,1.21)	1.22(0.99,1.50)		***1.41(1.13,1.75)***	***1.51(1.15,1.98)***
Dominant	244/432	0.97(0.79,1.20)	1.22(0.93,1.60)	168/254	***1.51(1.14,1.99)***	***1.75(1.23,2.49)***
Recessive	47/66	1.27(0.86,1.87)	1.52(0.96,2.41)	29/35	1.60(0.96,2.67)	1.47(0.79,2.74)
MIR-27 rs895819						
TT	247/413	1.00	1.00	154/256	1.00	1.00
TC	207/411	0.84(0.67,1.06)	0.92(0.70,1.22)	118/267	***0.73(0.55,0.99)***	0.88(0.61,1.27)
CC	57/86	1.11(0.77,1.60)	1.03(0.65,1.63)	28/45	1.03(0.62,1.73)	1.20(0.64,2.28)
Missing	100/130			59/66		
Log-additive		0.97(0.82,1.15)	0.98(0.80,1.20)		0.89(0.71,1.11)	1.00(0.76,1.32)
Dominant	264/497	0.89(0.72,1.10)	0.94(0.72,1.23)	146/312	0.78(0.59,1.03)	0.93(0.65,1.32)
Recessive	57/86	1.20(0.84,1.71)	1.07(0.70,1.66)	28/45	1.20(0.73,1.96)	1.28(0.69,2.37)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.3 Crude and adjusted associations between selected SNPs and lung cancer, stratified by pathology types (NSCLC vs. SCLC)

SNP	NSCLC			SCLC		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	169/305	1.00	1.00	24/305	1.00	1.00
AC	207/479	0.78(0.61,1.00)	0.76(0.56,1.04)	24/479	0.64(0.36,1.14)	0.54(0.27,1.07)
CC	89/146	1.10(0.80,1.52)	1.18(0.79,1.78)	17/146	1.48(0.77,2.84)	1.79(0.79,4.02)
Missing	71/110			10/110		
Log-additive		1.00(0.85,1.17)	1.03(0.84,1.26)		1.14(0.79,1.65)	1.19(0.76,1.86)
Dominant	296/625	0.85(0.68,1.08)	0.85(0.63,1.14)	41/625	0.83(0.49,1.41)	0.74(0.40,1.38)
Recessive	89/146	1.27(0.95,1.70)	1.40(0.98,2.01)	17/146	***1.90(1.06,3.40)***	***2.61(1.27,5.35)***
RAN rs14035						
CC	212/463	1.00	1.00	32/463	1.00	1.00
CT	207/366	1.24(0.98,1.56)	***1.48(1.11,1.96)***	26/366	1.03(0.60,1.76)	1.46(0.79,2.69)
TT	42/92	1.00(0.67,1.49)	0.92(0.57,1.49)	6/92	0.94(0.38,2.32)	1.15(0.44,3.04)
Missing	75/119			11/119		
Log-additive		1.08(0.91,1.28)	1.12(0.92,1.37)		0.99(0.68,1.45)	1.18(0.78,1.78)
Dominant	249/458	1.19(0.95,1.49)	***1.35(1.03,1.77)***	32/458	1.01(0.61,1.68)	1.37(0.77,2.44)
Recessive	42/92	0.90(0.62,1.33)	0.77(0.49,1.21)	6/92	0.93(0.39,2.22)	0.98(0.39,2.49)
DICER1 rs3742330						
AA	373/717	1.00	1.00	49/717	1.00	1.00
AG	82/200	0.79(0.59,1.05)	0.78(0.55,1.10)	17/200	1.24(0.70,2.21)	1.35(0.70,2.59)
GG	13/12	2.08(0.94,4.61)	2.00(0.80,4.99)	0/12		0.49(0.02,13.04)
Missing	68/111			9/111		
Log-additive		0.95(0.75,1.21)	0.94(0.70,1.27)		1.08(0.63,1.84)	1.14(0.62,2.10)
Dominant	95/212	0.86(0.66,1.13)	0.84(0.60,1.17)	17/212	1.17(0.66,2.08)	1.27(0.66,2.43)
Recessive	13/12	2.18(0.99,4.82)	2.18(0.88,5.40)	0/12		
AGO2 rs4961280						
CC	319/594	1.00	1.00	46/594	1.00	1.00
CA	124/279	0.83(0.64,1.06)	0.94(0.69,1.27)	17/279	0.79(0.44,1.40)	0.85(0.45,1.61)

SNP		NSCLC			SCLC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	14/47	0.56(0.30,1.02)	0.90(0.45,1.79)	1/47	0.27(0.04,2.04)	0.60(0.10,3.79)
Missing	79/120			11/120		
Log-additive		***0.79(0.65,0.97)***	0.94(0.74,1.20)		0.70(0.43,1.14)	0.80(0.46,1.38)
Dominant	138/326	0.79(0.62,1.00)	0.93(0.70,1.25)	18/326	0.71(0.41,1.25)	0.81(0.43,1.51)
Recessive	14/47	0.59(0.32,1.08)	0.92(0.46,1.82)	1/47	0.29(0.04,2.17)	0.64(0.10,4.00)
GEMIN3 rs197412						
TT	144/307	1.00	1.00	31/307	1.00	1.00
TC	228/434	1.12(0.87,1.44)	1.14(0.84,1.56)	24/434	***0.55(0.32,0.95)***	***0.45(0.24,0.86)***
CC	90/180	1.07(0.77,1.47)	0.80(0.54,1.20)	11/180	0.61(0.30,1.23)	0.57(0.25,1.31)
Missing	74/119			9/119		
Log-additive		1.04(0.89,1.22)	0.92(0.76,1.12)		0.72(0.50,1.03)	0.66(0.44,1.01)
Dominant	318/614	1.10(0.87,1.40)	1.04(0.78,1.40)	35/614	***0.56(0.34,0.93)***	***0.48(0.27,0.86)***
Recessive	90/180	1.00(0.75,1.32)	0.74(0.52,1.05)	11/180	0.82(0.42,1.61)	0.87(0.41,1.88)
GEMIN4 rs7813						
CC	214/378	1.00	1.00	28/378	1.00	1.00
CT	173/400	***0.76(0.60,0.98)***	0.93(0.69,1.26)	28/400	0.95(0.55,1.63)	0.92(0.49,1.72)
TT	62/134	0.82(0.58,1.15)	0.89(0.58,1.35)	9/134	0.91(0.42,1.97)	0.81(0.33,1.99)
Missing	87/128			10/128		
Log-additive		0.86(0.74,1.02)	0.94(0.77,1.14)		0.95(0.66,1.37)	0.90(0.59,1.36)
Dominant	235/534	***0.78(0.62,0.98)***	0.92(0.70,1.22)	37/534	0.94(0.56,1.56)	0.88(0.49,1.59)
Recessive	62/134	0.93(0.67,1.29)	0.92(0.62,1.36)	9/134	0.93(0.45,1.93)	0.85(0.37,1.97)
GEMIN4 rs2740348						
CC	335/640	1.00	1.00	47/640	1.00	1.00
CG	104/250	0.79(0.61,1.04)	0.83(0.60,1.15)	18/250	0.98(0.56,1.72)	0.75(0.39,1.45)
GG	11/28	0.75(0.37,1.53)	0.53(0.22,1.26)	1/28	0.49(0.06,3.65)	0.84(0.14,4.98)
Missing	86/122			9/122		
Log-additive		0.82(0.65,1.02)	0.80(0.61,1.04)		0.89(0.55,1.46)	0.76(0.43,1.36)
Dominant	115/278	0.79(0.61,1.02)	0.80(0.59,1.08)	19/278	0.93(0.54,1.61)	0.73(0.38,1.40)
Recessive	11/28	0.80(0.39,1.61)	0.56(0.23,1.32)	1/28	0.49(0.07,3.65)	0.91(0.16,5.40)
miRNA downstream						
CDK6 rs42031						

SNP		NSCLC			SCLC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	338/656	1.00	1.00	42/656	1.00	1.00
AT	106/241	0.85(0.66,1.11)	1.04(0.75,1.43)	21/241	1.36(0.79,2.35)	1.73(0.92,3.24)
TT	13/27	0.93(0.48,1.83)	0.67(0.28,1.60)	3/27	1.74(0.51,5.95)	2.06(0.53,7.98)
Missing	79/116			9/116		
Log-additive		0.89(0.72,1.11)	0.96(0.73,1.25)		1.34(0.87,2.07)	1.55(0.95,2.55)
Dominant	119/268	0.86(0.67,1.11)	0.99(0.73,1.35)	24/268	1.40(0.83,2.36)	1.74(0.95,3.19)
Recessive	13/27	0.97(0.50,1.90)	0.67(0.28,1.58)	3/27	1.58(0.47,5.36)	1.73(0.46,6.50)
TP53INP1 rs896849						
TT	301/666	1.00	1.00	45/666	1.00	1.00
TC	141/232	***1.34(1.05,1.73)***	1.18(0.87,1.61)	19/232	1.21(0.69,2.11)	1.13(0.59,2.14)
CC	25/31	***1.78(1.04,3.07)***	1.50(0.76,2.96)	2/31	0.95(0.22,4.12)	1.52(0.35,6.61)
Missing	69/111			9/111		
Log-additive		***1.34(1.10,1.63)***	1.20(0.94,1.54)		1.12(0.71,1.75)	1.14(0.67,1.92)
Dominant	166/263	***1.40(1.10,1.77)***	1.21(0.90,1.63)	21/263	1.18(0.69,2.02)	1.14(0.61,2.12)
Recessive	25/31	1.64(0.96,2.81)	1.40(0.71,2.73)	2/31	0.91(0.21,3.87)	1.47(0.34,6.32)
CXCL12 rs1804429						
TT	426/858	1.00	1.00	59/858	1.00	1.00
TG	37/73	1.02(0.68,1.54)	1.03(0.63,1.68)	7/73	1.39(0.61,3.16)	1.49(0.55,4.04)
GG	3/1	6.03(0.63,58.09)	2.12(0.19,23.81)	0/1		
Missing	70/108			9/108		
Log-additive		1.15(0.79,1.68)	1.08(0.69,1.70)		1.34(0.60,3.01)	1.46(0.55,3.88)
Dominant	40/74	1.09(0.73,1.63)	1.06(0.66,1.71)	7/74	1.38(0.61,3.12)	1.48(0.55,4.00)
Recessive	3/1	6.02(0.63,57.99)	2.12(0.19,23.73)	0/1		
E2F2 rs2075993						
GG	161/291	1.00	1.00	23/291	1.00	1.00
GA	197/455	0.78(0.61,1.01)	0.82(0.60,1.13)	33/455	0.92(0.53,1.59)	0.77(0.40,1.49)
AA	106/179	1.07(0.79,1.46)	1.22(0.83,1.80)	11/179	0.78(0.37,1.63)	0.70(0.29,1.65)
Missing	72/115			8/115		
Log-additive		1.00(0.86,1.17)	1.08(0.89,1.31)		0.89(0.62,1.27)	0.82(0.54,1.26)
Dominant	303/634	0.86(0.68,1.09)	0.92(0.69,1.25)	44/634	0.88(0.52,1.48)	0.74(0.40,1.39)
Recessive	106/179	1.23(0.94,1.62)	1.38(0.99,1.92)	11/179	0.82(0.42,1.59)	0.83(0.39,1.77)

SNP		NSCLC			SCLC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
DOCK4 rs3801790						
AA	204/376	1.00	1.00	29/376	1.00	1.00
AG	208/427	0.90(0.71,1.14)	1.02(0.77,1.36)	29/427	0.88(0.52,1.50)	1.19(0.65,2.19)
GG	54/126	0.79(0.55,1.13)	0.88(0.57,1.36)	8/126	0.82(0.37,1.85)	1.21(0.49,3.02)
Missing	70/111			9/111		
Log-additive		0.89(0.76,1.05)	0.96(0.79,1.17)		0.90(0.62,1.30)	1.12(0.73,1.70)
Dominant	262/553	0.87(0.70,1.09)	0.99(0.75,1.30)	37/553	0.87(0.52,1.44)	1.18(0.66,2.11)
Recessive	54/126	0.84(0.59,1.17)	0.87(0.58,1.31)	8/126	0.88(0.41,1.88)	1.11(0.48,2.60)
IL6R rs4072391						
CC	287/593	1.00	1.00	47/593	1.00	1.00
CT	158/279	1.17(0.92,1.49)	1.16(0.86,1.55)	17/279	0.77(0.43,1.36)	0.64(0.34,1.24)
TT	16/49	0.67(0.38,1.21)	0.61(0.31,1.20)	4/49	1.03(0.36,2.98)	1.34(0.43,4.15)
Missing	75/119			7/119		
Log-additive		1.01(0.83,1.22)	0.98(0.77,1.23)		0.88(0.57,1.36)	0.85(0.52,1.40)
Dominant	174/328	1.10(0.87,1.38)	1.07(0.81,1.41)	21/328	0.81(0.47,1.37)	0.72(0.39,1.31)
Recessive	16/49	0.64(0.36,1.14)	0.58(0.30,1.14)	4/49	1.11(0.39,3.18)	1.56(0.51,4.74)
HIF1A						
HIF1A rs2057482						
CC	303/672	1.00	1.00	51/672	1.00	1.00
CT	138/234	***1.31(1.02,1.68)***	1.17(0.86,1.58)	12/234	0.68(0.35,1.29)	0.72(0.35,1.46)
TT	23/23	***2.22(1.22,4.02)***	***2.40(1.17,4.91)***	3/23	1.72(0.50,5.92)	1.52(0.32,7.20)
Missing	72/111			9/111		
Log-additive		***1.38(1.13,1.69)***	***1.31(1.02,1.67)***		0.89(0.54,1.48)	0.86(0.48,1.53)
Dominant	161/257	***1.39(1.09,1.76)***	1.26(0.94,1.69)	15/257	0.77(0.42,1.39)	0.77(0.39,1.50)
Recessive	23/23	***2.05(1.14,3.70)***	***2.28(1.12,4.64)***	3/23	1.88(0.55,6.42)	1.65(0.35,7.79)
HIF1A rs2301113						
AA	205/467	1.00	1.00	33/467	1.00	1.00
AC	170/310	1.25(0.97,1.60)	1.13(0.84,1.53)	20/310	0.91(0.51,1.62)	1.01(0.53,1.92)
CC	72/100	***1.64(1.16,2.32)***	1.13(0.71,1.80)	10/100	1.42(0.68,2.97)	1.26(0.48,3.30)
Missing	89/163			12/163		
Log-additive		***1.27(1.08,1.49)***	1.08(0.88,1.34)		1.12(0.78,1.60)	1.08(0.69,1.68)

SNP		NSCLC			SCLC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Dominant	242/410	***1.34(1.07,1.69)***	1.13(0.85,1.51)	30/410	1.04(0.62,1.73)	1.05(0.57,1.92)
Recessive	72/100	***1.49(1.08,2.07)***	1.06(0.68,1.63)	10/100	1.47(0.72,2.97)	1.26(0.50,3.16)
miRNAs						
MIR-26A1 rs7372209						
CC	253/494	1.00	1.00	34/494	1.00	1.00
CT	171/366	0.91(0.72,1.16)	1.16(0.87,1.56)	26/366	1.03(0.61,1.75)	1.23(0.67,2.27)
TT	40/66	1.18(0.78,1.80)	1.58(0.96,2.59)	7/66	1.54(0.66,3.62)	2.32(0.90,6.00)
Missing	72/114			8/114		
Log-additive		1.01(0.85,1.20)	1.22(0.98,1.51)		1.16(0.79,1.70)	1.40(0.90,2.17)
Dominant	211/432	0.95(0.76,1.19)	1.23(0.93,1.62)	33/432	1.11(0.68,1.82)	1.37(0.77,2.44)
Recessive	40/66	1.23(0.82,1.85)	1.47(0.92,2.36)	7/66	1.52(0.67,3.46)	2.14(0.86,5.31)
MIR-27 rs895819						
TT	217/413	1.00	1.00	30/413	1.00	1.00
TC	180/411	0.83(0.66,1.06)	0.93(0.70,1.24)	27/411	0.90(0.53,1.55)	1.05(0.57,1.94)
CC	49/86	1.08(0.74,1.60)	1.00(0.62,1.60)	8/86	1.28(0.57,2.89)	1.64(0.63,4.22)
Missing	90/130			10/130		
Log-additive		0.96(0.81,1.14)	0.97(0.79,1.20)		1.05(0.72,1.54)	1.19(0.77,1.85)
Dominant	229/497	0.88(0.70,1.10)	0.94(0.72,1.24)	35/497	0.97(0.59,1.61)	1.13(0.63,2.02)
Recessive	49/86	1.18(0.82,1.71)	1.03(0.66,1.62)	8/86	1.35(0.62,2.91)	1.61(0.66,3.92)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.4 Crude and adjusted associations between selected SNPs and lung cancer, stratified by subtypes of NSCLC

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA processing and maturation									
XPO5 rs11077									
AA	26/305	1.00	1.00	94/305	1.00	1.00	35/305	1.00	1.00
AC	36/479	0.88 (0.52,1.49)	0.56 (0.28,1.11)	117/479	0.79 (0.58,1.08)	0.83 (0.58,1.20)	47/479	0.86 (0.54,1.36)	0.66 (0.38,1.17)
CC	22/146	1.77 (0.97,3.22)	1.50 (0.67,3.33)	49/146	1.09 (0.73,1.62)	1.36 (0.85,2.18)	14/146	0.84 (0.44,1.60)	0.91 (0.41,2.00)
Missing	11/110			37/110			19/110		
Log-add		1.30 (0.94,1.80)	1.17 (0.76,1.80)		1.00 (0.81,1.22)	1.11 (0.87,1.41)		0.90 (0.66,1.23)	0.88 (0.59,1.31)
Dominant	58/625	1.09 (0.67,1.76)	0.74 (0.39,1.38)	166/625	0.86 (0.65,1.15)	0.94 (0.66,1.32)	61/625	0.85 (0.55,1.32)	0.71 (0.41,1.22)
Recessive	22/146	***1.91 (1.14,3.20)***	***2.20 (1.12,4.32)***	49/146	1.25 (0.87,1.78)	***1.53 (1.01,2.31)***	14/146	0.92 (0.51,1.66)	1.19 (0.59,2.39)
RAN rs14035									
CC	41/463	1.00	1.00	122/463	1.00	1.00	38/463	1.00	1.00
CT	34/366	1.05 (0.65,1.69)	1.53 (0.85,2.77)	118/366	1.22 (0.92,1.63)	***1.46 (1.05,2.02)***	45/366	1.50 (0.95,2.36)	***1.91 (1.12,3.28)***
TT	8/92	0.98 (0.45,2.16)	0.91 (0.34,2.43)	18/92	0.74 (0.43,1.28)	0.76 (0.42,1.37)	12/92	1.59 (0.80,3.16)	1.46 (0.65,3.29)
Missing	12/119			39/119			20/119		
Log-add		1.01 (0.72,1.42)	1.12 (0.75,1.68)		1.00 (0.81,1.23)	1.07 (0.85,1.35)		1.32 (0.97,1.80)	1.36 (0.96,1.94)
Dominant	42/458	1.04 (0.66,1.62)	1.37 (0.78,2.41)	136/458	1.13 (0.85,1.49)	1.30 (0.95,1.78)	57/458	1.52 (0.99,2.33)	***1.80 (1.08,3.01)***
Recessive	8/92	0.96 (0.45,2.06)	0.75 (0.30,1.92)	18/92	0.68 (0.40,1.14)	0.64 (0.36,1.13)	12/92	1.30 (0.69,2.48)	1.05 (0.49,2.25)

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
DICER1 rs3742330									
AA	71/717	1.00	1.00	203/717	1.00	1.00	78/717	1.00	1.00
AG	13/200	0.66 (0.36,1.21)	0.73 (0.35,1.54)	47/200	0.83 (0.58,1.18)	0.76 (0.50,1.13)	20/200	0.92 (0.55,1.54)	1.03 (0.56,1.89)
GG	1/12	0.84 (0.11,6.57)	1.10 (0.10,11.88)	10/12	***2.94 (1.25,6.91)***	2.18 (0.82,5.76)	0/12	-	-
Missing	10/111			37/111			14/117		
Log-add		0.70 (0.41,1.22)	0.80 (0.41,1.55)		1.08 (0.81,1.43)	0.97 (0.69,1.35)		0.83 (0.51,1.35)	0.88 (0.50,1.55)
Dominant	14/212	0.67 (0.37,1.21)	0.75 (0.36,1.55)	57/212	0.95 (0.68,1.32)	0.84 (0.57,1.23)	20/212	0.87 (0.52,1.45)	0.96 (0.52,1.76)
Recessive	1/12	0.91 (0.12,7.08)	1.20 (0.11,12.93)	10/12	***3.06 (1.31,7.16)***	2.40 (0.92,6.28)	0/12	-	-
AGO2 rs4961280									
CC	57/594	1.00	1.00	170/594	1.00	1.00	70/594	1.00	1.00
CA	22/279	0.82 (0.49,1.37)	1.15 (0.62,2.15)	76/279	0.95 (0.70,1.29)	1.05 (0.74,1.48)	23/279	0.70 (0.43,1.14)	0.72 (0.40,1.28)
AA	1/47	0.22 (0.03,1.64)	0.60 (0.07,4.97)	10/47	0.74 (0.37,1.50)	1.16 (0.54,2.47)	3/47	0.54 (0.16,1.79)	1.02 (0.28,3.74)
Missing	15/120			41/120			19/120		
Log-add		0.71 (0.45,1.10)	1.03 (0.60,1.77)		0.91 (0.72,1.16)	1.06 (0.80,1.40)		0.71 (0.48,1.07)	0.82 (0.51,1.32)
Dominant	23/326	0.74 (0.45,1.22)	1.10 (0.60,2.04)	86/326	0.92 (0.69,1.23)	1.06 (0.76,1.48)	26/326	0.68 (0.42,1.08)	0.75 (0.43,1.30)
Recessive	1/47	0.24 (0.03,1.73)	0.57 (0.07,4.65)	10/47	0.76 (0.38,1.52)	1.14 (0.54,2.41)	3/47	0.60 (0.18,1.96)	1.13 (0.31,4.11)
GEMIN3 rs197412									
TT	26/307	1.00	1.00	85/307	1.00	1.00	28/307	1.00	1.00
TC	38/434	1.03 (0.62,1.74)	1.13 (0.59,2.15)	126/434	1.05 (0.77,1.43)	1.05 (0.73,1.49)	49/434	1.24 (0.76,2.01)	1.28 (0.72,2.28)

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
CC	20/180	1.31 (0.71,2.42)	1.03 (0.46,2.28)	47/180	0.94 (0.63,1.41)	0.76 (0.47,1.21)	18/180	1.10 (0.59,2.04)	1.06 (0.51,2.23)
Missing	11/119			39/119			20/119		
Log-add		1.14 (0.83,1.55)	1.02 (0.69,1.51)		0.98 (0.81,1.19)	0.89 (0.71,1.12)		1.07 (0.79,1.43)	1.05 (0.74,1.51)
Dominant	58/614	1.12 (0.69,1.81)	1.10 (0.59,2.03)	173/614	1.02 (0.76,1.36)	0.96 (0.69,1.34)	67/614	1.20 (0.75,1.90)	1.22 (0.70,2.13)
Recessive	20/180	1.29 (0.76,2.18)	0.95 (0.48,1.88)	47/180	0.92 (0.64,1.31)	0.74 (0.49,1.11)	18/180	0.96 (0.56,1.65)	0.90 (0.48,1.70)
GEMIN4 rs7813									
CC	39/378	1.00	1.00	123/378	1.00	1.00	43/378	1.00	1.00
CT	32/400	0.78 (0.48,1.26)	1.18 (0.63,2.19)	99/400	0.76 (0.56,1.03)	0.88 (0.63,1.25)	33/400	0.73 (0.45,1.17)	0.86 (0.49,1.50)
TT	9/134	0.65 (0.31,1.38)	0.73 (0.29,1.85)	32/134	0.73 (0.48,1.14)	0.76 (0.46,1.26)	15/134	0.98 (0.53,1.83)	1.00 (0.48,2.10)
Missing	15/128			43/128			24/128		
Log-add		0.80 (0.57,1.12)	0.93 (0.62,1.40)		0.83 (0.68,1.01)	0.87 (0.69,1.10)		0.92 (0.68,1.26)	0.97 (0.68,1.39)
Dominant	41/534	0.74 (0.47,1.18)	1.05 (0.58,1.88)	131/534	***0.75 (0.57,1.00)***	0.85 (0.62,1.18)	48/534	0.79 (0.51,1.22)	0.90 (0.54,1.50)
Recessive	9/134	0.74 (0.36,1.51)	0.68 (0.28,1.63)	32/134	0.84 (0.55,1.27)	0.81 (0.50,1.30)	15/134	1.15 (0.64,2.05)	1.08 (0.54,2.15)
GEMIN4 rs2740348									
CC	61/640	1.00	1.00	190/640	1.00	1.00	67/640	1.00	1.00
CG	16/250	0.67 (0.38,1.19)	0.63 (0.31,1.28)	58/250	0.78 (0.56,1.09)	0.80 (0.55,1.16)	23/250	0.88 (0.54,1.44)	0.89 (0.49,1.61)
GG	2/28	0.75 (0.17,3.22)	0.47 (0.08,2.74)	7/28	0.84 (0.36,1.96)	0.67 (0.25,1.76)	2/28	0.68 (0.16,2.93)	0.65 (0.14,3.16)
Missing	16/122			42/122			23/122		
Log-add		0.73	0.65		0.83	0.81		0.86	0.86

SNP		SQC			ADC			LCL	
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.45,1.18)	(0.37,1.16)		(0.63,1.09)	(0.59,1.10)		(0.56,1.32)	(0.53,1.41)
Dominant	18/278	0.68 (0.39,1.17)	0.61 (0.31,1.20)	65/278	0.79 (0.57,1.08)	0.78 (0.55,1.12)	25/278	0.86 (0.53,1.39)	0.86 (0.49,1.52)
Recessive	2/28	0.83 (0.19,3.53)	0.53 (0.09,3.08)	7/28	0.90 (0.39,2.08)	0.71 (0.27,1.87)	2/28	0.71 (0.17,3.01)	0.67 (0.14,3.23)
miRNA downstream									
CDK6 rs42031									
AA	66/656	1.00	1.00	181/656	1.00	1.00	71/656	1.00	1.00
AT	15/241	0.62 (0.35,1.11)	0.84 (0.42,1.68)	66/241	0.99 (0.72,1.36)	1.15 (0.80,1.65)	21/241	0.81 (0.48,1.34)	0.96 (0.53,1.75)
TT	1/27	0.37 (0.05,2.75)	0.14 (0.01,1.77)	7/27	0.94 (0.40,2.19)	0.82 (0.31,2.19)	4/27	1.37 (0.47,4.02)	0.88 (0.22,3.46)
Missing	13/116			43/116			19/116		
Log-add		0.62 (0.37,1.03)	0.67 (0.37,1.23)		0.98 (0.75,1.28)	1.06 (0.78,1.43)		0.94 (0.63,1.41)	0.95 (0.59,1.53)
Dominant	16/268	0.59 (0.34,1.04)	0.73 (0.37,1.44)	73/268	0.99 (0.73,1.34)	1.11 (0.78,1.58)	25/268	0.86 (0.53,1.39)	0.95 (0.54,1.69)
Recessive	1/27	0.41 (0.06,3.06)	0.15 (0.01,1.84)	7/27	0.94 (0.41,2.19)	0.79 (0.30,2.08)	4/27	1.44 (0.49,4.22)	0.89 (0.23,3.47)
TP53INP1 rs896849									
TT	48/666	1.00	1.00	166/666	1.00	1.00	68/666	1.00	1.00
TC	33/232	***1.97 (1.24,3.15)***	1.27 (0.70,2.32)	78/232	1.35 (0.99,1.83)	1.28 (0.90,1.82)	25/232	1.06 (0.65,1.71)	0.93 (0.53,1.64)
CC	2/31	0.90 (0.21,3.85)	0.78 (0.15,4.07)	17/31	***2.20 (1.19,4.07)***	1.92 (0.93,3.96)	5/31	1.58 (0.59,4.20)	1.40 (0.41,4.73)
Missing	12/111			36/111			17/111		
Log-add		***1.50 (1.03,2.19)***	1.12 (0.67,1.86)		***1.41 (1.12,1.79)***	***1.33 (1.01,1.75)***		1.15 (0.79,1.66)	1.03 (0.65,1.63)
Dominant	35/263	***1.85 (1.17,2.92)***	1.22 (0.68,2.21)	95/263	***1.45 (1.08,1.94)***	1.35 (0.96,1.89)	30/263	1.12 (0.71,1.76)	0.97 (0.57,1.68)

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Recessive	2/31	0.72 (0.17,3.04)	0.70 (0.14,3.56)	17/31	***2.02 (1.10,3.71)***	1.74 (0.85,3.55)	5/31	1.56 (0.59,4.10)	1.44 (0.43,4.77)
CXCL12 rs1804429									
TT	74/858	1.00	1.00	242/858	1.00	1.00	88/858	1.00	1.00
TG	8/73	1.27 (0.59,2.74)	1.12 (0.45,2.79)	19/73	0.92 (0.55,1.56)	0.96 (0.53,1.71)	8/73	1.07 (0.50,2.29)	0.80 (0.32,2.03)
GG	2/1	23.19 (2.08,258.73)	10.94 (0.70,170.31)	0/1			0/1		
Missing	11/108			36/108			19/108		
Log-add		1.80 (0.97,3.36)	1.51 (0.71,3.24)		0.90 (0.54,1.51)	0.92 (0.52,1.63)		1.04 (0.49,2.20)	0.79 (0.32,1.96)
Dominant	10/74	1.57 (0.78,3.16)	1.34 (0.57,3.14)	19/74	0.91 (0.54,1.54)	0.94 (0.52,1.68)	8/74	1.05 (0.49,2.26)	0.80 (0.32,2.00)
Recessive	2/1	22.71 (2.04,253.08)	10.74 (0.69,166.50)	0/1	-	-	0/1	-	-
E2F2 rs2075993									
GG	32/291	1.00	1.00	92/291	1.00	1.00	29/291	1.00	1.00
GA	32/455	0.64 (0.38,1.07)	0.68 (0.34,1.35)	108/455	0.75 (0.55,1.03)	0.77 (0.53,1.10)	45/455	0.99 (0.61,1.62)	1.01 (0.56,1.84)
AA	17/179	0.86 (0.47,1.60)	1.43 (0.64,3.22)	61/179	1.08 (0.74,1.57)	1.12 (0.72,1.74)	23/179	1.29 (0.72,2.30)	1.41 (0.69,2.87)
Missing	14/115			36/115			18/115		
Log-add		0.88 (0.64,1.22)	1.14 (0.74,1.75)		1.00 (0.83,1.22)	1.03 (0.82,1.29)		1.13 (0.84,1.51)	1.18 (0.82,1.69)
Dominant	49/634	0.70 (0.44,1.12)	0.84 (0.45,1.59)	169/634	0.84 (0.63,1.13)	0.86 (0.61,1.20)	68/634	1.08 (0.68,1.70)	1.12 (0.64,1.96)
Recessive	17/179	1.11 (0.63,1.94)	1.82 (0.91,3.67)	61/179	1.27 (0.91,1.77)	1.32 (0.90,1.93)	23/179	1.30 (0.79,2.13)	1.39 (0.77,2.53)
DOCK4 rs3801790									
AA	35/376	1.00	1.00	112/376	1.00	1.00	44/376	1.00	1.00

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AG	40/427	1.01 (0.63,1.62)	1.19 (0.66,2.12)	114/427	0.90 (0.67,1.20)	1.06 (0.76,1.47)	45/427	0.90 (0.58,1.40)	1.05 (0.63,1.75)
GG	9/126	0.77 (0.36,1.64)	0.97 (0.38,2.49)	33/126	0.88 (0.57,1.36)	1.02 (0.62,1.68)	10/126	0.68 (0.33,1.39)	0.74 (0.32,1.73)
Missing	11/111			38/111			16/111		
Log-add		0.92 (0.66,1.28)	1.05 (0.70,1.58)		0.93 (0.76,1.13)	1.02 (0.81,1.29)		0.85 (0.62,1.16)	0.92 (0.64,1.33)
Dominant	49/553	0.95 (0.61,1.50)	1.14 (0.66,1.99)	147/553	0.89 (0.68,1.18)	1.05 (0.76,1.44)	55/553	0.85 (0.56,1.29)	0.98 (0.60,1.60)
Recessive	9/126	0.76 (0.37,1.57)	0.89 (0.37,2.15)	33/126	0.93 (0.62,1.40)	0.99 (0.62,1.58)	10/126	0.72 (0.36,1.41)	0.72 (0.32,1.61)
IL6R rs4072391									
CC	52/593	1.00	1.00	153/593	1.00	1.00	63/593	1.00	1.00
CT	26/279	1.06 (0.65,1.74)	0.88 (0.48,1.62)	94/279	1.31 (0.97,1.75)	1.24 (0.89,1.73)	32/279	1.08 (0.69,1.69)	1.13 (0.67,1.92)
TT	4/49	0.93 (0.32,2.68)	0.66 (0.18,2.36)	9/49	0.71 (0.34,1.48)	0.74 (0.34,1.63)	3/49	0.58 (0.17,1.90)	0.61 (0.16,2.29)
Missing	13/119			41/119			17/119		
Log-add		1.02 (0.69,1.49)	0.84 (0.53,1.36)		1.08 (0.86,1.37)	1.06 (0.81,1.38)		0.94 (0.65,1.35)	0.97 (0.64,1.48)
Dominant	30/328	1.04 (0.65,1.67)	0.84 (0.47,1.51)	103/328	1.22 (0.92,1.62)	1.16 (0.84,1.60)	35/328	1.00 (0.65,1.55)	1.05 (0.63,1.75)
Recessive	4/49	0.91 (0.32,2.60)	0.69 (0.19,2.42)	9/49	0.65 (0.31,1.34)	0.68 (0.31,1.49)	3/49	0.56 (0.17,1.84)	0.59 (0.16,2.16)
HIF1A									
HIF1A rs2057482									
CC	51/672	1.00	1.00	171/672	1.00	1.00	67/672	1.00	1.00
CT	28/234	1.58 (0.97,2.56)	1.47 (0.80,2.67)	75/234	1.26 (0.92,1.72)	1.12 (0.79,1.60)	27/234	1.16 (0.72,1.85)	1.24 (0.71,2.16)
TT	3/23	1.72	1.51	14/23	***2.39***	***2.34***	3/23	1.31	1.21

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.50,5.92)	(0.33,6.93)		***(1.21,4.75)***	***(1.06,5.16)***		(0.38,4.47)	(0.28,5.15)
Missing	13/111			37/111			18/111		
Log-add		1.47	1.37		***1.38***	1.28		1.15	1.19
		(0.99,2.18)	(0.83,2.25)		***(1.08,1.76)***	(0.96,1.70)		(0.78,1.71)	(0.75,1.88)
Dominant	31/257	1.59	1.47	89/257	***1.36***	1.22	30/257	1.17	1.24
		(0.99,2.54)	(0.82,2.63)		***(1.01,1.83)***	(0.87,1.71)		(0.74,1.84)	(0.72,2.12)
Recessive	3/23	1.50	1.33	14/23	***2.24***	***2.25***	3/23	1.26	1.13
		(0.44,5.09)	(0.30,5.97)		***(1.14,4.42)***	***(1.03,4.93)***		(0.37,4.27)	(0.27,4.77)
HIF1A rs2301113									
AA	32/467	1.00	1.00	115/467	1.00	1.00	48/467	1.00	1.00
AC	34/310	1.60	1.35	94/310	1.23	1.14	35/310	1.10	1.03
		(0.97,2.65)	(0.72,2.53)		(0.90,1.68)	(0.81,1.62)		(0.69,1.74)	(0.60,1.79)
CC	13/100	1.90	0.86	41/100	***1.67***	1.08	12/100	1.17	0.74
		(0.96,3.74)	(0.33,2.27)		***(1.10,2.53)***	(0.63,1.85)		(0.60,2.28)	(0.30,1.83)
Missing	16/163			47/163			20/163		
Log-add		***1.42***	1.02		***1.28***	1.07		1.09	0.92
		(1.04,1.95)	(0.65,1.59)		***(1.05,1.55)***	(0.84,1.37)		(0.80,1.47)	(0.62,1.36)
Dominant	47/410	***1.67***	1.24	135/410	***1.34***	1.13	47/410	1.12	0.97
		(1.05,2.67)	(0.67,2.31)		***(1.01,1.77)***	(0.81,1.58)		(0.73,1.70)	(0.57,1.65)
Recessive	13/100	1.53	0.71	41/100	***1.52***	1.01	12/100	1.12	0.73
		(0.82,2.87)	(0.30,1.70)		***(1.03,2.26)***	(0.61,1.66)		(0.59,2.13)	(0.31,1.71)
miRNAs									
MIR-26A1 rs7372209									
CC	49/494	1.00	1.00	136/494	1.00	1.00	51/494	1.00	1.00
CT	29/366	0.80	1.35	95/366	0.94	1.18	41/366	1.09	1.37
		(0.50,1.29)	(0.73,2.49)		(0.70,1.27)	(0.84,1.66)		(0.70,1.67)	(0.81,2.32)
TT	6/66	0.92	1.96	27/66	1.49	***1.98***	6/66	0.88	1.12
		(0.38,2.22)	(0.70,5.50)		(0.91,2.42)	***(1.15,3.42)***		(0.36,2.13)	(0.41,3.02)
Missing	11/114			39/114			17/114		
Log-add		0.88	1.38		1.10	***1.32***		1.01	1.18

SNP	SQC			ADC			LCL		
	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/ Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.61,1.27)	(0.88,2.16)		(0.89,1.37)	***(1.04,1.69)***		(0.72,1.41)	(0.80,1.75)
Dominant	35/432	0.82	1.44	122/432	1.03	1.30	47/432	1.05	1.33
		(0.52,1.28)	(0.80,2.57)		(0.78,1.35)	(0.94,1.79)		(0.69,1.60)	(0.80,2.21)
Recessive	6/66	1.00	1.72	27/66	1.52	***1.84***	6/66	0.85	0.96
		(0.42,2.39)	(0.64,4.62)		(0.95,2.44)	***(1.09,3.09)***		(0.36,2.01)	(0.37,2.52)
MIR-27 rs895819									
TT	37/413	1.00	1.00	121/413	1.00	1.00	44/413	1.00	1.00
TC	33/411	0.90	0.94	102/411	0.85	0.95	40/411	0.91	1.05
		(0.55,1.46)	(0.52,1.70)		(0.63,1.14)	(0.68,1.33)		(0.58,1.43)	(0.62,1.79)
CC	9/86	1.17	0.82	27/86	1.07	0.99	10/86	1.09	1.15
		(0.54,2.51)	(0.31,2.17)		(0.66,1.73)	(0.58,1.71)		(0.53,2.25)	(0.48,2.75)
Missing	16/130			47/130			21/130		
Log-add		1.01	0.92		0.96	0.98		0.99	1.07
		(0.71,1.44)	(0.60,1.41)		(0.78,1.19)	(0.77,1.25)		(0.72,1.38)	(0.72,1.57)
Dominant	42/497	0.94	0.92	129/497	0.89	0.96	50/497	0.94	1.07
		(0.60,1.50)	(0.52,1.62)		(0.67,1.17)	(0.70,1.32)		(0.62,1.45)	(0.64,1.78)
Recessive	9/86	1.23	0.85	27/86	1.16	1.02	10/86	1.14	1.12
		(0.59,2.55)	(0.34,2.13)		(0.73,1.83)	(0.60,1.71)		(0.57,2.28)	(0.49,2.56)

* Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.5a Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung cancer, in the overall population

SNP	Cases/Controls	Crude OR (95% CI)	Bayesian posterior OR, crude (95% posterior limits)	Adjusted* OR (95% CI)	Bayesian posterior OR, adjusted* (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	193/305	1.00	1.00	1.00	1.00
AC	231/479	***0.76(0.60,0.97)***	***0.78(0.62,0.97)***	0.76(0.56,1.03)	0.78(0.59,1.02)
CC	106/146	1.15(0.84,1.56)	1.14(0.86,1.50)	1.23(0.83,1.83)	1.20(0.85,1.68)
Log-additive		1.01(0.87,1.18)	1.01(0.87,1.18)	1.05(0.86,1.28)	1.05(0.86,1.26)
Dominant	337/625	0.85(0.68,1.07)	0.87(0.70,1.07)	0.86(0.64,1.14)	0.88(0.67,1.14)
Recessive	106/146	***1.34(1.02,1.77)***	1.29(1.00,1.67)	***1.46(1.03,2.07)***	1.36(0.99,1.85)
RAN rs14035					
CC	244/463	1.00	1.00	1.00	1.00
CT	233/366	1.21(0.96,1.51)	1.19(0.96,1.47)	***1.44(1.09,1.90)***	***1.38(1.07,1.78)***
TT	48/92	0.99(0.68,1.45)	0.99(0.71,1.38)	0.92(0.58,1.46)	0.93(0.63,1.36)
Log-additive		1.07(0.91,1.26)	1.07(0.91,1.25)	1.11(0.91,1.35)	1.10(0.91,1.33)
Dominant	281/458	1.16(0.94,1.44)	1.15(0.94,1.41)	***1.32(1.02,1.72)***	***1.28(1.00,1.63)***
Recessive	48/92	0.91(0.63,1.31)	0.93(0.67,1.28)	0.78(0.50,1.21)	0.83(0.58,1.21)
AGO2 rs4961280					
CC	365/594	1.00	1.00	1.00	1.00
CA	141/279	0.82(0.65,1.05)	0.85(0.68,1.07)	0.91(0.68,1.22)	0.93(0.71,1.22)
AA	15/47	***0.52(0.29,0.94)***	0.68(0.44,1.06)	0.80(0.40,1.60)	0.90(0.55,1.45)
Log-additive		***0.78(0.64,0.95)***	***0.80(0.66,0.96)***	0.91(0.71,1.15)	0.92(0.73,1.15)
Dominant	156/326	***0.78(0.62,0.98)***	***0.80(0.64,0.99)***	0.90(0.68,1.19)	0.91(0.70,1.19)
Recessive	15/47	***0.55(0.31,1.00)***	0.70(0.45,1.09)	0.83(0.42,1.64)	0.91(0.56,1.47)
GEMIN4 rs7813					
CC	242/378	1.00	1.00	1.00	1.00
CT	201/400	***0.79(0.62,0.99)***	0.81(0.65,1.01)	0.91(0.68,1.21)	0.92(0.71,1.20)

SNP	Cases/Controls	Crude OR (95% CI)	Bayesian posterior OR, crude (95% posterior limits)	Adjusted* OR (95% CI)	Bayesian posterior OR, adjusted* (95% posterior limits)
TT	71/134	0.83(0.60,1.15)	0.87(0.64,1.16)	0.88(0.59,1.33)	0.92(0.64,1.30)
Log-additive		0.88(0.75,1.02)	0.88(0.76,1.03)	0.93(0.77,1.13)	0.93(0.78,1.13)
Dominant	272/534	***0.80(0.64,0.99)***	***0.81(0.66,1.00)***	0.90(0.69,1.18)	0.91(0.71,1.17)
Recessive	71/134	0.93(0.68,1.27)	0.94(0.71,1.25)	0.93(0.63,1.36)	0.94(0.67,1.32)
miRNA downstream					
TP53INP1 rs896849					
TT	346/666	1.00	1.00	1.00	1.00
TC	160/232	***1.33(1.05,1.69)***	***1.28(1.02,1.60)***	1.15(0.85,1.55)	1.11(0.85,1.46)
CC	27/31	1.68(0.99,2.85)	1.38(0.90,2.10)	1.47(0.75,2.86)	1.21(0.75,1.96)
Log-additive		***1.31(1.09,1.59)***	***1.29(1.07,1.55)***	1.18(0.92,1.50)	1.16(0.92,1.45)
Dominant	187/263	***1.37(1.09,1.72)***	***1.33(1.07,1.65)***	1.18(0.89,1.58)	1.15(0.88,1.51)
Recessive	27/31	1.55(0.91,2.62)	1.32(0.86,2.01)	1.38(0.72,2.67)	1.19(0.73,1.91)
HIF1A					
HIF1A rs2057482					
CC	354/672	1.00	1.00	1.00	1.00
CT	150/234	1.22(0.96,1.55)	1.17(0.94,1.48)	1.09(0.81,1.48)	1.06(0.80,1.39)
TT	26/23	***2.15(1.21,3.82)***	***1.57(1.01,2.44)***	***2.32(1.15,4.71)***	1.51(0.92,2.50)
Log-additive		***1.31(1.08,1.59)***	***1.29(1.06,1.55)***	1.25(0.98,1.59)	1.22(0.97,1.53)
Dominant	176/257	***1.30(1.03,1.64)***	***1.27(1.02,1.58)***	1.19(0.90,1.59)	1.16(0.89,1.51)
Recessive	26/23	***2.03(1.15,3.60)***	1.53(0.98,2.37)	***2.26(1.12,4.55)***	1.50(0.91,2.45)
HIF1A rs2301113					
AA	238/467	1.00	1.00	1.00	1.00
AC	190/310	1.20(0.95,1.53)	1.16(0.93,1.45)	1.12(0.83,1.50)	1.09(0.84,1.42)
CC	82/100	***1.61(1.16,2.24)***	***1.46(1.09,1.97)***	1.17(0.74,1.83)	1.11(0.76,1.61)
Log-additive		***1.25(1.07,1.46)***	***1.24(1.07,1.44)***	1.09(0.89,1.34)	1.08(0.89,1.32)
Dominant	272/410	***1.30(1.05,1.62)***	***1.27(1.03,1.57)***	1.13(0.85,1.49)	1.11(0.86,1.44)
Recessive	82/100	***1.49(1.09,2.04)***	***1.39(1.04,1.85)***	1.10(0.72,1.68)	1.07(0.75,1.54)

SNP	Cases/Controls	Crude OR (95% CI)	Bayesian posterior OR, crude (95% posterior limits)	Adjusted* OR (95% CI)	Bayesian posterior OR, adjusted* (95% posterior limits)
miRNAs					
MIR-26A1 rs7372209					
CC	287/494	1.00	1.00	1.00	1.00
CT	197/366	0.93(0.74,1.16)	0.93(0.75,1.15)	1.15(0.86,1.52)	1.10(0.85,1.42)
TT	47/66	1.23(0.82,1.83)	1.17(0.82,1.65)	***1.62(1.00,2.62)***	1.38(0.93,2.04)
Log-additive		1.03(0.87,1.21)	1.02(0.87,1.21)	1.22(0.99,1.50)	1.20(0.99,1.47)
Dominant	244/432	0.97(0.79,1.20)	0.97(0.79,1.20)	1.22(0.93,1.60)	1.19(0.92,1.53)
Recessive	47/66	1.27(0.86,1.87)	1.20(0.85,1.68)	1.52(0.96,2.41)	1.34(0.91,1.96)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.5b Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung cancer, in the Caucasians

SNP	Cases/Controls	Crude OR (95% CI)	Bayesian posterior OR, crude (95% posterior limits)	Adjusted* OR (95% CI)	Bayesian posterior OR, adjusted* (95% posterior limits)
Micro RNA processing and maturation					
GEMIN3 rs197412					
TT+TC	277/483	1.00	1.00	1.00	1.00
CC	34/89	0.67(0.44,1.02)	0.74(0.52,1.06)	***0.53(0.31,0.90)***	0.67(0.44,1.01)
miRNAs					
MIR-26A1 rs7372209					
CC	141/322	1.00	1.00	1.00	1.00
CT	139/219	***1.45(1.08,1.94)***	***1.34(1.02,1.74)***	***1.73(1.20,2.50)***	***1.49(1.08,2.05)***
TT	29/35	***1.89(1.11,3.22)***	1.47(0.96,2.24)	1.88(0.99,3.59)	1.36(0.85,2.19)
Missing	50/58				
Dominant	168/254	***1.51(1.14,1.99)***	***1.43(1.10,1.84)***	***1.75(1.23,2.49)***	***1.56(1.14,2.14)***
MIR-27 rs895819					
TT	154/256	1.00	1.00	1.00	1.00
TC	118/267	***0.73(0.55,0.99)***	0.77(0.59,1.01)	0.88(0.61,1.27)	0.90(0.65,1.24)
CC	28/45	1.03(0.62,1.73)	1.04(0.69,1.56)	1.20(0.64,2.28)	1.11(0.70,1.78)

Table 1.1.6 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and NSCLC

	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
RAN rs14035					
CC	212/463	1.00	1.00	1.00	1.00
CT	207/366	1.24(0.98,1.56)	1.21(0.97,1.51)	***1.48(1.11,1.96)***	***1.40(1.08,1.82)***
TT	42/92	1.00(0.67,1.49)	0.99(0.70,1.40)	0.92(0.57,1.49)	0.93(0.63,1.37)
Log-additive		1.08(0.91,1.28)	1.08(0.91,1.27)	1.12(0.92,1.37)	1.11(0.92,1.35)
Dominant	249/458	1.19(0.95,1.49)	0.81(0.64,1.02)	***1.35(1.03,1.77)***	***1.30(1.01,1.67)***
Recessive	42/92	0.90(0.62,1.33)	0.93(0.66,1.29)	0.77(0.49,1.21)	0.83(0.57,1.21)
AGO2 rs4961280					
CC	319/594	1.00	1.00	1.00	1.00
CA	124/279	0.83(0.64,1.06)	0.86(0.68,1.08)	0.94(0.69,1.27)	0.95(0.72,1.25)
AA	14/47	0.56(0.30,1.02)	0.71(0.46,1.11)	0.90(0.45,1.79)	0.95(0.58,1.54)
Log-additive		***0.79(0.65,0.97)***	***0.81(0.67,0.98)***	0.94(0.74,1.20)	0.95(0.75,1.19)
Dominant	138/326	0.79(0.62,1.00)	0.81(0.64,1.02)	0.93(0.70,1.25)	0.94(0.72,1.23)
Recessive	14/47	0.59(0.32,1.08)	0.74(0.47,1.15)	0.92(0.46,1.82)	0.96(0.59,1.55)
GEMIN4 rs7813					
CC	214/378	1.00	1.00	1.00	1.00
CT	173/400	***0.76(0.60,0.98)***	***0.79(0.63,1.00)***	0.93(0.69,1.26)	0.95(0.72,1.25)
TT	62/134	0.82(0.58,1.15)	0.86(0.63,1.17)	0.89(0.58,1.35)	0.92(0.64,1.31)
Log-additive		0.86(0.74,1.02)	0.87(0.74,1.02)	0.94(0.77,1.14)	0.94(0.78,1.14)
Dominant	235/534	***0.78(0.62,0.98)***	***0.80(0.64,0.99)***	0.92(0.70,1.22)	0.93(0.72,1.21)
Recessive	62/134	0.93(0.67,1.29)	0.94(0.70,1.26)	0.92(0.62,1.36)	0.94(0.66,1.32)
miRNA downstream					
TP53INP1 rs896849					
TT	301/666	1.00	1.00	1.00	1.00

	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
TC	141/232	***1.34(1.05,1.73)***	***1.28(1.02,1.62)***	1.18(0.87,1.61)	1.13(0.86,1.50)
CC	25/31	***1.78(1.04,3.07)***	1.42(0.92,2.19)	1.50(0.76,2.96)	1.22(0.75,1.99)
Log-additive		***1.34(1.10,1.63)***	***1.31(1.09,1.58)***	1.20(0.94,1.54)	1.18(0.93,1.49)
Dominant	166/263	***1.40(1.10,1.77)***	***1.35(1.08,1.69)***	1.21(0.90,1.63)	1.18(0.90,1.55)
Recessive	25/31	1.64(0.96,2.81)	1.36(0.88,2.09)	1.40(0.71,2.73)	1.19(0.73,1.93)
HIF1A					
HIF1A rs2057482					
CC	303/672	1.00	1.00	1.00	1.00
CT	138/234	***1.31(1.02,1.68)***	1.25(0.99,1.58)	1.17(0.86,1.58)	1.11(0.84,1.47)
TT	23/23	***2.22(1.22,4.02)***	1.57(1.00,2.48)	***2.40(1.17,4.91)***	1.52(0.92,2.50)
Log-additive		***1.38(1.13,1.69)***	***1.34(1.11,1.63)***	***1.31(1.02,1.67)***	1.27(1.00,1.60)
Dominant	161/257	***1.39(1.09,1.76)***	***1.34(1.07,1.68)***	1.26(0.94,1.69)	1.22(0.93,1.60)
Recessive	23/23	***2.05(1.14,3.70)***	1.52(0.97,2.38)	***2.28(1.12,4.64)***	1.49(0.91,2.46)
HIF1A rs2301113					
AA	205/467	1.00	1.00	1.00	1.00
AC	170/310	1.25(0.97,1.60)	1.19(0.95,1.51)	1.13(0.84,1.53)	1.10(0.84,1.45)
CC	72/100	***1.64(1.16,2.32)***	***1.47(1.08,2.01)***	1.13(0.71,1.80)	1.08(0.74,1.59)
Log-additive		***1.27(1.08,1.49)***	***1.26(1.08,1.47)***	1.08(0.88,1.34)	1.08(0.88,1.32)
Dominant	242/410	***1.34(1.07,1.69)***	***1.31(1.05,1.62)***	1.13(0.85,1.51)	1.11(0.85,1.45)
Recessive	72/100	***1.49(1.08,2.07)***	***1.39(1.03,1.87)***	1.06(0.68,1.63)	1.04(0.72,1.50)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.7 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and SCLC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	24/305	1.00	1.00	1.00	1.00
AC	24/479	0.64(0.36,1.14)	0.72(0.47,1.11)	0.54(0.27,1.07)	0.67(0.42,1.07)
CC	17/146	1.48(0.77,2.84)	1.30(0.81,2.09)	1.79(0.79,4.02)	1.39(0.81,2.36)
Log-additive		1.14(0.79,1.65)	1.11(0.80,1.54)	1.19(0.76,1.86)	1.13(0.77,1.66)
Dominant	41/625	0.83(0.49,1.41)	0.89(0.59,1.35)	0.74(0.40,1.38)	0.85(0.53,1.37)
Recessive	17/146	***1.90(1.06,3.40)***	1.45(0.91,2.29)	***2.61(1.27,5.35)***	1.55(0.92,2.61)
GEMIN3 rs197412					
TT	31/307	1.00	1.00	1.00	1.00
TC	24/434	***0.55(0.32,0.95)***	0.72(0.47,1.10)	***0.45(0.24,0.86)***	0.68(0.43,1.08)
CC	11/180	0.61(0.30,1.23)	0.82(0.51,1.33)	0.57(0.25,1.31)	0.84(0.50,1.43)
Log-additive		0.72(0.50,1.03)	0.77(0.56,1.06)	0.66(0.44,1.01)	0.74(0.51,1.07)
Dominant	35/614	***0.56(0.34,0.93)***	0.69(0.46,1.04)	***0.48(0.27,0.86)***	0.65(0.41,1.03)
Recessive	11/180	0.82(0.42,1.61)	0.90(0.56,1.45)	0.87(0.41,1.88)	0.93(0.55,1.56)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.8 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung SQC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	26/305	1.00	1.00	1.00	1.00
AC	36/479	0.88(0.52,1.49)	0.86(0.58,1.28)	0.56(0.28,1.11)	0.68(0.43,1.08)
CC	22/146	1.77(0.97,3.22)	1.42(0.91,2.22)	1.50(0.67,3.33)	1.31(0.78,2.18)
Log-additive		1.30(0.94,1.80)	1.24(0.92,1.66)	1.17(0.76,1.80)	1.12(0.78,1.62)
Dominant	58/625	1.09(0.67,1.76)	1.06(0.71,1.57)	0.74(0.39,1.38)	0.84(0.53,1.35)
Recessive	22/146	***1.91(1.14,3.20)***	1.50(0.98,2.30)	***2.20(1.12,4.32)***	1.49(0.91,2.44)
miRNA downstream					
TP53INP1 rs896849					
TT	48/666	1.00	1.00	1.00	1.00
TC	33/232	***1.97(1.24,3.15)***	***1.60(1.08,2.36)***	1.27(0.70,2.32)	1.16(0.74,1.82)
CC	2/31	0.90(0.21,3.85)	0.96(0.52,1.79)	0.78(0.15,4.07)	0.95(0.51,1.79)
Log-additive		***1.50(1.03,2.19)***	1.36(0.97,1.91)	1.12(0.67,1.86)	1.07(0.71,1.62)
Dominant	35/263	***1.85(1.17,2.92)***	***1.53(1.04,2.25)***	1.22(0.68,2.21)	1.12(0.71,1.76)
Recessive	2/31	0.72(0.17,3.04)	0.93(0.51,1.72)	0.70(0.14,3.56)	0.94(0.50,1.77)
CXCL12 rs1804429					
TT	74/858	1.00	1.00	1.00	1.00
TG	8/73	1.27(0.59,2.74)	1.10(0.65,1.85)	1.12(0.45,2.79)	1.03(0.59,1.78)
GG	2/1	23.19(2.08,258.73)	1.24(0.63,2.45)	10.94(0.70,170.31)	1.14(0.58,2.25)
Log-additive		1.80(0.97,3.36)	1.37(0.84,2.22)	1.51(0.71,3.24)	1.20(0.72,2.02)
Dominant	10/74	1.57(0.78,3.16)	1.24(0.74,2.06)	1.34(0.57,3.14)	1.12(0.65,1.93)
Recessive	2/1	22.71(2.04,253.08)	1.24(0.63,2.44)	10.74(0.69,166.50)	1.14(0.58,2.25)
HIF1A					
HIF1A rs2301113					

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
AA	32/467	1.00	1.00	1.00	1.00
AC	34/310	1.60(0.97,2.65)	1.30(0.87,1.93)	1.35(0.72,2.53)	1.21(0.77,1.89)
CC	13/100	1.90(0.96,3.74)	1.33(0.81,2.18)	0.86(0.33,2.27)	0.92(0.53,1.59)
Log-additive		***1.42(1.04,1.95)***	1.34(1.00,1.78)	1.02(0.65,1.59)	1.01(0.70,1.48)
Dominant	47/410	***1.67(1.05,2.67)***	1.43(0.97,2.10)	1.24(0.67,2.31)	1.13(0.71,1.79)
Recessive	13/100	1.53(0.82,2.87)	1.26(0.78,2.03)	0.71(0.30,1.70)	0.87(0.51,1.50)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.9 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung ADC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	94/305	1.00	1.00	1.00	1.00
AC	117/479	0.79(0.58,1.08)	0.82(0.62,1.08)	0.83(0.58,1.20)	0.84(0.62,1.15)
CC	49/146	1.09(0.73,1.62)	1.08(0.77,1.53)	1.36(0.85,2.18)	1.26(0.86,1.85)
Log-additive		1.00(0.81,1.22)	1.00(0.82,1.21)	1.11(0.87,1.41)	1.10(0.88,1.38)
Dominant	166/625	0.86(0.65,1.15)	0.88(0.68,1.15)	0.94(0.66,1.32)	0.95(0.70,1.29)
Recessive	49/146	1.25(0.87,1.78)	1.19(0.86,1.64)	***1.53(1.01,2.31)***	1.37(0.95,1.95)
RAN rs14035					
CC	122/463	1.00	1.00	1.00	1.00
CT	118/366	1.22(0.92,1.63)	1.20(0.93,1.57)	***1.46(1.05,2.02)***	***1.38(1.03,1.85)***
TT	18/92	0.74(0.43,1.28)	0.82(0.54,1.25)	0.76(0.42,1.37)	0.83(0.54,1.30)
Log-additive		1.00(0.81,1.23)	1.00(0.82,1.22)	1.07(0.85,1.35)	1.06(0.85,1.32)
Dominant	136/458	1.13(0.85,1.49)	1.11(0.86,1.43)	1.30(0.95,1.78)	1.24(0.94,1.65)
Recessive	18/92	0.68(0.40,1.14)	0.78(0.52,1.17)	0.64(0.36,1.13)	0.76(0.50,1.17)
DICER1 rs3742330					
AA	203/717	1.00	1.00	1.00	1.00
AG	47/200	0.83(0.58,1.18)	0.85(0.62,1.16)	0.76(0.50,1.13)	0.79(0.56,1.12)
GG	10/12	***2.94(1.25,6.91)***	1.52(0.87,2.64)	2.18(0.82,5.76)	1.30(0.74,2.31)
Log-additive		1.08(0.81,1.43)	1.06(0.82,1.39)	0.97(0.69,1.35)	0.97(0.72,1.31)
Dominant	57/212	0.95(0.68,1.32)	0.96(0.71,1.29)	0.84(0.57,1.23)	0.87(0.62,1.22)
Recessive	10/12	***3.06(1.31,7.16)***	1.54(0.88,2.67)	2.40(0.92,6.28)	1.34(0.76,2.37)
GEMIN4 rs7813					
CC	123/378	1.00	1.00	1.00	1.00
CT	99/400	0.76(0.56,1.03)	0.81(0.61,1.06)	0.88(0.63,1.25)	0.92(0.68,1.25)

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
TT	32/134	0.73(0.48,1.14)	0.81(0.56,1.17)	0.76(0.46,1.26)	0.84(0.56,1.26)
Log-additive		0.83(0.68,1.01)	0.84(0.69,1.02)	0.87(0.69,1.10)	0.89(0.71,1.11)
Dominant	131/534	***0.75(0.57,1.00)***	0.78(0.61,1.02)	0.85(0.62,1.18)	0.88(0.65,1.18)
Recessive	32/134	0.84(0.55,1.27)	0.88(0.62,1.25)	0.81(0.50,1.30)	0.86(0.59,1.27)
miRNA downstream					
TP53INP1 rs896849					
TT	166/666	1.00	1.00	1.00	1.00
TC	78/232	1.35(0.99,1.83)	1.26(0.95,1.66)	1.28(0.90,1.82)	1.19(0.87,1.62)
CC	17/31	***2.20(1.19,4.07)***	1.53(0.95,2.45)	1.92(0.93,3.96)	1.35(0.81,2.24)
Log-additive		***1.41(1.12,1.79)***	***1.36(1.09,1.70)***	***1.33(1.01,1.75)***	1.28(0.99,1.65)
Dominant	95/263	***1.45(1.08,1.94)***	***1.37(1.05,1.79)***	1.35(0.96,1.89)	1.27(0.94,1.73)
Recessive	17/31	***2.02(1.10,3.71)***	1.47(0.92,2.36)	1.74(0.85,3.55)	1.30(0.79,2.16)
HIF1A					
HIF1A rs2057482					
CC	171/672	1.00	1.00	1.00	1.00
CT	75/234	1.26(0.92,1.72)	1.19(0.90,1.57)	1.12(0.79,1.60)	1.07(0.78,1.46)
TT	14/23	***2.39(1.21,4.75)***	1.53(0.92,2.52)	***2.34(1.06,5.16)***	1.43(0.84,2.43)
Log-additive		***1.38(1.08,1.76)***	***1.33(1.05,1.68)***	1.28(0.96,1.70)	1.23(0.95,1.60)
Dominant	89/257	***1.36(1.01,1.83)***	1.30(0.99,1.70)	1.22(0.87,1.71)	1.18(0.87,1.59)
Recessive	14/23	***2.24(1.14,4.42)***	1.49(0.91,2.46)	***2.25(1.03,4.93)***	1.42(0.83,2.40)
HIF1A rs2301113					
AA	115/467	1.00	1.00	1.00	1.00
AC	94/310	1.23(0.90,1.68)	1.16(0.88,1.53)	1.14(0.81,1.62)	1.11(0.82,1.51)
CC	41/100	***1.67(1.10,2.53)***	***1.44(1.00,2.06)***	1.08(0.63,1.85)	1.04(0.68,1.59)
Log-additive		***1.28(1.05,1.55)***	***1.25(1.04,1.51)***	1.07(0.84,1.37)	1.06(0.84,1.34)
Dominant	135/410	***1.34(1.01,1.77)***	1.28(0.99,1.67)	1.13(0.81,1.58)	1.11(0.82,1.49)
Recessive	41/100	***1.52(1.03,2.26)***	1.37(0.97,1.94)	1.01(0.61,1.66)	1.00(0.67,1.51)

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
miRNAs					
MIR-26A1 rs7372209					
CC	136/494	1.00	1.00	1.00	1.00
CT	95/366	0.94(0.70,1.27)	0.94(0.72,1.22)	1.18(0.84,1.66)	1.10(0.81,1.48)
TT	27/66	1.49(0.91,2.42)	1.31(0.87,1.95)	***1.98(1.15,3.42)***	1.51(0.98,2.33)
Log-additive		1.10(0.89,1.37)	1.09(0.89,1.34)	***1.32(1.04,1.69)***	***1.28(1.02,1.61)***
Dominant	122/432	1.03(0.78,1.35)	1.02(0.79,1.32)	1.30(0.94,1.79)	1.24(0.93,1.66)
Recessive	27/66	1.52(0.95,2.44)	1.33(0.90,1.98)	***1.84(1.09,3.09)***	1.47(0.96,2.25)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.10 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung LCL

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
RAN rs14035					
CC	38/463	1.00	1.00	1.00	1.00
CT	45/366	1.50(0.95,2.36)	1.29(0.89,1.86)	***1.91(1.12,3.28)***	1.47(0.97,2.22)
TT	12/92	1.59(0.80,3.16)	1.22(0.75,2.01)	1.46(0.65,3.29)	1.11(0.66,1.88)
Log-additive		1.32(0.97,1.80)	1.26(0.95,1.67)	1.36(0.96,1.94)	1.28(0.93,1.75)
Dominant	57/458	1.52(0.99,2.33)	1.35(0.94,1.94)	***1.80(1.08,3.01)***	1.47(0.98,2.21)
Recessive	12/92	1.30(0.69,2.48)	1.15(0.71,1.86)	1.05(0.49,2.25)	1.02(0.61,1.71)

*Adjusted for age, gender, ethnicity, smoking as pack-years, and education level as high school, college and beyond college.

Table 1.1.11. Multiplicative interactions between selected SNPs and smoking status in lung cancer

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**	
	Cases/Controls	Adjusted* OR (95% CI)	Cases/Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Micro RNA processing and maturation						
XPO5 rs11077						
AA	43/159	1.00	150/146	1.00		
AC	32/218	0.89(0.49,1.59)	199/261	***0.69(0.48,0.99)***		
CC	17/62	1.84(0.87,3.90)	89/84	1.09(0.68,1.75)		
Missing	18/52		63/58			
Log-additive		1.27(0.86,1.86)		0.99(0.78,1.24)		
Dominant	49/280	1.07(0.62,1.85)	288/345	0.77(0.55,1.09)	0.84(0.46,1.52)	0.56
Recessive	17/62	***1.98(1.01,3.86)***	89/84	1.39(0.92,2.10)	0.88(0.42,1.85)	0.74
RAN rs14035						
CC	41/223	1.00	203/240	1.00		
CT	44/169	***1.75(1.04,2.95)***	189/197	1.33(0.95,1.85)		
TT	6/43	0.88(0.33,2.33)	42/49	0.96(0.56,1.64)		
Missing	19/56		67/63			
Log-additive		1.20(0.83,1.74)		1.09(0.86,1.38)		
Dominant	50/212	1.56(0.95,2.59)	231/246	1.24(0.91,1.70)	0.87(0.49,1.55)	0.64
Recessive	6/43	0.67(0.26,1.71)	42/49	0.84(0.51,1.40)	1.39(0.48,3.98)	0.55
DICER1 rs3742330						
AA	60/341	1.00	362/376	1.00		
AG	26/91	0.99(0.55,1.79)	73/109	0.77(0.52,1.14)		
GG	7/5	3.00(0.81,11.07)	6/7	1.10(0.29,4.16)		
Missing	17/54		60/57			
Log-additive		1.26(0.79,2.01)		0.83(0.58,1.18)		
Dominant	33/96	1.13(0.64,1.97)	79/116	0.79(0.53,1.16)	0.58(0.31,1.11)	0.10
Recessive	7/5	3.01(0.83,10.86)	6/7	1.20(0.32,4.48)	0.29(0.05,1.78)	0.18
AGO2 rs4961280						
CC	63/282	1.00	302/312	1.00		
CA	22/128	0.67(0.38,1.20)	119/151	1.03(0.73,1.45)		

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**	
	Cases/Controls	Adjusted* OR (95% CI)	Cases/Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	6/25	0.79(0.28,2.21)	9/22	0.77(0.30,1.99)		
Missing	19/56		71/64			
Log-additive		0.79(0.51,1.20)		0.97(0.73,1.31)		
Dominant	28/153	0.69(0.40,1.19)	128/173	1.00(0.72,1.40)	1.23(0.67,2.27)	0.51
Recessive	6/25	0.91(0.33,2.49)	9/22	0.76(0.30,1.96)	0.68(0.18,2.58)	0.57
GEMIN3 rs197412						
TT	35/136	1.00	140/171	1.00		
TC	42/223	0.58(0.34,1.01)	210/211	1.26(0.88,1.80)		
CC	16/79	0.57(0.27,1.18)	85/101	0.87(0.55,1.38)		
Missing	17/53		66/66			
Log-additive		0.72(0.50,1.03)		0.97(0.77,1.22)		
Dominant	58/302	***0.58(0.34,0.97)***	295/312	1.14(0.81,1.60)	1.68(0.93,3.06)	0.09
Recessive	16/79	0.78(0.41,1.51)	85/101	0.75(0.50,1.13)	1.01(0.48,2.11)	0.99
GEMIN4 rs7813						
CC	43/164	1.00	199/214	1.00		
CT	34/192	0.78(0.45,1.34)	167/208	0.92(0.65,1.30)		
TT	13/74	0.86(0.41,1.80)	58/60	0.89(0.54,1.46)		
Missing	20/61		77/67			
Log-additive		0.89(0.62,1.27)		0.94(0.74,1.18)		
Dominant	47/266	0.80(0.48,1.33)	225/268	0.91(0.66,1.26)	1.08(0.60,1.93)	0.80
Recessive	13/74	0.97(0.49,1.95)	58/60	0.93(0.58,1.48)	0.95(0.42,2.15)	0.89
GEMIN4 rs2740348						
CC	70/285	1.00	312/355	1.00		
CG	18/134	0.58(0.32,1.05)	104/116	0.93(0.64,1.35)		
GG	1/15	0.21(0.03,1.69)	11/13	0.57(0.22,1.50)		
Missing	21/57		74/65			
Log-additive		***0.54(0.32,0.92)***		0.87(0.64,1.18)		
Dominant	19/149	***0.53(0.29,0.95)***	115/129	0.89(0.62,1.27)	1.43(0.73,2.79)	0.30
Recessive	1/15	0.25(0.03,1.99)	11/13	0.58(0.22,1.52)	1.59(0.16,15.48)	0.69
miRNA downstream						
CDK6 rs42031						

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**	
	Cases/Controls	Adjusted* OR (95% CI)	Cases/Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	70/310	1.00	310/346	1.00		
AT	20/119	1.08(0.60,1.96)	107/122	1.09(0.75,1.57)		
TT	2/6	3.58(0.61,21.06)	14/21	0.58(0.24,1.38)		
Missing	18/56		70/60			
Log-additive		1.24(0.73,2.11)		0.94(0.70,1.26)		
Dominant	22/125	1.16(0.66,2.06)	121/143	1.01(0.71,1.43)	0.99(0.52,1.89)	0.97
Recessive	2/6	3.50(0.60,20.33)	14/21	0.57(0.24,1.34)	0.21(0.03,1.39)	0.11
TP53INP1 rs896849						
TT	66/319	1.00	280/347	1.00		
TC	27/106	1.45(0.82,2.55)	133/126	1.07(0.75,1.53)		
CC	2/13	1.24(0.25,6.17)	25/18	1.47(0.69,3.13)		
Missing	15/53		63/58			
Log-additive		1.33(0.82,2.15)		1.13(0.85,1.50)		
Dominant	29/119	1.43(0.82,2.49)	158/144	1.11(0.79,1.57)	0.98(0.53,1.81)	0.95
Recessive	2/13	1.06(0.22,5.19)	25/18	1.43(0.68,3.01)	1.88(0.34,10.42)	0.47
CXCL12 rs1804429						
TT	79/409	1.00	406/449	1.00		
TG	13/28	1.81(0.82,3.97)	31/45	0.79(0.44,1.40)		
GG	0/1		3/0			
Missing	18/53		61/55			
Log-additive		1.62(0.77,3.41)		0.93(0.55,1.56)		
Dominant	13/29	1.74(0.80,3.78)	34/45	0.85(0.49,1.49)	0.42(0.16,1.08)	0.07
Recessive	0/1		3/0			
E2F2 rs2075993						
GG	27/144	1.00	157/147	1.00		
GA	41/202	1.25(0.70,2.24)	189/253	***0.68(0.47,0.98)***		
AA	26/90	1.59(0.81,3.12)	91/89	0.94(0.59,1.49)		
Missing	16/55		64/60			
Log-additive		1.26(0.90,1.77)		0.94(0.75,1.19)		
Dominant	67/292	1.35(0.79,2.33)	280/342	0.74(0.52,1.05)	0.55(0.30,1.01)	0.05
Recessive	26/90	1.39(0.78,2.47)	91/89	1.22(0.82,1.80)	0.82(0.42,1.61)	0.56

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**	
	Cases/Controls	Adjusted* OR (95% CI)	Cases/Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
DOCK4 rs3801790						
AA	37/180	1.00	196/196	1.00		
AG	41/193	0.96(0.56,1.65)	196/234	1.05(0.75,1.46)		
GG	16/66	0.73(0.35,1.52)	46/60	0.96(0.57,1.62)		
Missing	16/52		63/59			
Log-additive		0.88(0.62,1.24)		1.00(0.79,1.27)		
Dominant	57/259	0.90(0.54,1.48)	242/294	1.03(0.75,1.41)	1.00(0.56,1.79)	0.99
Recessive	16/66	0.75(0.38,1.46)	46/60	0.93(0.57,1.53)	0.95(0.42,2.14)	0.91
IL6R rs4072391						
CC	66/272	1.00	268/321	1.00		
CT	26/140	0.78(0.45,1.35)	149/139	1.29(0.92,1.81)		
TT	0/22	0.06(0.003,0.98)	20/27	1.12(0.54,2.33)		
Missing	18/57		64/62			
Log-additive		***0.55(0.34,0.89)***		1.18(0.90,1.54)		
Dominant	26/162	0.61(0.36,1.06)	169/166	1.27(0.92,1.75)	***2.10(1.14,3.89)***	***0.02***
Recessive	0/22	0.06(0.003,1.06)	20/27	1.03(0.50,2.12)	-	-
HIF1A						
HIF1A rs2057482						
CC	66/317	1.00	288/355	1.00		
CT	19/115	0.78(0.42,1.43)	131/119	1.25(0.88,1.79)		
TT	9/8	8.96(2.86,28.11)	17/15	1.18(0.51,2.75)		
Missing	16/51		65/60			
Log-additive		1.50(0.96,2.35)		1.18(0.89,1.58)		
Dominant	28/123	1.12(0.65,1.93)	148/134	1.25(0.88,1.75)	1.27(0.68,2.37)	0.44
Recessive	9/8	9.60(3.10,29.74)	17/15	1.10(0.48,2.54)	***0.17(0.04,0.67)***	***0.01***
HIF1A rs2301113						
AA	41/233	1.00	197/234	1.00		
AC	32/148	1.11(0.64,1.93)	158/162	1.08(0.76,1.54)		
CC	17/36	***3.19(1.36,7.47)***	65/64	0.84(0.49,1.42)		
Missing	20/74		81/89			
Log-additive		***1.52(1.04,2.24)***		0.96(0.75,1.23)		

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**	
	Cases/Controls	Adjusted* OR (95% CI)	Cases/Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Dominant	49/184	1.37(0.82,2.29)	223/226	1.03(0.73,1.44)	0.83(0.46,1.49)	0.53
Recessive	17/36	***3.04(1.34,6.86)***	65/64	0.80(0.49,1.31)	0.48(0.21,1.08)	0.08
miRNAs						
MIR-26A1 rs7372209						
CC	49/226	1.00	238/268	1.00		
CT	35/181	0.73(0.42,1.26)	162/185	1.31(0.93,1.85)		
TT	10/30	1.13(0.47,2.69)	37/36	***1.84(1.02,3.32)***		
Missing	16/54		64/60			
Log-additive		0.92(0.62,1.38)		***1.34(1.04,1.72)***		
Dominant	45/211	0.79(0.47,1.32)	199/221	***1.39(1.01,1.93)***	1.32(0.75,2.33)	0.34
Recessive	10/30	1.33(0.58,3.03)	37/36	1.63(0.92,2.88)	1.01(0.38,2.67)	0.98
MIR-27 rs895819						
TT	40/189	1.00	207/224	1.00		
TC	37/205	1.02(0.60,1.74)	170/206	0.90(0.64,1.25)		
CC	8/37	1.04(0.41,2.60)	49/49	0.99(0.58,1.68)		
Missing	25/60		75/70			
Log-additive		1.02(0.69,1.51)		0.96(0.76,1.21)		
Dominant	45/242	1.02(0.61,1.70)	219/255	0.91(0.67,1.25)	0.98(0.55,1.77)	0.96
Recessive	8/37	1.03(0.43,2.47)	49/49	1.04(0.63,1.73)	1.11(0.41,2.99)	0.84

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, and smoking as pack-years, if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and smoking was dichotomized as nonsmoking vs smoking.

Table 1.1.12. Semi-Bayesian shrinkage of multiplicative interactions between selected SNPs and smoking status in lung cancer

SNP	Nonsmokers		Smokers		SNP-Smoking product terms**		Bayesian Shrinkage for product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity	Adjusted* OR (95% posterior limits)	P-value* for heterogeneity
miRNA downstream								
IL6R								
rs4072391								
CC	66/272	1.00	268/321	1.00				
CT+TT	26/162	0.61(0.36,1.06)	169/166	1.27(0.92,1.75)	***2.10(1.14,3.89)***	***0.02***	1.52(0.96,2.40)	0.07
HIF1A								
HIF1A								
rs2057482								
CC+CT	85/432	1.00	288/355	1.00				
TT	9/8	9.60(3.10,29.74)	17/15	1.10(0.48,2.54)	***0.17(0.04,0.67)***	***0.01***	0.70(0.38,1.31)	0.27

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, and smoking as pack-years, if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and smoking was dichotomized as nonsmoking vs smoking.

Section II

Table 1.2.1 Crude and adjusted associations between selected SNPs and UADT cancers

SNP	Cases* (%)	Controls* (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)
Micro RNA processing and maturation				
XPO5 rs11077				
AA	184(40.2)	305(32.8)	1.00	1.00
AC	192(41.9)	479(51.5)	***0.66(0.52,0.85)***	***0.66(0.50,0.87)***
CC	82(17.9)	146(15.7)	0.93(0.67,1.29)	0.93(0.64,1.34)
Missing	143(24)	110(10)		
Log-additive			0.90(0.76,1.06)	0.90(0.75,1.08)
Dominant	274(59.8)	625(67.2)	***0.73(0.58,0.92)***	***0.72(0.55,0.93)***
Recessive	82(17.9)	146(15.7)	1.17(0.87,1.58)	1.19(0.86,1.66)
RAN rs14035				
CC	218(47.8)	463(50.3)	1.00	1.00
CT	191(41.9)	366(39.7)	1.11(0.87,1.41)	1.11(0.85,1.44)
TT	47(10.3)	92(10.0)	1.09(0.74,1.60)	1.20(0.79,1.83)
Missing	145(24)	119(11)		
Log-additive			1.06(0.90,1.26)	1.10(0.91,1.32)
Dominant	238(52.2)	458(49.7)	1.10(0.88,1.38)	1.13(0.88,1.44)
Recessive	47(10.3)	92(10.0)	1.04(0.72,1.50)	1.14(0.76,1.72)
DICER1 rs3742330				
AA	367(79.4)	717(77.2)	1.00	1.00
AG	91(19.7)	200(21.5)	0.89(0.67,1.17)	0.76(0.55,1.05)
GG	4(0.9)	12(1.3)	0.65(0.21,2.03)	0.36(0.10,1.31)
Missing	139(23)	111(11)		
Log-additive			0.87(0.68,1.12)	***0.73(0.54,0.98)***
Dominant	95(20.6)	212(22.8)	0.88(0.67,1.15)	0.74(0.54,1.01)
Recessive	4(0.9)	12(1.3)	0.67(0.21,2.08)	0.40(0.11,1.45)
AGO2 rs4961280				
CC	307(67.2)	594(64.6)	1.00	1.00

SNP	Cases* (%)	Controls* (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)
CA	136(29.8)	279(30.3)	0.94(0.74,1.21)	1.05(0.80,1.38)
AA	14(3.1)	47(5.1)	0.58(0.31,1.06)	0.68(0.35,1.31)
Missing	144(24)	120(12)		
Log-additive			0.86(0.71,1.06)	0.95(0.76,1.18)
Dominant	150(32.8)	326(35.4)	0.89(0.70,1.13)	1.00(0.76,1.30)
Recessive	14(3.1)	47(5.1)	0.59(0.32,1.08)	0.67(0.35,1.28)
GEMIN3 rs197412				
TT	139(30.1)	307(33.3)	1.00	1.00
TC	218(47.2)	434(47.1)	1.11(0.86,1.44)	1.15(0.87,1.53)
CC	105(22.7)	180(19.5)	1.29(0.94,1.76)	1.29(0.90,1.83)
Missing	139(23)	119(11)		
Log-additive			1.13(0.97,1.32)	1.13(0.95,1.35)
Dominant	323(69.9)	614(66.7)	1.16(0.91,1.48)	1.19(0.91,1.55)
Recessive	105(22.7)	180(19.5)	1.21(0.92,1.59)	1.18(0.87,1.60)
GEMIN4 rs7813				
CC	193(42.5)	378(41.5)	1.00	1.00
CT	198(43.6)	400(43.9)	0.97(0.76,1.24)	1.02(0.78,1.33)
TT	63(13.9)	134(14.7)	0.92(0.65,1.30)	1.03(0.71,1.52)
Missing	147(24)	128(12)		
Log-additive			0.96(0.82,1.13)	1.02(0.85,1.22)
Dominant	261(57.5)	534(58.6)	0.96(0.76,1.20)	1.02(0.79,1.32)
Recessive	63(13.9)	134(14.7)	0.94(0.68,1.29)	1.02(0.72,1.46)
GEMIN4 rs2740348				
CC	336(73.9)	640(69.7)	1.00	1.00
CG	109(24.0)	250(27.2)	0.83(0.64,1.08)	0.83(0.62,1.10)
GG	10(2.2)	28(3.1)	0.68(0.33,1.42)	0.62(0.28,1.39)
Missing	146(24)	122(12)		
Log-additive			0.83(0.66,1.03)	0.81(0.64,1.04)
Dominant	119(26.2)	278(30.3)	0.82(0.63,1.05)	0.80(0.61,1.06)
Recessive	10(2.2)	28(3.1)	0.71(0.34,1.48)	0.66(0.30,1.46)
miRNA downstream				
CDK6 rs42031				

SNP	Cases* (%)	Controls* (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)
AA	326(70.7)	656(71.0)	1.00	1.00
AT	120(26.0)	241(26.1)	1.00(0.78,1.29)	1.09(0.82,1.45)
TT	15(3.3)	27(2.9)	1.12(0.59,2.13)	1.01(0.50,2.02)
Missing	140(23)	116(11)		
Log-additive			1.02(0.83,1.26)	1.06(0.84,1.33)
Dominant	135(29.3)	268(29.0)	1.01(0.79,1.30)	1.08(0.82,1.42)
Recessive	15(3.3)	27(2.9)	1.12(0.59,2.12)	0.98(0.49,1.95)
TP53INP1 rs896849				
TT	304(65.7)	666(71.7)	1.00	1.00
TC	132(28.5)	232(25.0)	1.25(0.97,1.61)	1.29(0.98,1.71)
CC	27(5.8)	31(3.3)	***1.91(1.12,3.25)***	***1.93(1.06,3.51)***
Missing	138(23)	111(11)		
Log-additive			***1.31(1.08,1.59)***	***1.34(1.07,1.67)***
Dominant	159(34.3)	263(28.3)	***1.32(1.04,1.68)***	***1.36(1.04,1.78)***
Recessive	27(5.8)	31(3.3)	***1.79(1.06,3.04)***	1.76(0.98,3.18)
CXCL12 rs1804429				
TT	422(91.3)	858(92.1)	1.00	1.00
TG	39(8.4)	73(7.8)	1.09(0.72,1.63)	0.77(0.49,1.21)
GG	1(0.2)	1(0.1)	2.03(0.13,32.58)	3.92(0.24,64.33)
Missing	139(23)	108(10)		
Log-additive			1.11(0.75,1.64)	0.83(0.54,1.28)
Dominant	40(8.7)	74(7.9)	1.10(0.74,1.64)	0.80(0.51,1.24)
Recessive	1(0.2)	1(0.1)	2.02(0.13,32.36)	4.02(0.25,65.81)
E2F2 rs2075993				
GG	151(32.9)	291(31.5)	1.00	1.00
GA	214(46.6)	455(49.2)	0.91(0.70,1.17)	0.89(0.67,1.19)
AA	94(20.5)	179(19.4)	1.01(0.74,1.39)	1.03(0.72,1.48)
Missing	142(24)	115(11)		
Log-additive			0.99(0.85,1.16)	1.00(0.84,1.20)
Dominant	308(67.1)	634(68.5)	0.94(0.74,1.19)	0.93(0.70,1.22)
Recessive	94(20.5)	179(19.4)	1.07(0.81,1.42)	1.11(0.82,1.52)
DOCK4 rs3801790				
AA	187(40.3)	376(40.5)	1.00	1.00

SNP	Cases* (%)	Controls* (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)
AG	208(44.8)	427(46.0)	0.98(0.77,1.25)	0.98(0.75,1.28)
GG	69(14.9)	126(13.6)	1.10(0.78,1.55)	1.07(0.73,1.57)
Missing	137(23)	111(11)		
Log-additive			1.03(0.88,1.21)	1.02(0.85,1.22)
Dominant	277(59.7)	553(59.5)	1.01(0.80,1.26)	1.00(0.78,1.28)
Recessive	69(14.9)	126(13.6)	1.11(0.81,1.53)	1.08(0.76,1.54)
IL6R rs4072391				
CC	273(60.1)	593(64.4)	1.00	1.00
CT	152(33.5)	279(30.3)	1.18(0.93,1.51)	1.16(0.89,1.51)
TT	29(6.4)	49(5.3)	1.29(0.80,2.08)	1.34(0.79,2.26)
Missing	147(24)	119(11)		
Log-additive			1.16(0.96,1.39)	1.16(0.94,1.42)
Dominant	181(39.9)	328(35.6)	1.20(0.95,1.51)	1.18(0.92,1.53)
Recessive	29(6.4)	49(5.3)	1.21(0.76,1.95)	1.27(0.76,2.13)
HIF1A				
HIF1A rs2057482				
CC	321(70.2)	672(72.3)	1.00	1.00
CT	121(26.5)	234(25.2)	1.08(0.84,1.40)	1.15(0.87,1.53)
TT	15(3.3)	23(2.5)	1.37(0.70,2.65)	1.20(0.57,2.52)
Missing	144(24)	111(11)		
Log-additive			1.11(0.90,1.38)	1.13(0.89,1.43)
Dominant	136(29.8)	257(27.7)	1.11(0.87,1.42)	1.16(0.88,1.52)
Recessive	15(3.3)	23(2.5)	1.34(0.69,2.59)	1.15(0.55,2.40)
HIF1A rs2301113				
AA	219(50.2)	467(53.3)	1.00	1.00
AC	152(34.9)	310(35.4)	1.05(0.81,1.35)	1.00(0.76,1.32)
CC	65(14.9)	100(11.4)	1.39(0.98,1.97)	1.30(0.85,2.00)
Missing	165(27)	163(16)		
Log-additive			1.14(0.97,1.34)	1.09(0.90,1.33)
Dominant	217(49.8)	410(46.8)	1.13(0.90,1.42)	1.06(0.81,1.37)
Recessive	65(14.9)	100(11.4)	1.36(0.97,1.91)	1.30(0.87,1.96)
miRNAs				
MIR-26A1				

SNP	Cases* (%)	Controls* (%)	Crude OR (95% CI)	Adjusted** OR (95% CI)
rs7372209				
CC	258(56.2)	494(53.4)	1.00	1.00
CT	164(35.7)	366(39.5)	0.86(0.68,1.09)	0.89(0.68,1.16)
TT	37(8.1)	66(7.1)	1.07(0.70,1.65)	1.11(0.69,1.78)
Missing	142(24)	114(11)		
Log-additive			0.95(0.80,1.14)	0.98(0.80,1.19)
Dominant	201(43.8)	432(46.7)	0.89(0.71,1.12)	0.92(0.72,1.19)
Recessive	37(8.1)	66(7.1)	1.14(0.75,1.74)	1.17(0.74,1.84)
MIR-27 rs895819				
TT	193(42.6)	413(45.4)	1.00	1.00
TC	204(45.0)	411(45.2)	1.06(0.84,1.35)	1.04(0.80,1.35)
CC	56(12.4)	86(9.5)	1.39(0.96,2.03)	1.36(0.90,2.07)
Missing	148(25)	130(12)		
Log-additive			1.14(0.96,1.35)	1.12(0.93,1.36)
Dominant	260(57.4)	497(54.6)	1.12(0.89,1.41)	1.09(0.85,1.41)
Recessive	56(12.4)	86(9.5)	1.35(0.95,1.93)	1.34(0.90,1.98)

*The proportions of genotypes were among nonmissing only.

**Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.2a Crude and adjusted associations between selected SNPs and UADT SQC, both in the overall population and in the Caucasians

SNP	Overall			Caucasians		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	142/305	1.00	1.00	79/192	1.00	1.00
AC	154/479	***0.69(0.53,0.90)***	***0.63(0.47,0.86)***	95/308	0.75(0.53,1.06)	***0.67(0.46,0.97)***
CC	72/146	1.06(0.75,1.50)	0.97(0.66,1.44)	36/78	1.12(0.70,1.80)	1.04(0.62,1.72)
Missing	129/110			70/56		
Log-additive		0.96(0.81,1.14)	0.92(0.76,1.12)		0.98(0.78,1.24)	0.93(0.72,1.20)
Dominant	226/625	***0.78(0.60,1.00)***	***0.71(0.53,0.95)***	131/386	0.82(0.59,1.15)	0.74(0.52,1.06)
Recessive	72/146	1.31(0.96,1.79)	1.29(0.91,1.82)	36/78	1.33(0.86,2.04)	1.30(0.82,2.07)
RAN rs14035						
CC	180/463	1.00	1.00	108/271	1.00	1.00
CT	147/366	1.03(0.80,1.34)	1.02(0.77,1.36)	84/251	0.84(0.60,1.17)	0.79(0.55,1.12)
TT	39/92	1.09(0.72,1.65)	1.20(0.76,1.88)	17/51	0.84(0.46,1.51)	1.05(0.56,1.99)
Missing	131/119			71/61		
Log-additive		1.04(0.87,1.25)	1.07(0.88,1.30)		0.88(0.69,1.13)	0.91(0.69,1.20)
Dominant	186/458	1.04(0.82,1.33)	1.06(0.81,1.38)	101/302	0.84(0.61,1.15)	0.82(0.59,1.16)
Recessive	39/92	1.07(0.72,1.60)	1.18(0.77,1.83)	17/51	0.91(0.51,1.61)	1.18(0.64,2.18)
DICER1 rs3742330						
AA	297/717	1.00	1.00	185/466	1.00	1.00
AG	71/200	0.86(0.63,1.16)	0.76(0.54,1.08)	30/106	0.71(0.46,1.11)	0.70(0.43,1.12)
GG	4/12	0.80(0.26,2.52)	0.51(0.14,1.85)	1/5	0.50(0.06,4.34)	0.37(0.03,4.06)
Missing	125/111			64/57		
Log-additive		0.87(0.66,1.14)	0.75(0.55,1.03)		0.71(0.47,1.08)	0.68(0.44,1.07)
Dominant	75/212	0.85(0.64,1.15)	0.75(0.53,1.05)	31/111	0.70(0.46,1.08)	0.68(0.43,1.09)
Recessive	4/12	0.83(0.27,2.59)	0.56(0.16,2.04)	1/5	0.53(0.06,4.58)	0.40(0.04,4.36)
AGO2 rs4961280						
CC	253/594	1.00	1.00	149/379	1.00	1.00

SNP	Overall			Caucasians		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
CA	104/279	0.88(0.67,1.15)	0.99(0.73,1.33)	56/169	0.84(0.59,1.20)	0.88(0.60,1.29)
AA	10/47	0.50(0.25,1.00)	0.65(0.31,1.36)	6/24	0.64(0.25,1.59)	0.74(0.28,1.96)
Missing	130/120			69/62		
Log-additive		0.81(0.65,1.01)	0.91(0.71,1.16)		0.83(0.62,1.11)	0.87(0.63,1.19)
Dominant	114/326	0.82(0.63,1.06)	0.94(0.71,1.26)	62/193	0.82(0.58,1.15)	0.86(0.59,1.24)
Recessive	10/47	0.52(0.26,1.04)	0.65(0.31,1.36)	6/24	0.67(0.27,1.66)	0.77(0.29,2.02)
GEMIN3 rs197412						
TT	108/307	1.00	1.00	74/220	1.00	1.00
TC	174/434	1.14(0.86,1.51)	1.13(0.83,1.55)	99/263	1.12(0.79,1.59)	1.19(0.82,1.74)
CC	90/180	***1.42(1.02,1.99)***	1.33(0.91,1.94)	42/89	1.40(0.89,2.20)	1.38(0.85,2.26)
Missing	125/119			65/62		
Log-additive		***1.19(1.01,1.41)***	1.15(0.95,1.39)		1.17(0.94,1.46)	1.18(0.93,1.50)
Dominant	264/614	1.22(0.94,1.59)	1.19(0.89,1.59)	141/352	1.19(0.86,1.65)	1.24(0.87,1.77)
Recessive	90/180	1.31(0.99,1.75)	1.23(0.89,1.70)	42/89	1.32(0.88,1.98)	1.26(0.81,1.95)
GEMIN4 rs7813						
CC	157/378	1.00	1.00	79/202	1.00	1.00
CT	156/400	0.94(0.72,1.22)	1.01(0.75,1.35)	91/270	0.86(0.61,1.23)	0.85(0.58,1.24)
TT	51/134	0.92(0.63,1.33)	1.03(0.68,1.56)	39/97	1.03(0.65,1.62)	1.03(0.63,1.68)
Missing	133/128			71/65		
Log-additive		0.95(0.80,1.13)	1.01(0.83,1.23)		0.99(0.79,1.23)	0.98(0.77,1.25)
Dominant	207/534	0.93(0.73,1.19)	1.01(0.77,1.33)	130/367	0.91(0.65,1.26)	0.89(0.63,1.27)
Recessive	51/134	0.95(0.67,1.34)	1.03(0.70,1.50)	39/97	1.12(0.74,1.68)	1.13(0.73,1.76)
GEMIN4 rs2740348						
CC	276/640	1.00	1.00	152/390	1.00	1.00
CG	82/250	0.76(0.57,1.01)	0.74(0.54,1.01)	51/166	0.79(0.55,1.14)	0.72(0.48,1.07)
GG	7/28	0.58(0.25,1.34)	0.53(0.21,1.33)	5/15	0.86(0.31,2.39)	0.55(0.18,1.67)
Missing	132/122			72/63		
Log-additive		***0.76(0.60,0.97)***	***0.73(0.56,0.96)***		0.83(0.60,1.13)	0.72(0.52,1.02)
Dominant	89/278	***0.74(0.56,0.98)***	***0.71(0.53,0.97)***	56/181	0.79(0.56,1.13)	0.70(0.48,1.03)
Recessive	7/28	0.62(0.27,1.44)	0.58(0.23,1.44)	5/15	0.91(0.33,2.54)	0.60(0.20,1.82)
miRNA downstream						

SNP	Overall			Caucasians		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
CDK6 rs42031						
AA	268/656	1.00	1.00	141/371	1.00	1.00
AT	92/241	0.93(0.71,1.24)	1.02(0.75,1.39)	63/180	0.92(0.65,1.30)	0.95(0.66,1.38)
TT	11/27	1.00(0.49,2.04)	0.89(0.41,1.92)	10/23	1.14(0.53,2.46)	0.94(0.41,2.12)
Missing	126/116			66/60		
Log-additive		0.96(0.76,1.21)	0.99(0.77,1.27)		0.98(0.74,1.30)	0.96(0.71,1.29)
Dominant	103/268	0.94(0.72,1.23)	1.00(0.75,1.35)	73/203	0.95(0.68,1.32)	0.95(0.67,1.36)
Recessive	11/27	1.02(0.50,2.07)	0.88(0.41,1.90)	10/23	1.17(0.55,2.51)	0.95(0.42,2.13)
TP53INP1 rs896849						
TT	241/666	1.00	1.00	142/418	1.00	1.00
TC	108/232	1.29(0.98,1.69)	1.28(0.95,1.72)	64/139	1.36(0.95,1.93)	1.37(0.94,2.00)
CC	24/31	***2.14(1.23,3.72)***	***1.91(1.02,3.58)***	9/20	1.32(0.59,2.98)	1.38(0.57,3.30)
Missing	124/111			65/57		
Log-additive		***1.37(1.11,1.69)***	***1.33(1.05,1.68)***		1.26(0.96,1.67)	1.28(0.95,1.73)
Dominant	132/263	***1.39(1.07,1.79)***	***1.35(1.01,1.79)***	73/159	1.35(0.97,1.89)	1.37(0.95,1.97)
Recessive	24/31	***1.99(1.15,3.44)***	1.75(0.94,3.25)	9/20	1.22(0.55,2.72)	1.26(0.53,3.00)
CXCL12 rs1804429						
TT	342/858	1.00	1.00	203/548	1.00	1.00
TG	31/73	1.07(0.69,1.65)	0.76(0.47,1.23)	11/32	0.93(0.46,1.88)	0.54(0.25,1.18)
GG	0/1			0/0		
Missing	124/108			66/54		
Log-additive		1.04(0.67,1.60)	0.75(0.46,1.21)		0.93(0.46,1.88)	0.54(0.25,1.18)
Dominant	31/74	1.05(0.68,1.63)	0.75(0.46,1.22)	11/32	0.93(0.46,1.88)	0.54(0.25,1.18)
Recessive	0/1			0/0		
E2F2 rs2075993						
GG	126/291	1.00	1.00	50/142	1.00	1.00
GA	177/455	0.90(0.68,1.18)	0.93(0.68,1.27)	119/311	1.09(0.74,1.60)	1.04(0.68,1.58)
AA	66/179	0.85(0.60,1.21)	0.92(0.61,1.37)	43/123	0.99(0.62,1.59)	0.99(0.60,1.65)
Missing	128/115			68/58		
Log-additive		0.92(0.77,1.09)	0.95(0.78,1.17)		1.00(0.79,1.26)	1.00(0.77,1.29)
Dominant	243/634	0.89(0.69,1.14)	0.93(0.69,1.25)	162/434	1.06(0.73,1.53)	1.03(0.69,1.53)

SNP	Overall			Caucasians		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Recessive	66/179	0.91(0.66,1.24)	0.96(0.68,1.36)	43/123	0.94(0.63,1.38)	0.97(0.64,1.47)
DOCK4 rs3801790						
AA	157/376	1.00	1.00	100/253	1.00	1.00
AG	159/427	0.89(0.69,1.16)	0.93(0.70,1.24)	88/266	0.84(0.60,1.17)	0.85(0.59,1.22)
GG	58/126	1.10(0.77,1.58)	1.12(0.75,1.68)	28/58	1.22(0.74,2.03)	1.16(0.67,2.00)
Missing	123/111			64/57		
Log-additive		1.01(0.85,1.20)	1.03(0.85,1.24)		1.01(0.80,1.28)	1.00(0.77,1.28)
Dominant	217/553	0.94(0.74,1.20)	0.97(0.74,1.27)	116/324	0.91(0.66,1.24)	0.91(0.65,1.27)
Recessive	58/126	1.17(0.83,1.64)	1.17(0.80,1.69)	28/58	1.33(0.82,2.16)	1.25(0.74,2.11)
IL6R rs4072391						
CC	218/593	1.00	1.00	129/377	1.00	1.00
CT	123/279	1.20(0.92,1.56)	1.14(0.85,1.52)	68/177	1.12(0.80,1.58)	1.15(0.79,1.66)
TT	23/49	1.28(0.76,2.15)	1.26(0.71,2.22)	12/19	1.85(0.87,3.91)	1.73(0.77,3.89)
Missing	133/119			71/61		
Log-additive		1.16(0.95,1.42)	1.13(0.91,1.41)		1.22(0.93,1.61)	1.22(0.91,1.63)
Dominant	146/328	1.21(0.94,1.55)	1.16(0.88,1.52)	80/196	1.19(0.86,1.66)	1.21(0.85,1.72)
Recessive	23/49	1.20(0.72,2.00)	1.20(0.69,2.10)	12/19	1.78(0.85,3.73)	1.65(0.74,3.68)
HIF1A						
HIF1A rs2057482						
CC	255/672	1.00	1.00	149/428	1.00	1.00
CT	100/234	1.13(0.86,1.48)	1.17(0.87,1.59)	54/135	1.15(0.80,1.66)	1.23(0.83,1.83)
TT	12/23	1.37(0.67,2.80)	1.14(0.51,2.52)	6/15	1.15(0.44,3.02)	1.09(0.38,3.14)
Missing	130/111			71/56		
Log-additive		1.14(0.91,1.44)	1.13(0.88,1.46)		1.12(0.83,1.52)	1.16(0.84,1.61)
Dominant	112/257	1.15(0.88,1.50)	1.17(0.87,1.57)	60/150	1.15(0.81,1.63)	1.22(0.83,1.78)
Recessive	12/23	1.33(0.66,2.70)	1.09(0.49,2.40)	6/15	1.11(0.42,2.90)	1.04(0.36,2.98)
HIF1A rs2301113						
AA	174/467	1.00	1.00	116/325	1.00	1.00
AC	117/310	1.01(0.77,1.33)	0.95(0.70,1.28)	64/186	0.96(0.68,1.37)	0.95(0.65,1.40)
CC	58/100	***1.56(1.08,2.25)***	1.34(0.85,2.11)	19/34	1.57(0.86,2.85)	1.48(0.77,2.86)
Missing	148/163			81/89		

SNP		Overall			Caucasians	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Log-additive		1.19(1.00,1.41)	1.09(0.89,1.34)		1.12(0.87,1.45)	1.10(0.83,1.45)
Dominant	175/410	1.15(0.89,1.47)	1.02(0.77,1.36)	83/220	1.06(0.76,1.47)	1.04(0.73,1.48)
Recessive	58/100	***1.55(1.09,2.20)***	1.38(0.90,2.11)	19/34	1.59(0.88,2.85)	1.51(0.79,2.87)
miRNAs						
MIR-26A1 rs7372209						
CC	210/494	1.00	1.00	109/322	1.00	1.00
CT	132/366	0.85(0.66,1.10)	0.89(0.67,1.19)	87/219	1.17(0.84,1.63)	1.13(0.79,1.61)
TT	28/66	1.00(0.62,1.60)	1.05(0.63,1.76)	16/35	1.35(0.72,2.54)	1.29(0.66,2.55)
Missing	127/114			68/58		
Log-additive		0.93(0.76,1.12)	0.96(0.78,1.20)		1.17(0.91,1.50)	1.13(0.86,1.49)
Dominant	160/432	0.87(0.68,1.11)	0.91(0.70,1.20)	103/254	1.20(0.87,1.64)	1.15(0.82,1.62)
Recessive	28/66	1.07(0.67,1.69)	1.11(0.67,1.82)	16/35	1.26(0.68,2.33)	1.23(0.63,2.38)
MIR-27 rs895819						
TT	151/413	1.00	1.00	95/256	1.00	1.00
TC	166/411	1.10(0.85,1.43)	1.10(0.83,1.46)	96/267	0.97(0.70,1.35)	1.04(0.73,1.49)
CC	46/86	1.46(0.98,2.19)	1.38(0.88,2.17)	20/45	1.20(0.67,2.13)	1.29(0.70,2.39)
Missing	134/130			69/66		
Log-additive		1.17(0.98,1.41)	1.15(0.94,1.41)		1.04(0.81,1.34)	1.10(0.84,1.43)
Dominant	212/497	1.17(0.91,1.49)	1.14(0.87,1.50)	116/312	1.00(0.73,1.38)	1.08(0.76,1.52)
Recessive	46/86	1.39(0.95,2.03)	1.32(0.86,2.01)	20/45	1.22(0.70,2.11)	1.27(0.70,2.27)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.2b Crude and adjusted associations between selected SNPs and esophageal ADC

SNP	Esophageal ADC		
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA processing and maturation			
XPO5 rs11077			
AA	29/305	1.00	1.00
AC	29/479	0.64(0.37,1.09)	0.69(0.39,1.20)
CC	9/146	0.65(0.30,1.41)	0.81(0.37,1.78)
Missing	7/110		
Log-additive		0.75(0.52,1.10)	0.83(0.56,1.23)
Dominant	38/625	0.64(0.39,1.06)	0.71(0.42,1.20)
Recessive	9/146	0.83(0.40,1.72)	1.01(0.49,2.09)
RAN rs14035			
CC	27/463	1.00	1.00
CT	35/366	1.64(0.97,2.76)	1.64(0.96,2.81)
TT	5/92	0.93(0.35,2.48)	1.42(0.55,3.67)
Missing	7/119		
Log-additive		1.18(0.82,1.70)	1.33(0.90,1.96)
Dominant	40/458	1.50(0.90,2.48)	1.59(0.94,2.67)
Recessive	5/92	0.73(0.29,1.85)	1.11(0.45,2.75)
DICER1 rs3742330			
AA	55/717	1.00	1.00
AG	12/200	0.78(0.41,1.49)	0.76(0.39,1.47)
GG	0/12		0.30(0.01,7.09)
Missing	7/111		
Log-additive		0.71(0.39,1.32)	0.67(0.36,1.27)
Dominant	12/212	0.74(0.39,1.40)	0.71(0.36,1.37)
Recessive	0/12		0.34(0.01,7.84)
AGO2 rs4961280			
CC	39/594	1.00	1.00
CA	25/279	1.36(0.81,2.30)	1.34(0.78,2.28)
AA	3/47	0.97(0.29,3.26)	1.12(0.34,3.65)

SNP		Esophageal ADC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Missing	7/120		
Log-additive		1.17(0.78,1.76)	1.18(0.77,1.79)
Dominant	28/326	1.31(0.79,2.17)	1.29(0.77,2.16)
Recessive	3/47	0.87(0.26,2.87)	1.01(0.32,3.24)
GEMIN3 rs197412			
TT	22/307	1.00	1.00
TC	34/434	1.09(0.63,1.91)	1.22(0.69,2.16)
CC	11/180	0.85(0.40,1.80)	1.13(0.53,2.40)
Missing	7/119		
Log-additive		0.95(0.67,1.35)	1.08(0.75,1.55)
Dominant	45/614	1.02(0.60,1.73)	1.18(0.69,2.04)
Recessive	11/180	0.81(0.42,1.57)	1.02(0.52,1.98)
GEMIN4 rs7813			
CC	23/378	1.00	1.00
CT	35/400	1.44(0.83,2.48)	1.35(0.77,2.38)
TT	9/134	1.10(0.50,2.45)	1.09(0.49,2.42)
Missing	7/128		
Log-additive		1.13(0.79,1.60)	1.09(0.76,1.57)
Dominant	44/534	1.35(0.80,2.28)	1.27(0.74,2.18)
Recessive	9/134	0.90(0.44,1.86)	0.92(0.44,1.90)
GEMIN4 rs2740348			
CC	46/640	1.00	1.00
CG	19/250	1.06(0.61,1.84)	0.98(0.56,1.72)
GG	2/28	0.99(0.23,4.30)	0.93(0.23,3.71)
Missing	7/122		
Log-additive		1.04(0.65,1.64)	0.95(0.60,1.51)
Dominant	21/278	1.05(0.62,1.79)	0.96(0.55,1.65)
Recessive	2/28	0.98(0.23,4.20)	0.94(0.24,3.72)
miRNA downstream			
CDK6 rs42031			
AA	42/656	1.00	1.00

SNP		Esophageal ADC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AT	22/241	1.43(0.83,2.44)	1.45(0.83,2.53)
TT	3/27	1.74(0.51,5.95)	1.23(0.36,4.24)
Missing	7/116		
Log-additive		1.38(0.90,2.12)	1.25(0.81,1.94)
Dominant	25/268	1.46(0.87,2.44)	1.40(0.82,2.40)
Recessive	3/27	1.56(0.46,5.27)	1.09(0.32,3.68)
TP53INP1 rs896849			
TT	47/666	1.00	1.00
TC	18/232	1.10(0.63,1.93)	1.21(0.68,2.15)
CC	2/31	0.91(0.21,3.94)	1.62(0.41,6.41)
Missing	7/111		
Log-additive		1.04(0.66,1.65)	1.20(0.75,1.93)
Dominant	20/263	1.08(0.63,1.85)	1.22(0.70,2.13)
Recessive	2/31	0.89(0.21,3.81)	1.55(0.40,6.08)
CXCL12 rs1804429			
TT	60/858	1.00	1.00
TG	6/73	1.18(0.49,2.81)	1.14(0.47,2.78)
GG	1/1	14.30(0.88,231.46)	
Missing	7/108		
Log-additive		1.51(0.71,3.19)	1.61(0.73,3.57)
Dominant	7/74	1.35(0.60,3.07)	1.36(0.59,3.15)
Recessive	1/1	14.11(0.87,228.07)	
E2F2 rs2075993			
GG	21/291	1.00	1.00
GA	25/455	0.76(0.42,1.39)	0.54(0.29,1.01)
AA	21/179	1.63(0.86,3.06)	1.45(0.75,2.80)
Missing	7/115		
Log-additive		1.27(0.90,1.80)	1.19(0.82,1.73)
Dominant	46/634	1.01(0.59,1.72)	0.76(0.44,1.32)
Recessive	21/179	***1.90(1.11,3.27)***	***2.11(1.20,3.73)***
DOCK4 rs3801790			

SNP		Esophageal ADC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	23/376	1.00	1.00
AG	37/427	1.42(0.83,2.43)	1.33(0.77,2.30)
GG	7/126	0.91(0.38,2.17)	0.84(0.35,2.03)
Missing	7/111		
Log-additive		1.07(0.74,1.53)	1.01(0.70,1.47)
Dominant	44/553	1.30(0.77,2.19)	1.21(0.71,2.05)
Recessive	7/126	0.74(0.33,1.66)	0.72(0.32,1.62)
IL6R rs4072391			
CC	44/593	1.00	1.00
CT	20/279	0.97(0.56,1.67)	1.15(0.66,2.00)
TT	3/49	0.83(0.25,2.75)	1.16(0.36,3.78)
Missing	7/119		
Log-additive		0.94(0.61,1.44)	1.09(0.71,1.69)
Dominant	23/328	0.95(0.56,1.59)	1.13(0.66,1.92)
Recessive	3/49	0.83(0.25,2.75)	1.12(0.35,3.59)
HIF1A			
HIF1A rs2057482			
CC	47/672	1.00	1.00
CT	19/234	1.16(0.67,2.02)	1.49(0.85,2.63)
TT	1/23	0.62(0.08,4.70)	0.68(0.10,4.65)
Missing	7/111		
Log-additive		1.05(0.65,1.69)	1.21(0.75,1.98)
Dominant	20/257	1.11(0.65,1.91)	1.38(0.79,2.41)
Recessive	1/23	0.60(0.08,4.49)	0.63(0.09,4.21)
HIF1A rs2301113			
AA	31/467	1.00	1.00
AC	28/310	1.36(0.80,2.31)	1.43(0.83,2.44)
CC	5/100	0.75(0.29,1.98)	1.16(0.43,3.17)
Missing	10/163		
Log-additive		1.03(0.71,1.49)	1.20(0.81,1.79)
Dominant	33/410	1.21(0.73,2.01)	1.37(0.81,2.29)

SNP		Esophageal ADC	
	Cases/Controls	Crude OR (95% CI)	Adjusted* OR (95% CI)
Recessive	5/100	0.66(0.26,1.68)	1.00(0.38,2.64)
miRNAs			
MIR-26A1 rs7372209			
CC	38/494	1.00	1.00
CT	24/366	0.85(0.50,1.45)	0.84(0.49,1.44)
TT	4/66	0.79(0.27,2.28)	0.89(0.32,2.50)
Missing	8/114		
Log-additive		0.87(0.58,1.31)	0.88(0.57,1.34)
Dominant	28/432	0.84(0.51,1.40)	0.83(0.50,1.40)
Recessive	4/66	0.84(0.30,2.38)	0.97(0.35,2.65)
MIR-27 rs895819			
TT	29/413	1.00	1.00
TC	30/411	1.04(0.61,1.76)	1.06(0.62,1.83)
CC	8/86	1.33(0.59,3.00)	1.79(0.78,4.11)
Missing	7/130		
Log-additive		1.11(0.76,1.62)	1.23(0.83,1.82)
Dominant	38/497	1.09(0.66,1.80)	1.16(0.69,1.94)
Recessive	8/86	1.30(0.60,2.81)	1.75(0.80,3.84)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.3 Crude and adjusted associations between selected SNPs and squamous UADT cancers, stratified by cancer sites

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
Micro RNA biogenesis									
XPO5 rs11077									
AA	91/305	1.00	1.00	23/305	1.00	1.00	12/305	1.00	1.00
AC	91/479	***0.64 (0.46,0.88)***	***0.60 (0.42,0.85)***	36/479	1.00 (0.58,1.71)	0.53 (0.27,1.02)	12/479	0.64 (0.28,1.44)	0.55 (0.23,1.35)
CC	49/146	1.13 (0.75,1.68)	1.06 (0.68,1.65)	15/146	1.36 (0.69,2.69)	0.75 (0.32,1.72)	2/146	0.35 (0.08,1.58)	0.41 (0.10,1.69)
Missing	104/110			16/110			6/110		
Log-add		0.98 (0.79,1.20)	0.95 (0.76,1.19)		1.15 (0.81,1.62)	0.81 (0.52,1.26)		0.61 (0.33,1.13)	0.58 (0.30,1.15)
Dominant	140/625	0.75 (0.56,1.01)	***0.70 (0.50,0.97)***	51/625	1.08 (0.65,1.80)	0.58 (0.31,1.08)	14/625	0.57 (0.26,1.25)	0.50 (0.21,1.21)
Recessive	49/146	***1.45 (1.01,2.08)***	1.44 (0.98,2.14)	15/146	1.37 (0.75,2.47)	1.15 (0.56,2.35)	2/146	0.45 (0.10,1.91)	0.61 (0.17,2.29)
RAN rs14035									
CC	122/463	1.00	1.00	35/463	1.00	1.00	7/463	1.00	1.00
CT	91/366	0.94 (0.70,1.28)	0.91 (0.66,1.26)	23/366	0.83 (0.48,1.43)	0.90 (0.48,1.68)	18/366	***3.25 (1.34,7.87)***	***4.55 (1.88,10.99)***
TT	18/92	0.74 (0.43,1.28)	0.87 (0.49,1.53)	14/92	***2.01 (1.04,3.89)***	***2.32 (1.07,5.03)***	3/92	2.16 (0.55,8.49)	2.87 (0.78,10.54)
Missing	104/119			18/119			4/119		
Log-add		0.89 (0.72,1.12)	0.92 (0.73,1.17)		1.27 (0.90,1.78)	1.36 (0.92,2.01)		***1.72 (1.02,2.92)***	***2.02 (1.21,3.40)***
Dominant	109/458	0.90 (0.68,1.21)	0.90 (0.66,1.23)	37/458	1.07 (0.66,1.73)	1.19 (0.69,2.08)	21/458	***3.03 (1.28,7.20)***	***4.07 (1.74,9.55)***
Recessive	18/92	0.76 (0.45,1.29)	0.90 (0.52,1.57)	14/92	***2.18 (1.17,4.05)***	***2.42 (1.16,5.05)***	3/92	1.08 (0.32,3.65)	1.32 (0.42,4.14)
DICER1 rs3742330									
AA	193/717	1.00	1.00	61/717	1.00	1.00	23/717	1.00	1.00

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
AG	39/200	0.72 (0.50,1.06)	0.69 (0.46,1.05)	14/200	0.82 (0.45,1.50)	0.84 (0.41,1.73)	4/200	0.69 (0.25,1.91)	0.52 (0.18,1.47)
GG	2/12	0.62 (0.14,2.79)	0.50 (0.10,2.48)	1/12	0.98 (0.13,7.66)	1.01 (0.09,11.53)	0/12	1.22 (0.06,23.82)	0.70 (0.03,15.86)
Missing	101/111			14/111			5/111		
Log-add		0.74 (0.52,1.04)	0.70 (0.48,1.02)		0.86 (0.50,1.47)	0.87 (0.45,1.68)		0.58 (0.21,1.63)	0.49 (0.18,1.32)
Dominant	41/212	0.72 (0.50,1.04)	0.68 (0.46,1.02)	15/212	0.83 (0.46,1.49)	0.84 (0.41,1.72)	4/212	0.59 (0.20,1.72)	0.48 (0.17,1.38)
Recessive	2/12	0.66 (0.15,2.97)	0.56 (0.11,2.76)	1/12	1.02 (0.13,7.94)	1.09 (0.10,12.12)	0/12	1.34 (0.07,25.92)	0.93 (0.04,20.17)
AGO2 rs4961280									
CC	158/594	1.00	1.00	47/594	1.00	1.00	23/594	1.00	1.00
CA	68/279	0.92 (0.67,1.26)	1.07 (0.76,1.51)	23/279	1.04 (0.62,1.75)	1.33 (0.71,2.50)	4/279	0.41 (0.15,1.13)	0.43 (0.16,1.16)
AA	5/47	0.40 (0.16,1.02)	0.53 (0.20,1.41)	3/47	0.81 (0.24,2.69)	2.35 (0.63,8.83)	0/47	0.27 (0.02,4.58)	0.36 (0.02,5.75)
Missing	104/120			17/120			5/120		
Log-add		0.81 (0.62,1.05)	0.94 (0.70,1.24)		0.98 (0.65,1.47)	1.42 (0.85,2.36)		***0.33 (0.12,0.91)***	0.39 (0.15,1.00)
Dominant	73/326	0.84 (0.62,1.15)	1.01 (0.72,1.40)	26/326	1.01 (0.61,1.66)	1.41 (0.77,2.59)	4/326	***0.32 (0.11,0.92)***	0.38 (0.14,1.03)
Recessive	5/47	0.41 (0.16,1.05)	0.52 (0.20,1.36)	3/47	0.80 (0.24,2.62)	2.10 (0.58,7.69)	0/47	0.33 (0.02,5.73)	0.48 (0.03,7.57)
GEMIN3 rs197412									
TT	67/307	1.00	1.00	18/307	1.00	1.00	8/307	1.00	1.00
TC	113/434	1.19 (0.85,1.67)	1.30 (0.90,1.86)	34/434	1.34 (0.74,2.41)	1.20 (0.60,2.38)	14/434	1.24 (0.51,2.99)	1.00 (0.42,2.40)
CC	54/180	1.37 (0.92,2.06)	1.42 (0.91,2.23)	24/180	***2.27 (1.20,4.31)***	1.74 (0.82,3.70)	3/180	0.64 (0.17,2.44)	0.58 (0.17,2.05)
Missing	101/119			14/119			7/119		

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
Log-add		1.17 (0.96,1.43)	1.20 (0.96,1.50)		***1.52 (1.10,2.10)***	1.33 (0.91,1.94)		0.88 (0.50,1.55)	0.80 (0.45,1.42)
Dominant	167/614	1.25 (0.91,1.71)	1.33 (0.94,1.88)	58/614	1.61 (0.93,2.78)	1.37 (0.72,2.59)	17/614	1.06 (0.45,2.49)	0.87 (0.37,2.04)
Recessive	54/180	1.24 (0.87,1.74)	1.21 (0.82,1.77)	24/180	***1.90 (1.14,3.17)***	1.55 (0.85,2.83)	3/180	0.56 (0.17,1.90)	0.59 (0.19,1.80)
GEMIN4 rs7813									
CC	91/378	1.00	1.00	34/378	1.00	1.00	10/378	1.00	1.00
CT	100/400	1.04 (0.76,1.43)	1.06 (0.75,1.48)	34/400	0.95 (0.58,1.55)	1.31 (0.72,2.38)	10/400	0.95 (0.39,2.30)	1.36 (0.56,3.30)
TT	38/134	1.18 (0.77,1.81)	1.23 (0.78,1.95)	5/134	0.42 (0.16,1.08)	0.40 (0.13,1.23)	5/134	1.41 (0.47,4.20)	1.74 (0.57,5.30)
Missing	106/128			17/128			7/128		
Log-add		1.08 (0.88,1.32)	1.10 (0.88,1.37)		0.76 (0.53,1.08)	0.84 (0.55,1.27)		1.14 (0.66,2.00)	1.31 (0.76,2.27)
Dominant	138/534	1.07 (0.80,1.44)	1.10 (0.80,1.51)	39/534	0.81 (0.50,1.31)	1.06 (0.60,1.88)	15/534	1.06 (0.47,2.39)	1.43 (0.63,3.27)
Recessive	38/134	1.16 (0.78,1.71)	1.20 (0.79,1.82)	5/134	0.43 (0.17,1.08)	0.35 (0.12,1.02)	5/134	1.45 (0.54,3.93)	1.51 (0.56,4.11)
GEMIN4 rs2740348									
CC	166/640	1.00	1.00	58/640	1.00	1.00	22/640	1.00	1.00
CG	55/250	0.85 (0.60,1.19)	0.84 (0.59,1.21)	16/250	0.71 (0.40,1.25)	0.54 (0.27,1.07)	4/250	0.51 (0.18,1.42)	0.44 (0.16,1.20)
GG	6/28	0.83 (0.34,2.03)	0.72 (0.27,1.89)	1/28	0.39 (0.05,2.95)	0.29 (0.03,2.47)	0/28	0.50 (0.03,8.87)	0.40 (0.02,6.98)
Missing	108/122			15/122			6/122		
Log-add		0.87 (0.65,1.15)	0.85 (0.62,1.14)		0.69 (0.41,1.14)	***0.54 (0.30,0.98)***		0.42 (0.15,1.17)	0.41 (0.16,1.05)
Dominant	61/278	0.85 (0.61,1.17)	0.83 (0.59,1.18)	17/278	0.67 (0.39,1.18)	***0.51 (0.26,1.00)***	4/278	0.42 (0.14,1.23)	0.40 (0.15,1.08)
Recessive	6/28	0.86	0.75	1/28	0.43	0.35	0/28	0.59	0.51

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.35,2.11)	(0.29,1.98)		(0.06,3.20)	(0.04,2.92)		(0.03,10.41)	(0.03,8.83)
miRNA downstream									
CDK6 rs42031									
AA	165/656	1.00	1.00	57/656	1.00	1.00	20/656	1.00	1.00
AT	58/241	0.96 (0.69,1.34)	0.95 (0.66,1.36)	18/241	0.88 (0.51,1.51)	1.13 (0.61,2.11)	8/241	1.13 (0.50,2.55)	1.57 (0.69,3.60)
TT	8/27	1.18 (0.53,2.64)	0.94 (0.40,2.20)	0/27	0.21 (0.01,3.63)	0.19 (0.01,3.73)	0/27	0.58 (0.03,10.39)	0.91 (0.05,15.59)
Missing	104/116			15/116			4/116		
Log-add		1.00 (0.76,1.32)	0.96 (0.72,1.28)		0.72 (0.44,1.20)	0.84 (0.48,1.48)		0.88 (0.42,1.86)	1.25 (0.60,2.59)
Dominant	66/268	0.98 (0.71,1.35)	0.95 (0.67,1.34)	18/268	0.77 (0.45,1.34)	0.97 (0.51,1.83)	8/268	0.98 (0.43,2.25)	1.44 (0.63,3.30)
Recessive	8/27	1.19 (0.53,2.66)	0.96 (0.41,2.22)	0/27	0.22 (0.01,3.77)	0.19 (0.01,3.59)	0/27	0.57 (0.03,10.12)	0.79 (0.05,13.40)
TP53INP1 rs896849									
TT	152/666	1.00	1.00	46/666	1.00	1.00	18/666	1.00	1.00
TC	71/232	1.34 (0.97,1.84)	1.30 (0.93,1.84)	20/232	1.25 (0.72,2.15)	1.14 (0.61,2.16)	8/232	1.28 (0.55,2.97)	1.36 (0.58,3.15)
CC	12/31	1.70 (0.85,3.38)	1.50 (0.71,3.18)	8/31	***3.74 (1.62,8.59)***	2.90 (0.97,8.68)	1/31	1.19 (0.15,9.23)	2.34 (0.38,14.29)
Missing	100/111			16/111			5/111		
Log-add		***1.32 (1.03,1.70)***	1.27 (0.97,1.66)		***1.63 (1.12,2.39)***	1.43 (0.89,2.30)		1.20 (0.61,2.35)	1.35 (0.67,2.72)
Dominant	83/263	***1.38 (1.02,1.87)***	1.33 (0.96,1.84)	28/263	1.54 (0.94,2.52)	1.33 (0.73,2.40)	9/263	1.27 (0.56,2.85)	1.38 (0.61,3.13)
Recessive	12/31	1.56 (0.79,3.09)	1.37 (0.65,2.88)	8/31	***3.51 (1.55,7.94)***	2.75 (0.95,7.98)	1/31	1.11 (0.15,8.48)	2.10 (0.35,12.48)
CXCL12 rs1804429									
TT	218/858	1.00	1.00	68/858	1.00	1.00	24/858	1.00	1.00
TG	15/73	0.81	0.57	8/73	1.38	0.67	3/73	1.47	0.90

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.45,1.44)	(0.30,1.06)		(0.64,2.99)	(0.27,1.66)		(0.43,5.00)	(0.27,3.00)
GG	0/1	-	-	0/1	-	-	0/1	-	-
Missing	102/108			14/108			5/108		
Log-add		0.79	0.56		1.33	0.66		1.41	0.90
		(0.45,1.40)	(0.30,1.04)		(0.63,2.84)	(0.27,1.64)		(0.43,4.69)	(0.27,2.97)
Dominant	15/74	0.80	0.56	8/74	1.36	0.66	3/74	1.45	0.90
		(0.45,1.42)	(0.30,1.05)		(0.63,2.95)	(0.27,1.65)		(0.43,4.93)	(0.27,2.99)
Recessive	0/1			0/1			0/1		
E2F2 rs2075993									
GG	72/291	1.00	1.00	33/291	1.00	1.00	12/291	1.00	1.00
GA	122/455	1.08	1.02	31/455	0.60	0.62	9/455	0.48	0.41
		(0.78,1.50)	(0.71,1.46)		(0.36,1.00)	(0.33,1.17)		(0.20,1.15)	(0.17,1.00)
AA	38/179	0.86	0.86	11/179	0.54	0.75	5/179	0.68	0.71
		(0.56,1.33)	(0.53,1.39)		(0.27,1.10)	(0.32,1.76)		(0.23,1.95)	(0.24,2.07)
Missing	103/115			15/115			6/115		
Log-add		0.95	0.94		***0.70***	0.81		0.74	0.73
		(0.77,1.17)	(0.74,1.19)		***(0.49,0.99)***	(0.53,1.25)		(0.42,1.30)	(0.40,1.32)
Dominant	160/634	1.02	0.98	42/634	***0.58***	0.65	14/634	0.54	0.47
		(0.75,1.39)	(0.69,1.39)		***(0.36,0.94)***	(0.36,1.18)		(0.24,1.17)	(0.21,1.06)
Recessive	38/179	0.82	0.85	11/179	0.72	1.02	5/179	0.99	1.22
		(0.56,1.20)	(0.56,1.29)		(0.37,1.39)	(0.47,2.18)		(0.37,2.67)	(0.46,3.22)
DOCK4 rs3801790									
AA	94/376	1.00	1.00	36/376	1.00	1.00	12/376	1.00	1.00
AG	105/427	0.98	1.00	29/427	0.71	0.83	11/427	0.81	0.77
		(0.72,1.34)	(0.72,1.39)		(0.43,1.18)	(0.46,1.49)		(0.35,1.85)	(0.34,1.77)
GG	36/126	1.14	1.18	10/126	0.83	0.95	4/126	0.99	0.75
		(0.74,1.76)	(0.73,1.88)		(0.40,1.72)	(0.40,2.25)		(0.32,3.14)	(0.23,2.43)
Missing	100/111			15/111			5/111		
Log-add		1.05	1.06		0.84	0.93		0.94	0.83
		(0.85,1.29)	(0.85,1.33)		(0.59,1.20)	(0.62,1.40)		(0.54,1.66)	(0.47,1.46)
Dominant	141/553	1.02	1.04	39/553	0.74	0.85	15/553	0.85	0.75

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.76,1.37)	(0.76,1.42)		(0.46,1.18)	(0.49,1.49)		(0.39,1.84)	(0.34,1.64)
Recessive	36/126	1.15	1.18	10/126	0.98	1.05	4/126	1.11	0.88
		(0.77,1.72)	(0.76,1.81)		(0.49,1.96)	(0.46,2.35)		(0.38,3.26)	(0.30,2.62)
IL6R rs4072391									
CC	148/593	1.00	1.00	38/593	1.00	1.00	15/593	1.00	1.00
CT	69/279	0.99	1.01	32/279	***1.79***	1.60	7/279	0.99	1.01
		(0.72,1.36)	(0.72,1.42)		***(1.10,2.93)***	(0.89,2.88)		(0.40,2.46)	(0.43,2.41)
TT	15/49	1.23	1.23	3/49	0.96	1.10	2/49	1.61	1.56
		(0.67,2.25)	(0.64,2.36)		(0.28,3.21)	(0.30,4.07)		(0.36,7.26)	(0.38,6.31)
Missing	103/119			17/119			8/119		
Log-add		1.05	1.06		1.35	1.31		1.14	1.11
		(0.83,1.33)	(0.82,1.37)		(0.92,1.96)	(0.83,2.05)		(0.59,2.21)	(0.59,2.07)
Dominant	84/328	1.03	1.04	35/328	***1.67***	1.53	9/328	1.08	1.06
		(0.76,1.38)	(0.76,1.43)		***(1.03,2.69)***	(0.87,2.70)		(0.47,2.51)	(0.47,2.38)
Recessive	15/49	1.23	1.23	3/49	0.76	0.91	2/49	1.62	1.58
		(0.68,2.24)	(0.65,2.33)		(0.23,2.51)	(0.25,3.28)		(0.37,7.08)	(0.40,6.21)
HIF1A									
HIF1A rs2057482									
CC	160/672	1.00	1.00	48/672	1.00	1.00	19/672	1.00	1.00
CT	62/234	1.11	1.24	24/234	1.44	1.34	6/234	0.91	0.96
		(0.80,1.55)	(0.87,1.76)		(0.86,2.40)	(0.73,2.46)		(0.36,2.30)	(0.39,2.36)
TT	8/23	1.46	1.32	2/23	1.22	0.87	2/23	3.08	4.06
		(0.64,3.33)	(0.53,3.24)		(0.28,5.32)	(0.16,4.65)		(0.68,13.99)	(0.87,18.94)
Missing	105/111			16/111			5/111		
Log-add		1.15	1.21		1.31	1.18		1.27	1.36
		(0.87,1.51)	(0.90,1.61)		(0.85,2.01)	(0.71,1.95)		(0.64,2.54)	(0.69,2.69)
Dominant	70/257	1.14	1.25	26/257	1.42	1.29	8/257	1.10	1.16
		(0.83,1.57)	(0.89,1.75)		(0.86,2.33)	(0.72,2.32)		(0.48,2.55)	(0.51,2.66)
Recessive	8/23	1.42	1.23	2/23	1.09	0.80	2/23	3.15	4.18
		(0.63,3.22)	(0.50,3.01)		(0.25,4.73)	(0.15,4.22)		(0.70,14.10)	(0.91,19.16)
HIF1A rs2301113									

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
AA	116/467	1.00	1.00	28/467	1.00	1.00	10/467	1.00	1.00
AC	72/310	0.94 (0.67,1.30)	0.97 (0.68,1.38)	26/310	1.40 (0.80,2.43)	1.10 (0.58,2.10)	8/310	1.21 (0.47,3.09)	1.24 (0.50,3.06)
CC	35/100	1.41 (0.91,2.18)	1.45 (0.85,2.44)	16/100	***2.67 (1.39,5.12)***	1.67 (0.68,4.12)	5/100	2.34 (0.78,6.98)	2.17 (0.64,7.38)
Missing	112/163			20/163			9/163		
Log-add		1.12 (0.91,1.38)	1.12 (0.88,1.43)		***1.60 (1.15,2.22)***	1.25 (0.81,1.93)		1.48 (0.84,2.58)	1.40 (0.77,2.55)
Dominant	107/410	1.05 (0.78,1.41)	1.06 (0.76,1.47)	42/410	***1.71 (1.04,2.81)***	1.21 (0.66,2.23)	13/410	1.48 (0.64,3.41)	1.38 (0.59,3.22)
Recessive	35/100	1.45 (0.95,2.19)	1.47 (0.89,2.41)	16/100	***2.30 (1.27,4.18)***	1.58 (0.69,3.61)	5/100	2.16 (0.78,5.94)	2.00 (0.64,6.24)
miRNAs									
MIR-26A1 rs7372209									
CC	127/494	1.00	1.00	46/494	1.00	1.00	17/494	1.00	1.00
CT	87/366	0.92 (0.68,1.25)	0.95 (0.68,1.32)	22/366	0.65 (0.38,1.09)	0.80 (0.43,1.50)	9/366	0.71 (0.31,1.62)	0.97 (0.43,2.23)
TT	18/66	1.06 (0.61,1.85)	1.13 (0.62,2.05)	6/66	0.98 (0.40,2.37)	1.25 (0.44,3.57)	1/66	0.44 (0.06,3.36)	0.76 (0.14,4.04)
Missing	103/114			16/114			5/114		
Log-add		0.98 (0.78,1.23)	1.01 (0.79,1.30)		0.81 (0.55,1.21)	0.97 (0.61,1.55)		0.69 (0.35,1.36)	0.88 (0.46,1.68)
Dominant	105/432	0.95 (0.71,1.26)	0.98 (0.71,1.34)	28/432	0.70 (0.43,1.13)	0.87 (0.48,1.56)	10/432	0.67 (0.30,1.48)	0.90 (0.40,2.01)
Recessive	18/66	1.10 (0.64,1.88)	1.16 (0.65,2.06)	6/66	1.15 (0.48,2.75)	1.38 (0.50,3.79)	1/66	0.50 (0.07,3.75)	0.79 (0.15,4.00)
MIR-27 rs895819									
TT	97/413	1.00	1.00	29/413	1.00	1.00	12/413	1.00	1.00
TC	103/411	1.07 (0.78,1.45)	1.06 (0.76,1.47)	36/411	1.25 (0.75,2.07)	1.23 (0.68,2.22)	10/411	0.84 (0.36,1.96)	0.83 (0.36,1.93)
CC	31/86	1.54	1.53	6/86	0.99	0.68	4/86	1.60	1.31

SNP	Oral and oropharyngeal Cancer			Laryngeal Cancer			Esophageal Cancer		
	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)	Case/ Control	Crude OR (95% CI)	Adjusted* OR (95% CI)
		(0.96,2.45)	(0.93,2.54)		(0.40,2.47)	(0.23,1.99)		(0.50,5.08)	(0.40,4.32)
Missing	104/130			19/130			6/130		
Log-add		1.18	1.18		1.09	0.96		1.13	1.03
		(0.95,1.47)	(0.93,1.49)		(0.75,1.57)	(0.62,1.49)		(0.63,2.03)	(0.57,1.85)
Dominant	134/497	1.15	1.14	42/497	1.20	1.12	14/497	0.97	0.89
		(0.86,1.54)	(0.83,1.55)		(0.74,1.97)	(0.63,2.00)		(0.44,2.12)	(0.41,1.97)
Recessive	31/86	1.49	1.49	6/86	0.88	0.60	4/86	1.74	1.46
		(0.96,2.30)	(0.93,2.38)		(0.37,2.10)	(0.22,1.66)		(0.59,5.17)	(0.48,4.48)

* Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.4 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and UADT cancers

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	184/305	1.00	1.00	1.00	1.00
AC	192/479	***0.66(0.52,0.85)***	***0.70(0.55,0.88)***	***0.66(0.50,0.87)***	***0.70(0.54,0.90)***
CC	82/146	0.93(0.67,1.29)	0.96(0.72,1.29)	0.93(0.64,1.34)	0.97(0.70,1.33)
Log-additive		0.90(0.76,1.06)	0.90(0.77,1.06)	0.90(0.75,1.08)	0.91(0.76,1.08)
Dominant	274/625	***0.73(0.58,0.92)***	***0.75(0.60,0.94)***	***0.72(0.55,0.93)***	***0.75(0.58,0.96)***
Recessive	82/146	1.17(0.87,1.58)	1.14(0.87,1.50)	1.19(0.86,1.66)	1.16(0.86,1.56)
DICER1 rs3742330					
AA	367/717	1.00	1.00	1.00	
AG	91/200	0.89(0.67,1.17)	0.91(0.70,1.17)	0.76(0.55,1.05)	0.81(0.61,1.08)
GG	4/12	0.65(0.21,2.03)	0.89(0.50,1.58)	0.36(0.10,1.31)	0.78(0.43,1.43)
Log-additive		0.87(0.68,1.12)	0.89(0.70,1.13)	***0.73(0.54,0.98)***	0.77(0.58,1.00)
Dominant	95/212	0.88(0.67,1.15)	0.89(0.69,1.15)	0.74(0.54,1.01)	0.78(0.58,1.03)
Recessive	4/12	0.67(0.21,2.08)	0.89(0.50,1.59)	0.40(0.11,1.45)	0.80(0.44,1.46)
miRNA downstream					
TP53INP1 rs896849					
TT	304/666	1.00	1.00	1.00	1.00
TC	132/232	1.25(0.97,1.61)	1.20(0.95,1.52)	1.29(0.98,1.71)	1.23(0.95,1.59)
CC	27/31	***1.91(1.12,3.25)***	1.49(0.97,2.28)	***1.93(1.06,3.51)***	1.44(0.91,2.28)
Log-additive		***1.31(1.08,1.59)***	***1.28(1.06,1.55)***	***1.34(1.07,1.67)***	***1.30(1.05,1.61)***
Dominant	159/263	***1.32(1.04,1.68)***	***1.29(1.02,1.61)***	***1.36(1.04,1.78)***	***1.31(1.02,1.68)***
Recessive	27/31	***1.79(1.06,3.04)***	1.44(0.95,2.21)	1.76(0.98,3.18)	1.39(0.88,2.18)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.5a Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and UADT SQC, in the overall population

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	142/305	1.00	1.00	1.00	1.00
AC	154/479	***0.69(0.53,0.90)***	***0.72(0.56,0.92)***	***0.63(0.47,0.86)***	***0.68(0.52,0.90)***
CC	72/146	1.06(0.75,1.50)	1.07(0.79,1.45)	0.97(0.66,1.44)	1.01(0.72,1.42)
Log-additive		0.96(0.81,1.14)	0.96(0.81,1.14)	0.92(0.76,1.12)	0.93(0.77,1.12)
Dominant	226/625	***0.78(0.60,1.00)***	0.80(0.63,1.01)	***0.71(0.53,0.95)***	***0.75(0.57,0.97)***
Recessive	72/146	1.31(0.96,1.79)	1.25(0.94,1.66)	1.29(0.91,1.82)	1.22(0.90,1.67)
GEMIN3 rs197412					
TT	108/307	1.00	1.00	1.00	1.00
TC	174/434	1.14(0.86,1.51)	1.09(0.85,1.41)	1.13(0.83,1.55)	1.09(0.83,1.43)
CC	90/180	***1.42(1.02,1.99)***	1.32(0.98,1.78)	1.33(0.91,1.94)	1.23(0.89,1.71)
Log-additive		***1.19(1.01,1.41)***	***1.18(1.00,1.39)***	1.15(0.95,1.39)	1.14(0.95,1.37)
Dominant	264/614	1.22(0.94,1.59)	1.19(0.93,1.52)	1.19(0.89,1.59)	1.16(0.88,1.52)
Recessive	90/180	1.31(0.99,1.75)	1.26(0.97,1.65)	1.23(0.89,1.70)	1.18(0.88,1.59)
GEMIN4 rs2740348					
CC	276/640	1.00	1.00	1.00	1.00
CG	82/250	0.76(0.57,1.01)	0.80(0.61,1.04)	0.74(0.54,1.01)	0.78(0.59,1.04)
GG	7/28	0.58(0.25,1.34)	0.80(0.47,1.34)	0.53(0.21,1.33)	0.79(0.46,1.35)
Log-additive		***0.76(0.60,0.97)***	***0.78(0.62,0.99)***	***0.73(0.56,0.96)***	***0.76(0.60,0.98)***
Dominant	89/278	***0.74(0.56,0.98)***	***0.77(0.60,1.00)***	***0.71(0.53,0.97)***	***0.75(0.57,1.00)***
Recessive	7/28	0.62(0.27,1.44)	0.82(0.49,1.37)	0.58(0.23,1.44)	0.81(0.47,1.38)
miRNA downstream					
TP53INP1 rs896849					
TT	241/666	1.00	1.00	1.00	1.00

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
TC	108/232	1.29(0.98,1.69)	1.22(0.95,1.57)	1.28(0.95,1.72)	1.21(0.92,1.58)
CC	24/31	***2.14(1.23,3.72)***	***1.58(1.02,2.44)***	***1.91(1.02,3.58)***	1.41(0.88,2.26)
Log-additive		***1.37(1.11,1.69)***	***1.33(1.09,1.63)***	***1.33(1.05,1.68)***	***1.29(1.03,1.61)***
Dominant	132/263	***1.39(1.07,1.79)***	***1.33(1.05,1.70)***	***1.35(1.01,1.79)***	1.29(0.99,1.68)
Recessive	24/31	***1.99(1.15,3.44)***	1.52(0.99,2.36)	1.75(0.94,3.25)	1.36(0.85,2.17)
HIF1A					
HIF1A rs2301113					
AA	174/467	1.00	1.00	1.00	1.00
AC	117/310	1.01(0.77,1.33)	0.99(0.77,1.28)	0.95(0.70,1.28)	0.94(0.71,1.24)
CC	58/100	***1.56(1.08,2.25)***	***1.41(1.02,1.95)***	1.34(0.85,2.11)	1.23(0.85,1.80)
Log-additive		1.19(1.00,1.41)	1.17(0.99,1.39)	1.09(0.89,1.34)	1.08(0.89,1.32)
Dominant	175/410	1.15(0.89,1.47)	1.13(0.89,1.42)	1.02(0.77,1.36)	1.02(0.78,1.33)
Recessive	58/100	***1.55(1.09,2.20)***	***1.42(1.03,1.94)***	1.38(0.90,2.11)	1.26(0.87,1.82)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.5b Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and UADT SQC, in the Caucasians

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	79/192	1.00	1.00	1.00	1.00
AC	95/308	0.75(0.53,1.06)	0.78(0.58,1.06)	***0.67(0.46,0.97)***	0.73(0.53,1.00)
CC	36/78	1.12(0.70,1.80)	1.11(0.75,1.63)	1.04(0.62,1.72)	1.06(0.71,1.59)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.6 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and esophageal ADC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
miRNA downstream					
E2F2 rs2075993					
GG	21/291	1.00	1.00	1.00	1.00
GA	25/455	0.76(0.42,1.39)	0.79(0.52,1.22)	0.54(0.29,1.01)	0.66(0.42,1.03)
AA	21/179	1.63(0.86,3.06)	1.37(0.86,2.16)	1.45(0.75,2.80)	1.33(0.83,2.15)
Log-additive		1.27(0.90,1.80)	1.21(0.89,1.65)	1.19(0.82,1.73)	1.15(0.82,1.60)
Dominant	46/634	1.01(0.59,1.72)	1.00(0.66,1.53)	0.76(0.44,1.32)	0.85(0.55,1.33)
Recessive	21/179	***1.90(1.11,3.27)***	1.48(0.96,2.30)	***2.11(1.20,3.73)***	1.54(0.98,2.44)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.7 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and oral and oropharyngeal SQC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	91/305	1.00	1.00	1.00	1.00
AC	91/479	***0.64(0.46,0.88)***	***0.68(0.51,0.91)***	***0.60(0.42,0.85)***	***0.66(0.48,0.89)***
CC	49/146	1.13(0.75,1.68)	1.13(0.80,1.59)	1.06(0.68,1.65)	1.09(0.75,1.57)
Log-additive		0.98(0.79,1.20)	0.98(0.80,1.20)	0.95(0.76,1.19)	0.95(0.77,1.19)
Dominant	140/625	0.75(0.56,1.01)	0.79(0.60,1.03)	***0.70(0.50,0.97)***	***0.75(0.55,1.00)***
Recessive	49/146	***1.45(1.01,2.08)***	1.34(0.97,1.85)	1.44(0.98,2.14)	1.32(0.94,1.86)
miRNA downstream					
TP53INP1 rs896849					
TT	152/666	1.00	1.00	1.00	1.00
TC	71/232	1.34(0.97,1.84)	1.26(0.94,1.68)	1.30(0.93,1.84)	1.22(0.90,1.66)
CC	12/31	1.70(0.85,3.38)	1.29(0.78,2.12)	1.50(0.71,3.18)	1.19(0.71,2.00)
Log-additive		***1.32(1.03,1.70)***	***1.28(1.01,1.62)***	1.27(0.97,1.66)	1.23(0.95,1.58)
Dominant	83/263	***1.38(1.02,1.87)***	1.31(0.99,1.73)	1.33(0.96,1.84)	1.26(0.94,1.70)
Recessive	12/31	1.56(0.79,3.09)	1.25(0.76,2.05)	1.37(0.65,2.88)	1.16(0.69,1.93)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.8 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and laryngeal SQC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA biogenesis					
RAN rs14035					
CC	35/463	1.00	1.00	1.00	1.00
CT	23/366	0.83(0.48,1.43)	0.84(0.56,1.27)	0.90(0.48,1.68)	0.88(0.56,1.39)
TT	14/92	***2.01(1.04,3.89)***	1.46(0.89,2.38)	***2.32(1.07,5.03)***	1.46(0.86,2.47)
Log-additive		1.27(0.90,1.78)	1.21(0.89,1.65)	1.36(0.92,2.01)	1.27(0.90,1.78)
Dominant	37/458	1.07(0.66,1.73)	1.05(0.71,1.55)	1.19(0.69,2.08)	1.11(0.72,1.72)
Recessive	14/92	***2.18(1.17,4.05)***	1.51(0.93,2.46)	***2.42(1.16,5.05)***	1.49(0.89,2.51)
GEMIN3 rs197412					
TT	18/307	1.00	1.00	1.00	1.00
TC	34/434	1.34(0.74,2.41)	1.06(0.70,1.61)	1.20(0.60,2.38)	1.01(0.64,1.60)
CC	24/180	***2.27(1.20,4.31)***	1.54(0.98,2.42)	1.74(0.82,3.70)	1.29(0.79,2.10)
Log-additive		***1.52(1.10,2.10)***	***1.41(1.05,1.89)***	1.33(0.91,1.94)	1.24(0.89,1.73)
Dominant	58/614	1.61(0.93,2.78)	1.35(0.89,2.05)	1.37(0.72,2.59)	1.19(0.75,1.89)
Recessive	24/180	***1.90(1.14,3.17)***	1.51(0.99,2.30)	1.55(0.85,2.83)	1.28(0.81,2.03)
GEMIN4 rs2740348					
GG	58/640	1.00	1.00	1.00	1.00
GC	16/250	0.71(0.40,1.25)	0.82(0.53,1.27)	0.54(0.27,1.07)	0.74(0.46,1.19)
CC	1/28	0.39(0.05,2.95)	0.88(0.47,1.64)	0.29(0.03,2.47)	0.86(0.46,1.62)
Log-additive		0.69(0.41,1.14)	0.78(0.52,1.16)	***0.54(0.30,0.98)***	0.70(0.45,1.08)
Dominant	17/278	0.67(0.39,1.18)	0.79(0.51,1.20)	***0.51(0.26,1.00)***	0.70(0.44,1.12)
Recessive	1/28	0.43(0.06,3.20)	0.89(0.47,1.66)	0.35(0.04,2.92)	0.87(0.46,1.65)
miRNA downstream					
TP53INP1 rs896849					
TT	46/666	1.00	1.00	1.00	1.00
TC	20/232	1.25(0.72,2.15)	1.09(0.71,1.67)	1.14(0.61,2.16)	1.02(0.64,1.62)
CC	8/31	***3.74(1.62,8.59)***	1.60(0.90,2.85)	2.90(0.97,8.68)	1.32(0.72,2.42)

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Log-additive		***1.63(1.12,2.39)***	***1.46(1.04,2.04)***	1.43(0.89,2.30)	1.28(0.86,1.89)
Dominant	28/263	1.54(0.94,2.52)	1.33(0.89,2.00)	1.33(0.73,2.40)	1.18(0.75,1.85)
Recessive	8/31	***3.51(1.55,7.94)***	1.59(0.89,2.82)	2.75(0.95,7.98)	1.32(0.72,2.41)
E2F2 rs2075993					
GG	33/291	1.00	1.00	1.00	1.00
GA	31/455	0.60(0.36,1.00)	0.76(0.51,1.13)	0.62(0.33,1.17)	0.79(0.50,1.23)
AA	11/179	0.54(0.27,1.10)	0.77(0.48,1.23)	0.75(0.32,1.76)	0.94(0.55,1.59)
Log-additive		***0.70(0.49,0.99)***	0.75(0.55,1.02)	0.81(0.53,1.25)	0.86(0.60,1.24)
Dominant	42/634	***0.58(0.36,0.94)***	0.70 (0.47,1.03)	0.65(0.36,1.18)	0.78(0.50,1.23)
Recessive	11/179	0.72(0.37,1.39)	0.84(0.52,1.33)	1.02(0.47,2.18)	1.01(0.60,1.68)
IL6R rs4072391					
CC	38/593	1.00	1.00	1.00	1.00
CT	32/279	***1.79(1.10,2.93)***	1.48(0.99,2.21)	1.60(0.89,2.88)	1.31(0.84,2.05)
TT	3/49	0.96(0.28,3.21)	0.97(0.53,1.75)	1.10(0.30,4.07)	1.00(0.54,1.85)
Log-additive		1.35(0.92,1.96)	1.26(0.90,1.76)	1.31(0.83,2.05)	1.20(0.82,1.77)
Dominant	35/328	***1.67(1.03,2.69)***	1.41(0.95,2.10)	1.53(0.87,2.70)	1.29(0.83,2.00)
Recessive	3/49	0.76(0.23,2.51)	0.93(0.52,1.67)	0.91(0.25,3.28)	0.98(0.53,1.79)
HIF1A					
HIF1A rs2301113					
AA	28/467	1.00	1.00	1.00	1.00
AC	26/310	1.40(0.80,2.43)	1.13(0.74,1.72)	1.10(0.58,2.10)	1.00(0.63,1.58)
CC	16/100	***2.67(1.39,5.12)***	***1.63(1.01,2.65)***	1.67(0.68,4.12)	1.21(0.70,2.08)
Log-additive		***1.60(1.15,2.22)***	***1.47(1.09,1.98)***	1.25(0.81,1.93)	1.17(0.81,1.70)
Dominant	42/410	***1.71(1.04,2.81)***	1.43(0.96,2.13)	1.21(0.66,2.23)	1.11(0.70,1.76)
Recessive	16/100	***2.30(1.27,4.18)***	1.59(0.99,2.55)	1.58(0.69,3.61)	1.21(0.71,2.06)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.9 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and esophageal SQC

SNP	Cases/Controls	Crude OR (95% CI)	Crude Bayesian posterior OR (95% posterior limits)	Adjusted* OR (95% CI)	Adjusted* Bayesian posterior OR (95% posterior limits)
Micro RNA processing and maturation					
RAN rs14035					
CC	7/463	1.00	1.00	1.00	1.00
CT	18/366	***3.25(1.34,7.87)***	1.58(0.95,2.64)	***4.55(1.88,10.99)***	***1.79(1.05,3.03)***
TT	3/92	2.16(0.55,8.49)	1.07(0.58,1.99)	2.87(0.78,10.54)	1.09(0.58,2.04)
Log-additive		***1.72(1.02,2.92)***	1.41(0.92,2.15)	***2.02(1.21,3.40)***	***1.56(1.01,2.42)***
Dominant	21/458	***3.03(1.28,7.20)***	1.60(0.95,2.68)	***4.07(1.74,9.55)***	***1.81(1.07,3.07)***
Recessive	3/92	1.08(0.32,3.65)	1.02(0.56,1.87)	1.32(0.42,4.14)	1.04(0.56,1.92)
AGO2 rs4961280					
CC	23/594	1.00	1.00	1.00	1.00
CA	4/279	0.41(0.15,1.13)	0.73(0.42,1.26)	0.43(0.16,1.16)	0.76(0.43,1.33)
AA	0/47	0.27(0.02,4.58)	0.85(0.45,1.63)	0.36(0.02,5.75)	0.90(0.46,1.74)
Log-additive		***0.33(0.12,0.91)***	0.65(0.39,1.09)	0.39(0.15,1.00)	0.69(0.40,1.19)
Dominant	4/326	***0.32(0.11,0.92)***	0.67(0.39,1.15)	0.38(0.14,1.03)	0.71(0.41,1.25)
Recessive	0/47	0.33(0.02,5.73)	0.86(0.45,1.65)	0.48(0.03,7.57)	0.91(0.47,1.76)

*Adjusted for age, gender, ethnicity, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 1.2.10 Multiplicative interactions between selected SNPs and smoking status in UADT cancers

SNP	Nonsmokers		Smokers		SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Micro RNA processing and maturation						
XPO5 rs11077						
AA	54/159	1.00	130/146	1.00		
AC	60/218	0.90(0.57,1.41)	132/261	***0.54(0.37,0.77)***		
CC	29/62	1.49(0.82,2.72)	53/84	0.71(0.44,1.13)		
Missing	39/52		104/58			
Log-additive		1.16(0.86,1.56)		***0.78(0.62,0.99)***		
Dominant	89/280	1.02(0.66,1.56)	185/345	***0.58(0.41,0.81)***	***0.58(0.35,0.98)***	***0.04***
Recessive	29/62	1.59(0.93,2.73)	53/84	1.03(0.68,1.57)	0.69(0.36,1.33)	0.27
RAN rs14035						
CC	71/223	1.00	147/240	1.00		
CT	56/169	1.12(0.73,1.71)	135/197	1.13(0.81,1.58)		
TT	15/43	1.26(0.64,2.49)	32/49	1.20(0.69,2.06)		
Missing	40/56		105/63			
Log-additive		1.12(0.83,1.51)		1.11(0.87,1.40)		
Dominant	71/212	1.15(0.77,1.71)	167/246	1.14(0.83,1.57)	1.00(0.61,1.66)	0.99
Recessive	15/43	1.20(0.62,2.30)	32/49	1.13(0.67,1.91)	0.92(0.40,2.09)	0.83
DICER1 rs3742330						
AA	117/341	1.00	250/376	1.00		
AG	26/91	0.60(0.35,1.05)	65/109	0.85(0.57,1.27)		
GG	0/5		4/7	0.56(0.13,2.44)		
Missing	39/54		100/57			
Log-additive		***0.54(0.32,0.93)***		0.83(0.58,1.19)		
Dominant	26/96	***0.57(0.33,0.99)***	69/116	0.84(0.57,1.24)	1.33(0.70,2.52)	0.38
Recessive	0/5		4/7	0.60(0.14,2.57)	-	-
AGO2 rs4961280						
CC	86/282	1.00	221/312	1.00		
CA	50/128	1.28(0.83,1.96)	86/151	0.91(0.63,1.30)		

SNP	Nonsmokers		Smokers		SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	3/25	0.40(0.11,1.40)	11/22	0.86(0.38,1.96)		
Missing	43/56		101/64			
Log-additive		0.98(0.69,1.39)		0.92(0.69,1.22)		
Dominant	53/153	1.14(0.75,1.73)	97/173	0.90(0.64,1.27)	0.78(0.46,1.33)	0.37
Recessive	3/25	0.36(0.10,1.25)	11/22	0.89(0.40,2.01)	2.42(0.56,10.51)	0.24
GEMIN3 rs197412						
TT	37/136	1.00	102/171	1.00		
TC	72/223	1.34(0.83,2.15)	146/211	1.02(0.71,1.47)		
CC	33/79	1.64(0.91,2.94)	72/101	1.07(0.69,1.68)		
Missing	40/53		99/66			
Log-additive		1.28(0.96,1.71)		1.03(0.83,1.29)		
Dominant	105/302	1.41(0.90,2.22)	218/312	1.04(0.74,1.46)	0.75(0.43,1.30)	0.30
Recessive	33/79	1.35(0.83,2.22)	72/101	1.06(0.72,1.56)	0.79(0.43,1.45)	0.45
GEMIN4 rs7813						
CC	60/164	1.00	133/214	1.00		
CT	59/192	0.85(0.55,1.32)	139/208	1.14(0.81,1.61)		
TT	21/74	0.85(0.47,1.53)	42/60	1.16(0.70,1.93)		
Missing	42/61		105/67			
Log-additive		0.90(0.68,1.20)		1.10(0.87,1.39)		
Dominant	80/266	0.85(0.56,1.28)	181/268	1.15(0.83,1.59)	1.37(0.82,2.30)	0.22
Recessive	21/74	0.92(0.53,1.60)	42/60	1.08(0.68,1.73)	1.19(0.58,2.43)	0.64
GEMIN4 rs2740348						
CC	104/285	1.00	232/355	1.00		
CG	34/134	0.72(0.46,1.14)	75/116	0.88(0.60,1.28)		
GG	4/15	0.83(0.26,2.63)	6/13	0.49(0.17,1.42)		
Missing	40/57		106/65			
Log-additive		0.78(0.53,1.15)		0.82(0.59,1.12)		
Dominant	38/149	0.73(0.47,1.14)	81/129	0.83(0.58,1.20)	1.11(0.64,1.95)	0.71
Recessive	4/15	0.91(0.29,2.89)	6/13	0.50(0.17,1.47)	0.57(0.12,2.75)	0.49
miRNA downstream						
CDK6 rs42031						

SNP	Nonsmokers		Smokers		SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	99/310	1.00	227/346	1.00		
AT	37/119	1.10(0.70,1.73)	83/122	1.08(0.75,1.56)		
TT	5/6	2.87(0.83,9.90)	10/21	0.68(0.30,1.58)		
Missing	41/56		99/60			
Log-additive		1.26(0.85,1.86)		0.96(0.72,1.29)		
Dominant	42/125	1.19(0.77,1.84)	93/143	1.02(0.72,1.45)	0.90(0.52,1.56)	0.72
Recessive	5/6	2.79(0.81,9.54)	10/21	0.67(0.29,1.53)	0.26(0.06,1.15)	0.08
TP53INP1 rs896849						
TT	88/319	1.00	216/347	1.00		
TC	47/106	***1.68(1.08,2.62)***	85/126	1.11(0.77,1.59)		
CC	9/13	***2.70(1.03,7.07)***	18/18	1.74(0.80,3.77)		
Missing	38/53		100/58			
Log-additive		***1.66(1.17,2.37)***		1.20(0.90,1.60)		
Dominant	56/119	***1.78(1.16,2.72)***	103/144	1.18(0.83,1.66)	0.69(0.41,1.17)	0.17
Recessive	9/13	2.23(0.86,5.77)	18/18	1.67(0.78,3.60)	0.83(0.25,2.73)	0.76
CXCL12 rs1804429						
TT	130/409	1.00	292/449	1.00		
TG	12/28	0.97(0.46,2.05)	27/45	0.68(0.39,1.19)		
GG	1/1	3.04(0.18,51.38)	0/0			
Missing	39/53		100/55			
Log-additive		1.09(0.56,2.13)		0.68(0.39,1.19)		
Dominant	13/29	1.04(0.50,2.13)	27/45	0.68(0.39,1.19)	0.65(0.27,1.60)	0.35
Recessive	1/1	3.05(0.18,51.46)	0/0		-	-
E2F2 rs2075993						
GG	37/144	1.00	114/147	1.00		
GA	77/202	***1.62(1.00,2.63)***	137/253	***0.62(0.43,0.91)***		
AA	28/90	1.28(0.70,2.34)	66/89	0.92(0.57,1.48)		
Missing	40/55		102/60			
Log-additive		1.15(0.87,1.54)		0.92(0.72,1.16)		
Dominant	105/292	1.52(0.96,2.42)	203/342	***0.69(0.48,0.99)***	***0.50(0.29,0.87)***	***0.01***
Recessive	28/90	0.93(0.56,1.52)	66/89	1.25(0.83,1.88)	1.35(0.72,2.53)	0.35

SNP	Nonsmokers		Smokers		SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
DOCK4 rs3801790						
AA	57/180	1.00	130/196	1.00		
AG	65/193	1.04(0.68,1.60)	143/234	0.94(0.67,1.32)		
GG	21/66	0.78(0.42,1.47)	48/60	1.25(0.76,2.07)		
Missing	39/52		98/59			
Log-additive		0.92(0.69,1.23)		1.07(0.84,1.35)		
Dominant	86/259	0.98(0.65,1.47)	191/294	1.00(0.73,1.38)	1.01(0.61,1.69)	0.96
Recessive	21/66	0.76(0.43,1.37)	48/60	1.29(0.81,2.06)	1.62(0.79,3.31)	0.19
IL6R rs4072391						
CC	88/272	1.00	185/321	1.00		
CT	40/140	0.90(0.58,1.41)	112/139	1.35(0.96,1.90)		
TT	11/22	1.51(0.68,3.34)	18/27	1.19(0.60,2.40)		
Missing	43/57		104/62			
Log-additive		1.07(0.77,1.48)		1.22(0.93,1.58)		
Dominant	51/162	0.99(0.65,1.50)	130/166	1.32(0.96,1.83)	1.33(0.79,2.24)	0.28
Recessive	11/22	1.56(0.72,3.40)	18/27	1.08(0.54,2.14)	0.69(0.25,1.94)	0.49
HIF1A						
HIF1A rs2057482						
CC	103/317	1.00	218/355	1.00		
CT	35/115	1.01(0.64,1.59)	86/119	1.27(0.89,1.83)		
TT	4/8	1.64(0.46,5.83)	11/15	1.03(0.42,2.58)		
Missing	40/51		104/60			
Log-additive		1.08(0.73,1.60)		1.17(0.87,1.58)		
Dominant	39/123	1.05(0.68,1.63)	97/134	1.25(0.88,1.77)	1.18(0.68,2.06)	0.55
Recessive	4/8	1.63(0.46,5.78)	11/15	0.96(0.39,2.38)	0.62(0.13,2.91)	0.54
HIF1A rs2301113						
AA	74/233	1.00	145/234	1.00		
AC	47/148	1.03(0.67,1.60)	105/162	0.96(0.67,1.38)		
CC	16/36	1.40(0.65,3.00)	49/64	1.32(0.78,2.23)		
Missing	45/74		120/89			
Log-additive		1.12(0.81,1.54)		1.09(0.86,1.40)		

SNP	Nonsmokers		Smokers		SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Dominant	63/184	1.09(0.72,1.65)	154/226	1.04(0.74,1.45)	0.93(0.55,1.55)	0.77
Recessive	16/36	1.38(0.66,2.89)	49/64	1.34(0.82,2.21)	1.00(0.46,2.20)	0.99
miRNAs						
MIR-26A1 rs7372209						
CC	80/226	1.00	178/268	1.00		
CT	50/181	0.74(0.48,1.14)	114/185	0.99(0.70,1.40)		
TT	13/30	1.15(0.55,2.40)	24/36	1.07(0.58,1.98)		
Missing	39/54		103/60			
Log-additive		0.92(0.66,1.27)		1.02(0.79,1.31)		
Dominant	63/211	0.80(0.53,1.20)	138/221	1.00(0.72,1.39)	1.22(0.74,2.03)	0.43
Recessive	13/30	1.32(0.65,2.69)	24/36	1.08(0.59,1.95)	0.81(0.33,2.04)	0.66
MIR-27 rs895819						
TT	67/189	1.00	126/224	1.00		
TC	54/205	0.69(0.45,1.05)	150/206	1.36(0.97,1.91)		
CC	21/37	1.54(0.82,2.90)	35/49	1.25(0.72,2.17)		
Missing	40/60		108/70			
Log-additive		1.02(0.76,1.38)		1.19(0.94,1.53)		
Dominant	75/242	0.81(0.55,1.21)	185/255	1.34(0.97,1.86)	1.65(0.99,2.74)	0.05
Recessive	21/37	***1.85(1.02,3.37)***	35/49	1.06(0.63,1.77)	0.58(0.27,1.27)	0.17

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, alcohol drinking as alcoholic drinks per day and smoking as pack-years, if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and smoking was dichotomized as nonsmoking vs smoking.

Table 1.2.11 Bayesian shrinkage of multiplicative interactions between selected SNPs and smoking status in UADT cancers

SNP	Nonsmokers		Smokers		SNP-smoking product terms**		Bayesian shrinkage of SNP-smoking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity	Adjusted* OR (95% posterior limits)	P-value* for heterogeneity
Micro RNA processing and maturation								
XPO5 rs11077								
AA	54/159	1.00	130/146	1.00				
AC+CC	89/280	1.02(0.66,1.56)	185/345	***0.58(0.41,0.81)***	***0.58(0.35,0.98)***	***0.04***	0.71(0.47,1.08)	0.11
miRNA downstream								
E2F2 rs2075993								
GG	37/144	1.00	114/147	1.00				
GA+AA	105/292	1.52(0.96,2.42)	203/342	***0.69(0.48,0.99)***	***0.50(0.29,0.87)***	***0.01***	0.66(0.43,1.01)	0.05

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, alcohol drinking as alcoholic drinks per day and smoking as pack-years, if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and smoking was dichotomized as nonsmoking vs smoking.

Table 1.2.12 Multiplicative interactions between selected SNPs and alcohol drinking status in UADT cancers

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Micro RNA processing and maturation						
XPO5 rs11077						
AA	40/79	1.00	144/226	1.00		
AC	35/126	0.68(0.38,1.24)	157/353	***0.65(0.48,0.90)***		
CC	12/24	1.01(0.42,2.41)	69/122	0.91(0.61,1.38)		
Missing	30/35		112/75			
Log-additive		0.91(0.59,1.38)		0.92(0.75,1.12)		
Dominant	47/150	0.74(0.42,1.31)	226/475	***0.71(0.53,0.97)***	1.05(0.57,1.94)	0.87
Recessive	12/24	1.26(0.57,2.81)	69/122	1.18(0.82,1.70)	0.87(0.37,2.04)	0.75
RAN rs14035						
CC	41/125	1.00	177/338	1.00		
CT	33/81	1.34(0.75,2.38)	157/285	1.05(0.78,1.40)		
TT	12/21	1.61(0.67,3.91)	35/71	1.07(0.66,1.75)		
Missing	31/37		113/82			
Log-additive		1.29(0.87,1.91)		1.03(0.84,1.27)		
Dominant	45/102	1.40(0.82,2.39)	192/356	1.05(0.80,1.39)	0.76(0.42,1.37)	0.35
Recessive	12/21	1.43(0.61,3.34)	35/71	1.05(0.66,1.68)	0.71(0.28,1.79)	0.47
DICER1 rs3742330						
AA	66/163	1.00	301/554	1.00		
AG	21/58	0.81(0.41,1.57)	69/142	0.75(0.52,1.08)		
GG	0/5		4/7	0.69(0.16,2.95)		
Missing	30/38		108/73			
Log-additive		0.65(0.35,1.20)		0.77(0.55,1.08)		
Dominant	21/63	0.72(0.37,1.39)	73/149	0.75(0.52,1.08)	1.02(0.51,2.05)	0.96
Recessive	0/5		4/7	0.78(0.19,3.27)	-	-
AGO2 rs4961280						
CC	53/144	1.00	253/450	1.00		
CA	32/65	1.62(0.90,2.94)	104/214	0.92(0.67,1.26)		

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	2/16	0.45(0.09,2.16)	12/31	0.77(0.36,1.61)		
Missing	30/39		113/81			
Log-additive		1.11(0.70,1.77)		0.89(0.69,1.15)		
Dominant	34/81	1.41(0.79,2.51)	116/245	0.90(0.67,1.22)	0.70(0.38,1.29)	0.25
Recessive	2/16	0.37(0.08,1.73)	12/31	0.79(0.38,1.65)	2.36(0.44,12.80)	0.32
GEMIN3 rs197412						
TT	27/68	1.00	111/239	1.00		
TC	42/117	1.02(0.56,1.89)	176/317	1.20(0.87,1.66)		
CC	18/38	1.37(0.62,3.04)	87/142	1.29(0.87,1.92)		
Missing	30/41		108/78			
Log-additive		1.15(0.78,1.71)		1.16(0.96,1.41)		
Dominant	60/155	1.10(0.62,1.97)	263/459	1.23(0.90,1.66)	1.12(0.59,2.12)	0.72
Recessive	18/38	1.35(0.68,2.71)	87/142	1.15(0.82,1.62)	0.84(0.40,1.75)	0.64
GEMIN4 rs7813						
CC	34/93	1.00	158/285	1.00		
CT	40/87	1.29(0.71,2.35)	158/313	0.96(0.71,1.31)		
TT	12/41	1.03(0.46,2.31)	51/93	1.03(0.66,1.59)		
Missing	31/43		115/85			
Log-additive		1.06(0.73,1.55)		1.01(0.82,1.24)		
Dominant	52/128	1.21(0.69,2.13)	209/406	0.98(0.73,1.30)	0.87(0.47,1.59)	0.64
Recessive	12/41	0.90(0.43,1.88)	51/93	1.05(0.70,1.57)	1.20(0.52,2.75)	0.67
GEMIN4 rs2740348						
CC	67/152	1.00	268/488	1.00		
CG	17/61	0.69(0.36,1.33)	92/189	0.88(0.64,1.21)		
GG	4/10	1.31(0.36,4.74)	6/18	0.42(0.15,1.19)		
Missing	29/41		116/81			
Log-additive		0.88(0.53,1.45)		0.83(0.63,1.09)		
Dominant	21/71	0.76(0.41,1.41)	98/207	0.83(0.61,1.14)	1.19(0.60,2.33)	0.62
Recessive	4/10	1.46(0.41,5.22)	6/18	0.44(0.16,1.23)	0.37(0.07,1.85)	0.22
miRNA downstream						
CDK6 rs42031						

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
AA	65/165	1.00	260/491	1.00		
AT	15/59	0.73(0.37,1.45)	105/182	1.21(0.89,1.66)		
TT	6/2	6.08(1.16,31.93)	9/25	0.58(0.25,1.35)		
Missing	31/38		108/78			
Log-additive		1.23(0.74,2.05)		1.00(0.77,1.30)		
Dominant	21/61	0.98(0.52,1.82)	114/207	1.13(0.83,1.53)	1.23(0.63,2.42)	0.54
Recessive	6/2	6.52(1.25,34.02)	9/25	0.55(0.24,1.26)	***0.08(0.01,0.51)***	***0.01***
TP53INP1 rs896849						
TT	55/167	1.00	249/499	1.00		
TC	26/54	1.77(0.96,3.24)	106/178	1.20(0.87,1.64)		
CC	6/4	5.34(1.27,22.43)	20/27	1.54(0.79,3.00)		
Missing	30/39		107/72			
Log-additive		***1.97(1.20,3.23)***		1.20(0.94,1.54)		
Dominant	32/58	***1.99(1.12,3.56)***	126/205	1.24(0.92,1.67)	0.59(0.32,1.11)	0.10
Recessive	6/4	4.39(1.07,18.10)	20/27	1.44(0.75,2.79)	0.29(0.06,1.29)	0.10
CXCL12 rs1804429						
TT	77/216	1.00	344/642	1.00		
TG	10/12	1.89(0.71,5.07)	29/61	0.62(0.37,1.04)		
GG	0/1		1/0			
Missing	30/35		108/73			
Log-additive		1.50(0.61,3.71)		0.74(0.45,1.20)		
Dominant	10/13	1.72(0.65,4.53)	30/61	0.66(0.40,1.09)	0.38(0.13,1.10)	0.07
Recessive	0/1		1/0		-	-
E2F2 rs2075993						
GG	26/78	1.00	124/213	1.00		
GA	43/96	1.75(0.91,3.37)	171/359	0.75(0.54,1.05)		
AA	18/50	1.09(0.49,2.42)	76/129	1.04(0.69,1.58)		
Missing	30/40		111/75			
Log-additive		1.08(0.74,1.57)		0.98(0.79,1.20)		
Dominant	61/146	1.51(0.82,2.81)	247/488	0.82(0.60,1.12)	0.64(0.34,1.22)	0.18
Recessive	18/50	0.77(0.39,1.49)	76/129	1.26(0.88,1.80)	1.63(0.79,3.40)	0.19

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
DOCK4 rs3801790						
AA	30/83	1.00	156/293	1.00		
AG	46/107	1.21(0.67,2.18)	162/320	0.90(0.66,1.21)		
GG	11/36	1.06(0.45,2.48)	58/90	1.06(0.69,1.63)		
Missing	30/38		106/73			
Log-additive		1.07(0.72,1.59)		1.00(0.82,1.23)		
Dominant	57/143	1.18(0.67,2.07)	220/410	0.93(0.70,1.24)	0.79(0.42,1.45)	0.44
Recessive	11/36	0.94(0.43,2.04)	58/90	1.13(0.76,1.68)	1.25(0.53,2.92)	0.61
IL6R rs4072391						
CC	58/136	1.00	214/457	1.00		
CT	26/77	0.81(0.45,1.44)	126/202	1.29(0.95,1.75)		
TT	3/10	0.75(0.19,3.00)	26/39	1.55(0.87,2.75)		
Missing	30/41		116/78			
Log-additive		0.83(0.52,1.33)		***1.26(1.00,1.58)***		
Dominant	29/87	0.80(0.46,1.40)	152/241	1.33(1.00,1.77)	1.59(0.86,2.94)	0.14
Recessive	3/10	0.80(0.20,3.18)	26/39	1.42(0.81,2.49)	1.67(0.38,7.26)	0.49
HIF1A						
HIF1A rs2057482						
CC	67/158	1.00	253/514	1.00		
CT	17/62	0.66(0.35,1.28)	104/172	1.33(0.97,1.83)		
TT	3/8	0.54(0.12,2.39)	12/15	1.55(0.65,3.70)		
Missing	30/36		113/75			
Log-additive		0.69(0.41,1.16)		1.30(1.00,1.70)		
Dominant	20/70	0.65(0.35,1.20)	116/187	1.35(0.99,1.83)	1.83(0.93,3.60)	0.08
Recessive	3/8	0.59(0.13,2.61)	12/15	1.42(0.60,3.37)	2.11(0.38,11.79)	0.39
HIF1A rs2301113						
AA	52/107	1.00	167/360	1.00		
AC	23/83	0.56(0.30,1.04)	129/227	1.17(0.85,1.60)		
CC	9/27	***0.35(0.12,0.99)***	56/73	***1.79(1.11,2.89)***		
Missing	33/47		130/116			
Log-additive		***0.58(0.37,0.90)***		***1.28(1.03,1.59)***		

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity
Dominant	32/110	***0.50(0.28,0.91)***	185/300	1.28(0.95,1.72)	***2.11(1.15,3.90)***	***0.02***
Recessive	9/27	0.44(0.16,1.21)	56/73	***1.66(1.05,2.61)***	2.03(0.79,5.22)	0.14
miRNAs						
MIR-26A1 rs7372209						
CC	46/107	1.00	211/387	1.00		
CT	35/105	0.83(0.47,1.46)	129/261	0.90(0.67,1.22)		
TT	5/15	0.74(0.24,2.27)	32/51	1.19(0.70,2.01)		
Missing	31/37		110/77			
Log-additive		0.84(0.54,1.32)		1.01(0.81,1.26)		
Dominant	40/120	0.82(0.47,1.41)	161/312	0.95(0.71,1.26)	1.26(0.70,2.29)	0.44
Recessive	5/15	0.81(0.27,2.41)	32/51	1.24(0.75,2.07)	1.58(0.48,5.22)	0.45
MIR-27 rs895819						
TT	39/102	1.00	154/311	1.00		
TC	38/102	0.81(0.45,1.43)	165/309	1.11(0.83,1.50)		
CC	10/18	1.12(0.43,2.91)	46/68	1.45(0.91,2.31)		
Missing	30/42		117/88			
Log-additive		0.95(0.62,1.46)		1.17(0.95,1.44)		
Dominant	48/120	0.85(0.49,1.47)	211/377	1.17(0.88,1.56)	1.25(0.69,2.28)	0.46
Recessive	10/18	1.26(0.51,3.10)	46/68	1.37(0.88,2.12)	0.89(0.34,2.34)	0.81

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, smoking as pack-years, and alcohol drinking as alcoholic drinks per day if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and drinking was dichotomized as nondrinking vs drinking.

Table 1.2.13 Semi-Bayesian shrinkage of multiplicative interactions between selected SNPs and alcohol drinking status in UADT cancers

SNP	Nondrinkers		Drinkers		SNP-drinking product terms**		Bayesian Shrinkage of SNP-drinking product terms**	
	Cases/ Controls	Adjusted* OR (95% CI)	Cases/ Controls	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)	P-value* for heterogeneity	Adjusted* OR (95% posterior limits)	P-value* for heterogeneity
miRNA downstream								
CDK6								
rs42031								
AA+AT	80/224	1.00	260/491	1.00				
TT	6/2	6.52(1.25,34.02)	9/25	0.55(0.24,1.26)	***0.08(0.01,0.51)***	***0.01***	0.70(0.37,1.32)	0.27
HIF1A								
HIF1A								
rs2301113								
AA	52/107	1.00	167/360	1.00				
AC+CC	32/110	***0.50(0.28,0.91)***	185/300	1.28(0.95,1.72)	***2.11(1.15,3.90)***	***0.02***	1.52(0.97,2.41)	0.07

*Adjusted for age, gender, ethnicity, and education level as high school, college and beyond college, smoking as pack-years, and alcohol drinking as alcoholic drinks per day if applicable.

**For the product terms, SNPs were dichotomized in dominant or recessive models and drinking was dichotomized as nondrinking vs drinking.

Section III

Table 2.1.1 Demographic characteristics of patients of LA study

	Lung cancer (N = 611)				UADT (N = 601)			
	All, n	Death n (%)	Censored n (%)	Median survival years	All, n	Death n (%)	Censored n (%)	Median survival years
Survival	611	406 (66)	205 (34)	2.5	601	248 (41)	353 (59)	9.4
Age, mean (SD)		52.6±5.3	51.5±5.7			51.2±7.3	49.8±7.7	
<45	61	38 (62)	23 (38)	3.0	109	38 (35)	71 (65)	10.1
45-54	301	188 (62)	113 (38)	2.9	267	105 (39)	162 (61)	9.6
55+	249	180 (72)	69 (28)	2.2	225	105 (47)	120 (53)	9.0
Missing	0	0	0		0	0	0	
Sex								
Male	303	215 (71)	88 (29)	2.0	454	191 (42)	263 (58)	9.3
Female	308	191 (62)	117 (38)	3.7	147	57 (39)	90 (61)	9.7
Missing	0	0	0		0	0	0	
Ethnicity								
Caucasian	359	245 (68)	114 (32)	2.4	341	135 (40)	206 (60)	9.4
Hispanic	70	44 (63)	26 (37)	2.2	109	46 (42)	63 (58)	9.4
African-American	96	60 (62)	36 (38)	3.0	69	39 (56)	30 (43)	5.6
Asian-American	70	46 (66)	24 (34)	2.8	64	21 (33)	43 (67)	9.9

	Lung cancer (N = 611)				UADT (N = 601)			
	All, n	Death n (%)	Censored n (%)	Median survival years	All, n	Death n (%)	Censored n (%)	Median survival years
Other	15	10 (67)	5 (33)	4.1	16	6 (38)	10 (62)	9.0
Missing	1	1	0		2	1	1	
Histology								
Squamous cell	95	53 (56)	42 (44)	5.8	497	195 (39)	302 (61)	9.6
Adenocarcinoma	297	186 (63)	111 (34)	3.4	74	42 (57)	32 (43)	3.6
Large cell	115	85 (74)	30 (26)	2.1		-	-	
Small cell	75	60 (80)	15 (20)	1.4		-	-	
Other	29	22 (76)	7 (24)	1.5	30	11 (37)	19 (63)	9.9
Missing	0	0	0		0	0	0	
Education (years of schooling)		13.2±3.3	13.4±3.5			12.9±3.6	13.3±3.7	
0-12	265	181 (68)	84 (32)	2.6	273	117 (43)	156 (57)	9.3
13-16	275	181 (66)	94 (34)	2.4	259	110 (42)	149 (58)	9.4
>16	71	44 (62)	27 (38)	2.8	69	21 (30)	48 (70)	10.1
Missing	0	0	0		0	0	0	
Tumor cell differentiation								
Well to moderate	168	90 (54)	78 (46)	7.1	397	171 (43)	226 (57)	9.3

	Lung cancer (N = 611)				UADT (N = 601)			
	All, n	Death n (%)	Censored n (%)	Median survival years	All, n	Death n (%)	Censored n (%)	Median survival years
Poor to very poor	222	154 (69)	68 (31)	2.0	121	42 (35)	79 (65)	9.8
Undetermined	219	161 (74)	58 (26)	2.0	81	34 (42)	47 (58)	9.6
Missing	2	1	1		2	1	1	
Smoking (pack-years)		38.96±22.23	36.65±22.86			36.02±23.83	29.04±22.16	
Never	110	61 (55)	49 (44)	5.5	182	53 (29)	129 (71)	10.1
Ever	501	345 (69)	156 (31)	2.2	419	195 (46)	224 (53)	9.0
less than 20	98	63 (64)	35 (36)	2.6	145	51 (35)	94 (65)	9.7
20-less than 40	201	139 (69)	62 (31)	2.5	146	71 (49)	75 (51)	8.8
40 or more	202	143 (71)	59 (29)	1.9	128	73 (57)	55 (43)	6.8
Missing	0	0	0		0	0	0	
Alcohol drinking status (drink/day)		2.22±3.42	2.29±5.87			3.79±4.78	2.70±5.03	
Never	170	111 (65)	59 (34)	2.8	117	45 (38)	72 (62)	9.8
Ever	440	294 (67)	146 (33)	2.5	482	202 (42)	280 (58)	9.4
< 2 drinks/day	302	200 (66)	102 (34)	2.4	279	97 (35)	182 (65)	9.8
>= 2 drinks/day	138	94 (68)	44 (32)	2.8	203	105 (52)	98 (48)	8.2
Missing	1	1	0		2	1	1	

Table 2.1.2 Crude and adjusted associations between selected SNPs and lung cancer survival, both in the overall population and in the Caucasians

SNP	Overall			Caucasians		
	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	130/63	1.00	1.00	71/33	1.00	1.00
AC	160/71	1.02(0.81,1.29)	1.09(0.85,1.41)	108/46	1.04(0.77,1.41)	1.13(0.82,1.54)
CC	58/48	***0.69(0.51,0.94)***	***0.66(0.47,0.93)***	30/24	0.71(0.46,1.09)	0.65(0.42,1.01)
Missing	58/23			36/11		
Log-additive		***0.86(0.75,0.99)***	***0.85(0.73,1.00)***		0.88(0.73,1.07)	0.86(0.71,1.05)
Dominant	218/119	0.91(0.73,1.13)	0.95(0.75,1.21)	138/70	0.95(0.71,1.26)	0.98(0.72,1.31)
Recessive	58/48	***0.69(0.52,0.91)***	***0.62(0.46,0.85)***	30/24	0.69(0.47,1.02)	***0.60(0.40,0.90)***
RAN rs14035						
CC	171/73	1.00	1.00	97/49	1.00	1.00
CT	145/88	0.81(0.65,1.01)	0.84(0.67,1.05)	92/43	1.09(0.82,1.45)	1.12(0.83,1.50)
TT	28/20	0.74(0.50,1.11)	0.74(0.49,1.12)	14/11	0.77(0.44,1.34)	0.75(0.42,1.34)
Missing	62/24			42/11		
Log-additive		***0.84(0.71,0.99)***	0.85(0.71,1.01)		0.97(0.78,1.20)	0.97(0.78,1.21)
Dominant	173/108	***0.80(0.64,0.98)***	0.82(0.66,1.02)	106/54	1.03(0.78,1.36)	1.05(0.79,1.40)
Recessive	28/20	0.82(0.56,1.21)	0.81(0.54,1.21)	14/11	0.74(0.43,1.27)	0.71(0.41,1.25)
DICER1 rs3742330						
AA	272/150	1.00	1.00	171/90	1.00	1.00
AG	71/28	1.19(0.91,1.55)	1.18(0.90,1.56)	39/13	1.17(0.82,1.67)	1.08(0.75,1.55)
GG	9/4	0.93(0.48,1.81)	0.84(0.42,1.71)	1/0	0.95(0.13,6.79)	1.19(0.15,9.24)
Missing	54/23			34/11		
Log-additive		1.09(0.89,1.34)	1.07(0.85,1.34)		1.15(0.82,1.60)	1.08(0.77,1.53)
Dominant	80/32	1.15(0.90,1.48)	1.14(0.87,1.49)	40/13	1.17(0.82,1.65)	1.08(0.76,1.55)
Recessive	9/4	0.90(0.47,1.75)	0.80(0.40,1.62)	1/0	0.93(0.13,6.61)	1.18(0.15,9.08)
AGO2 rs4961280						
CC	233/132	1.00	1.00	131/68	1.00	1.00
CA	99/42	1.09(0.86,1.38)	1.21(0.94,1.54)	63/30	0.96(0.71,1.29)	1.06(0.78,1.45)

SNP	Overall			Caucasians		
	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	10/5	1.12(0.59,2.11)	1.45(0.76,2.79)	8/2	1.42(0.70,2.90)	***2.18(1.03,4.59)***
Missing	64/26			43/14		
Log-additive		1.08(0.89,1.32)	1.20(0.98,1.49)		1.04(0.80,1.34)	1.18(0.91,1.55)
Dominant	109/47	1.09(0.87,1.37)	1.22(0.96,1.55)	71/32	0.99(0.74,1.33)	1.12(0.83,1.51)
Recessive	10/5	1.09(0.58,2.05)	1.36(0.71,2.59)	8/2	1.44(0.71,2.92)	***2.13(1.02,4.44)***
GEMIN3 rs197412						
TT	119/56	1.00	1.00	76/41	1.00	1.00
TC	163/89	0.99(0.78,1.25)	1.08(0.84,1.38)	108/52	1.16(0.87,1.56)	1.27(0.94,1.73)
CC	67/34	0.98(0.73,1.33)	1.08(0.79,1.50)	24/10	1.10(0.69,1.74)	1.12(0.69,1.79)
Missing	57/26			37/11		
Log-additive		0.99(0.86,1.15)	1.05(0.89,1.22)		1.08(0.88,1.33)	1.11(0.90,1.37)
Dominant	230/123	0.99(0.79,1.23)	1.08(0.85,1.36)	132/62	1.15(0.87,1.52)	1.24(0.92,1.67)
Recessive	67/34	0.99(0.76,1.29)	1.04(0.78,1.38)	24/10	1.01(0.66,1.55)	0.98(0.63,1.51)
GEMIN4 rs7813						
CC	161/81	1.00	1.00	74/39	1.00	1.00
CT	132/69	0.97(0.77,1.23)	0.89(0.70,1.14)	95/42	1.14(0.84,1.54)	1.08(0.79,1.48)
TT	46/25	0.97(0.70,1.34)	0.93(0.66,1.30)	33/16	1.04(0.69,1.57)	1.08(0.71,1.64)
Missing	67/30			43/17		
Log-additive		0.98(0.84,1.14)	0.94(0.80,1.11)		1.04(0.86,1.26)	1.04(0.85,1.28)
Dominant	178/94	0.97(0.79,1.20)	0.90(0.72,1.13)	128/58	1.11(0.84,1.48)	1.08(0.80,1.45)
Recessive	46/25	0.98(0.72,1.34)	0.98(0.71,1.35)	33/16	0.97(0.67,1.41)	1.03(0.70,1.51)
GEMIN4 rs2740348						
CC	241/141	1.00	1.00	135/79	1.00	1.00
CG	88/34	***1.38(1.08,1.76)***	***1.33(1.03,1.71)***	60/20	***1.49(1.10,2.03)***	***1.63(1.18,2.26)***
GG	8/4	1.12(0.56,2.27)	1.27(0.62,2.59)	6/2	1.50(0.66,3.41)	2.01(0.87,4.67)
Missing	69/26			44/13		
Log-additive		***1.25(1.03,1.54)***	***1.25(1.01,1.55)***		***1.39(1.08,1.78)***	***1.55(1.18,2.03)***
Dominant	96/38	***1.35(1.07,1.72)***	***1.32(1.03,1.69)***	66/22	***1.50(1.11,2.01)***	***1.66(1.21,2.28)***
Recessive	8/4	1.04(0.52,2.10)	1.18(0.58,2.40)	6/2	1.35(0.60,3.04)	1.70(0.74,3.91)
miRNA downstream						
CDK6 rs42031						

SNP	Overall			Caucasians		
	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	247/133	1.00	1.00	135/67	1.00	1.00
AT	87/40	1.02(0.80,1.30)	0.99(0.77,1.27)	60/29	1.02(0.75,1.38)	0.98(0.72,1.34)
TT	13/3	1.12(0.63,2.00)	0.97(0.54,1.76)	11/2	1.28(0.67,2.44)	1.18(0.61,2.29)
Missing	59/29			39/16		
Log-additive		1.03(0.85,1.26)	0.99(0.81,1.21)		1.07(0.84,1.36)	1.03(0.81,1.31)
Dominant	100/43	1.03(0.82,1.30)	0.99(0.78,1.26)	71/31	1.05(0.79,1.40)	1.01(0.75,1.35)
Recessive	13/3	1.12(0.63,1.99)	0.97(0.54,1.76)	11/2	1.28(0.68,2.41)	1.19(0.62,2.28)
TP53INP1 rs896849						
TT	233/113	1.00	1.00	148/69	1.00	1.00
TC	103/57	0.96(0.76,1.21)	1.05(0.82,1.35)	57/32	0.93(0.69,1.27)	1.06(0.77,1.47)
CC	13/14	0.59(0.34,1.03)	***0.53(0.29,0.98)***	3/1	1.06(0.34,3.32)	1.07(0.33,3.41)
Missing	57/21			37/12		
Log-additive		0.87(0.73,1.05)	0.89(0.73,1.10)		0.95(0.72,1.26)	1.05(0.79,1.41)
Dominant	116/71	0.90(0.72,1.12)	0.97(0.76,1.25)	60/33	0.94(0.70,1.27)	1.06(0.77,1.46)
Recessive	13/14	0.60(0.34,1.04)	***0.52(0.29,0.94)***	3/1	1.08(0.35,3.38)	1.05(0.33,3.35)
CXCL12 rs1804429						
TT	318/167	1.00	1.00	190/99	1.00	1.00
TG	30/14	1.00(0.69,1.46)	1.10(0.74,1.62)	18/2	***1.75(1.08,2.84)***	***2.26(1.34,3.82)***
GG	2/1	0.91(0.23,3.67)	0.78(0.19,3.26)	1/0	1.17(0.16,8.39)	0.84(0.10,7.01)
Missing	56/23			36/13		
Log-additive		0.99(0.71,1.38)	1.04(0.74,1.45)		***1.54(1.02,2.34)***	***1.76(1.11,2.81)***
Dominant	32/15	1.00(0.69,1.43)	1.07(0.73,1.56)	19/2	***1.71(1.06,2.74)***	***2.12(1.27,3.56)***
Recessive	2/1	0.91(0.23,3.66)	0.78(0.19,3.24)	1/0	1.13(0.16,8.06)	0.74(0.09,6.15)
E2F2 rs2075993						
GG	118/66	1.00	1.00	51/27	1.00	1.00
GA	155/75	1.10(0.87,1.40)	1.10(0.85,1.42)	103/47	1.13(0.81,1.58)	1.13(0.80,1.59)
AA	75/42	0.96(0.72,1.29)	0.98(0.72,1.33)	55/29	0.96(0.65,1.41)	1.02(0.69,1.51)
Missing	58/22			36/11		
Log-additive		0.99(0.86,1.14)	1.00(0.86,1.16)		0.98(0.81,1.18)	1.01(0.83,1.22)
Dominant	230/117	1.05(0.84,1.31)	1.06(0.83,1.35)	158/76	1.06(0.78,1.46)	1.09(0.79,1.51)
Recessive	75/42	0.91(0.71,1.18)	0.92(0.71,1.21)	55/29	0.89(0.65,1.21)	0.94(0.69,1.30)

SNP	Overall			Caucasians		
	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
DOCK4 rs3801790						
AA	147/86	1.00	1.00	92/53	1.00	1.00
AG	163/74	1.15(0.92,1.44)	1.16(0.92,1.46)	96/38	1.14(0.85,1.51)	1.14(0.84,1.54)
GG	40/22	1.07(0.75,1.52)	1.10(0.77,1.59)	20/10	1.11(0.68,1.80)	1.19(0.72,1.95)
Missing	56/23			37/13		
Log-additive		1.07(0.92,1.25)	1.08(0.92,1.27)		1.08(0.88,1.33)	1.11(0.89,1.37)
Dominant	203/96	1.13(0.92,1.40)	1.15(0.92,1.43)	116/48	1.13(0.86,1.49)	1.15(0.86,1.53)
Recessive	40/22	1.00(0.72,1.39)	1.02(0.73,1.44)	20/10	1.04(0.66,1.65)	1.11(0.69,1.79)
IL6R rs4072391						
CC	216/118	1.00	1.00	135/69	1.00	1.00
CT	116/59	1.01(0.81,1.27)	1.06(0.84,1.33)	67/29	1.06(0.79,1.43)	1.12(0.83,1.51)
TT	15/5	1.17(0.69,1.98)	1.20(0.70,2.04)	5/4	0.67(0.28,1.65)	0.68(0.27,1.68)
Missing	59/23			38/12		
Log-additive		1.04(0.86,1.25)	1.07(0.89,1.30)		0.98(0.76,1.25)	1.01(0.78,1.29)
Dominant	131/64	1.03(0.83,1.28)	1.07(0.86,1.34)	72/33	1.02(0.77,1.36)	1.07(0.80,1.43)
Recessive	15/5	1.17(0.70,1.96)	1.17(0.69,1.99)	5/4	0.66(0.27,1.61)	0.66(0.27,1.61)
HIF1A						
HIF1A rs2057482						
CC	235/119	1.00	1.00	147/68	1.00	1.00
CT	100/50	1.06(0.84,1.34)	1.16(0.91,1.48)	52/31	0.88(0.64,1.21)	1.01(0.72,1.41)
TT	14/12	0.76(0.45,1.31)	0.75(0.43,1.31)	10/2	1.41(0.74,2.67)	1.43(0.73,2.81)
Missing	57/24			36/13		
Log-additive		0.97(0.81,1.16)	1.01(0.84,1.22)		1.00(0.78,1.29)	1.09(0.85,1.41)
Dominant	114/62	1.01(0.81,1.26)	1.08(0.86,1.37)	62/33	0.93(0.69,1.26)	1.06(0.78,1.45)
Recessive	14/12	0.75(0.44,1.28)	0.72(0.42,1.25)	10/2	1.46(0.77,2.75)	1.43(0.73,2.79)
HIF1A rs2301113						
AA	154/84	1.00	1.00	106/55	1.00	1.00
AC	128/62	1.12(0.89,1.42)	1.24(0.97,1.58)	72/40	1.00(0.74,1.35)	1.09(0.80,1.49)
CC	50/32	0.97(0.70,1.33)	1.14(0.80,1.64)	21/5	***1.61(1.01,2.58)***	***1.91(1.18,3.11)***
Missing	74/27			46/14		
Log-additive		1.01(0.87,1.17)	1.11(0.94,1.31)		1.16(0.94,1.44)	***1.27(1.01,1.59)***

SNP	Overall			Caucasians		
	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Dominant	178/94	1.07(0.86,1.33)	1.21(0.96,1.53)	73/45	1.10(0.83,1.45)	1.21(0.91,1.62)
Recessive	50/32	0.92(0.68,1.25)	1.02(0.73,1.44)	21/5	***1.61(1.02,2.53)***	***1.84(1.15,2.94)***
miRNAs						
MIR-26A1 rs7372209						
CC	186/101	1.00	1.00	95/46	1.00	1.00
CT	129/68	0.97(0.78,1.22)	0.95(0.75,1.22)	90/49	0.88(0.66,1.17)	0.80(0.59,1.07)
TT	34/13	1.24(0.86,1.79)	1.29(0.87,1.90)	22/7	1.13(0.71,1.80)	1.16(0.72,1.87)
Missing	57/23			38/12		
Log-additive		1.06(0.90,1.24)	1.06(0.89,1.27)		0.99(0.80,1.23)	0.96(0.77,1.20)
Dominant	163/81	1.02(0.83,1.26)	1.01(0.80,1.27)	112/56	0.92(0.70,1.21)	0.85(0.64,1.13)
Recessive	34/13	1.25(0.88,1.79)	1.32(0.91,1.90)	22/7	1.21(0.78,1.88)	1.29(0.82,2.04)
MIR-27 rs895819						
TT	173/74	1.00	1.00	110/44	1.00	1.00
TC	128/79	0.82(0.65,1.03)	0.83(0.65,1.05)	75/43	0.82(0.61,1.10)	0.83(0.61,1.14)
CC	35/22	0.87(0.61,1.25)	0.86(0.60,1.25)	17/11	0.81(0.49,1.36)	0.74(0.44,1.24)
Missing	70/30			43/16		
Log-additive		0.89(0.76,1.05)	0.89(0.75,1.06)		0.87(0.70,1.08)	0.85(0.68,1.06)
Dominant	163/101	0.83(0.67,1.03)	0.84(0.67,1.05)	92/54	0.82(0.62,1.08)	0.81(0.61,1.09)
Recessive	35/22	0.95(0.67,1.35)	0.95(0.66,1.35)	17/11	0.89(0.54,1.46)	0.80(0.48,1.32)

* Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college and pathology types, including squamous carcinoma, adenocarcinoma and large cell carcinoma and small cell carcinoma.

Table 2.1.3 Crude and adjusted associations between selected SNPs and lung cancer survival, stratified by pathology types (NSCLC vs. SCLC)

SNP	NSCLC			SCLC		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	112/57	1.00	1.00	18/6	1.00	1.00
AC	139/68	0.99(0.77,1.27)	1.06(0.80,1.39)	21/3	1.46(0.78,2.74)	1.16(0.56,2.38)
CC	46/43	***0.65(0.46,0.91)***	***0.65(0.44,0.95)***	12/5	0.88(0.42,1.82)	0.77(0.31,1.93)
Missing	49/22			9/1		
Log-additive		***0.84(0.72,0.98)***	0.85(0.71,1.01)		0.96(0.69,1.35)	0.90(0.58,1.40)
Dominant	185/111	0.87(0.69,1.10)	0.93(0.72,1.21)	33/8	1.17(0.66,2.09)	1.02(0.51,2.04)
Recessive	46/43	***0.65(0.48,0.90)***	***0.63(0.45,0.88)***	12/5	0.73(0.38,1.39)	0.70(0.32,1.56)
RAN rs14035						
CC	148/64	1.00	1.00	23/9	1.00	1.00
CT	122/85	***0.73(0.58,0.93)***	***0.71(0.56,0.91)***	23/3	1.78(0.99,3.18)	***2.12(1.11,4.05)***
TT	25/17	0.78(0.51,1.19)	0.72(0.46,1.11)	3/3	0.54(0.16,1.81)	0.90(0.24,3.37)
Missing	51/24			11/0		
Log-additive		***0.81(0.67,0.98)***	***0.78(0.65,0.95)***		1.03(0.69,1.52)	1.33(0.84,2.11)
Dominant	147/102	***0.74(0.59,0.93)***	***0.71(0.56,0.91)***	26(53.1)	1.40(0.80,2.46)	1.85(0.99,3.47)
Recessive	25/17	0.91(0.60,1.36)	0.85(0.55,1.30)	3(6.1)	0.43(0.13,1.38)	0.65(0.18,2.39)
DICER1 rs3742330						
AA	235/138	1.00	1.00	37/12	1.00	1.00
AG	57/25	1.14(0.85,1.53)	1.16(0.85,1.58)	14/3	1.29(0.70,2.40)	1.37(0.68,2.76)
GG	9/4	0.97(0.50,1.90)	0.87(0.42,1.77)			
Missing	45/23			9/0		
Log-additive		1.07(0.85,1.34)	1.05(0.82,1.34)		1.29(0.70,2.40)	1.37(0.68,2.76)
Dominant	66/29	1.11(0.85,1.47)	1.12(0.83,1.50)	14/3	1.29(0.70,2.40)	1.37(0.68,2.76)
Recessive	9/4	0.95(0.49,1.85)	0.83(0.41,1.68)	0/0		
AGO2 rs4961280						
CC	200/119	1.00	1.00	33/13	1.00	1.00
CA	83/41	1.04(0.81,1.35)	1.15(0.88,1.50)	16/1	1.50(0.83,2.73)	2.00(0.92,4.35)

SNP	NSCLC			SCLC		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	9/5	1.07(0.55,2.08)	1.34(0.67,2.67)	1/0	7.29(0.92,58.14)	15.77(1.54,161.49)
Missing	54/25			10/1		
Log-additive		1.04(0.84,1.29)	1.15(0.92,1.44)		1.65(0.94,2.89)	***2.29(1.10,4.75)***
Dominant	92/46	1.05(0.82,1.34)	1.17(0.90,1.51)	17/1	1.58(0.88,2.83)	2.11(0.99,4.52)
Recessive	9/5	1.05(0.54,2.04)	1.28(0.65,2.52)	1/0	6.49(0.82,51.21)	11.42(1.14,114.04)
GEMIN3 rs197412						
TT	95/49	1.00	1.00	24/7	1.00	1.00
TC	142/86	0.96(0.74,1.24)	0.98(0.75,1.28)	21/3	***1.96(1.08,3.53)***	***2.40(1.23,4.66)***
CC	60/30	1.05(0.76,1.45)	1.16(0.82,1.64)	7/4	0.71(0.31,1.66)	1.11(0.41,2.97)
Missing	49/25			8/1		
Log-additive		1.02(0.86,1.20)	1.06(0.89,1.26)		0.99(0.70,1.38)	1.29(0.86,1.95)
Dominant	202/116	0.98(0.77,1.26)	1.02(0.79,1.31)	28/7	1.36(0.79,2.34)	***1.92(1.04,3.56)***
Recessive	60/30	1.08(0.81,1.43)	1.17(0.87,1.58)	7/4	0.55(0.25,1.23)	0.81(0.32,2.09)
GEMIN4 rs7813						
CC	139/75	1.00	1.00	22/6	1.00	1.00
CT	110/63	0.95(0.74,1.22)	0.90(0.69,1.17)	22/6	1.11(0.62,2.01)	1.11(0.50,2.43)
TT	39/23	0.93(0.66,1.33)	0.90(0.62,1.31)	7/2	1.28(0.55,3.00)	1.29(0.51,3.24)
Missing	58/29			9/1		
Log-additive		0.96(0.82,1.13)	0.93(0.78,1.11)		1.13(0.76,1.68)	1.13(0.72,1.78)
Dominant	149/86	0.94(0.75,1.19)	0.90(0.70,1.15)	29/8	1.15(0.66,2.00)	1.17(0.58,2.35)
Recessive	39/23	0.96(0.68,1.34)	0.95(0.67,1.35)	7/2	1.21(0.55,2.70)	1.23(0.53,2.89)
GEMIN4 rs2740348						
CC	208/127	1.00	1.00	33/14	1.00	1.00
CG	71/33	1.25(0.95,1.64)	1.21(0.91,1.60)	17/1	***2.57(1.40,4.73)***	***2.58(1.29,5.18)***
GG	7/4	1.06(0.50,2.25)	1.17(0.54,2.50)	1/0	2.67(0.36,20.03)	3.08(0.12,76.67)
Missing	60/26			9/0		
Log-additive		1.16(0.93,1.45)	1.16(0.92,1.46)		***2.23(1.33,3.75)***	***2.45(1.27,4.70)***
Dominant	78/37	1.23(0.95,1.60)	1.20(0.92,1.58)	18/1	***2.58(1.42,4.69)***	***2.60(1.31,5.16)***
Recessive	7/4	1.00(0.47,2.12)	1.12(0.52,2.39)	1/0	1.96(0.27,14.43)	2.48(0.10,62.87)
miRNA downstream						
CDK6 rs42031						

SNP	NSCLC			SCLC		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	215/123	1.00	1.00	32/10	1.00	1.00
AT	69/37	0.95(0.73,1.25)	0.94(0.71,1.25)	18/3	1.29(0.72,2.30)	1.13(0.61,2.11)
TT	11/2	1.22(0.64,2.29)	1.11(0.58,2.12)	2/1	0.67(0.16,2.78)	0.31(0.07,1.44)
Missing	51/28			8/1		
Log-additive		1.01(0.81,1.26)	0.98(0.79,1.23)		1.04(0.67,1.62)	0.81(0.50,1.30)
Dominant	80/39	0.98(0.76,1.27)	0.96(0.74,1.25)	20/4	1.18(0.67,2.06)	0.93(0.51,1.69)
Recessive	11/2	1.23(0.65,2.31)	1.13(0.59,2.15)	2/1	0.61(0.15,2.52)	0.30(0.06,1.37)
TP53INP1 rs896849						
TT	198/103	1.00	1.00	35/10	1.00	1.00
TC	87/54	0.93(0.73,1.20)	1.03(0.78,1.35)	16/3	1.19(0.66,2.16)	1.00(0.50,2.01)
CC	13/12	0.69(0.39,1.21)	0.59(0.32,1.10)	0/2		
Missing	48/21			9/0		
Log-additive		0.88(0.73,1.08)	0.90(0.72,1.12)		0.82(0.50,1.36)	0.65(0.35,1.20)
Dominant	100/66	0.89(0.70,1.14)	0.96(0.73,1.26)	16/5	0.97(0.54,1.76)	0.82(0.40,1.66)
Recessive	13/12	0.70(0.40,1.23)	0.59(0.32,1.07)	0/2		
CXCL12 rs1804429						
TT	271/155	1.00	1.00	47/12	1.00	1.00
TG	25/12	1.05(0.70,1.59)	1.30(0.85,2.01)	5/2	0.71(0.28,1.78)	0.96(0.31,2.92)
GG	2/1	0.97(0.24,3.90)	0.77(0.19,3.24)			
Missing	48/22			8/1		
Log-additive		1.04(0.73,1.48)	1.15(0.80,1.65)		0.71(0.28,1.78)	0.96(0.31,2.92)
Dominant	27/13	1.05(0.71,1.56)	1.24(0.82,1.88)	5/2	0.71(0.28,1.78)	0.96(0.31,2.92)
Recessive	2/1	0.97(0.24,3.88)	0.76(0.18,3.17)	0/0		
E2F2 rs2075993						
GG	102/59	1.00	1.00	16/7	1.00	1.00
GA	127/70	1.05(0.81,1.36)	1.03(0.78,1.35)	28/5	1.41(0.76,2.62)	1.39(0.67,2.89)
AA	67/39	0.97(0.71,1.32)	0.98(0.70,1.37)	8/3	0.97(0.41,2.26)	0.83(0.33,2.09)
Missing	50/22			8/0		
Log-additive		0.99(0.85,1.15)	0.99(0.84,1.17)		1.04(0.71,1.52)	0.95(0.62,1.45)
Dominant	194/109	1.02(0.80,1.29)	1.01(0.78,1.31)	36/8	1.28(0.71,2.31)	1.18(0.60,2.34)
Recessive	67/39	0.94(0.72,1.24)	0.97(0.73,1.28)	8/3	0.79(0.37,1.67)	0.68(0.31,1.52)

SNP	NSCLC			SCLC		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
DOCK4 rs3801790						
AA	126/78	1.00	1.00	21/8	1.00	1.00
AG	139/69	1.12(0.88,1.42)	1.12(0.87,1.44)	24/5	1.43(0.79,2.57)	1.48(0.75,2.93)
GG	33/21	0.99(0.67,1.45)	0.98(0.66,1.47)	7/1	2.01(0.85,4.75)	1.61(0.63,4.11)
Missing	48/22			8/1		
Log-additive		1.03(0.87,1.22)	1.03(0.87,1.23)		1.42(0.95,2.12)	1.32(0.86,2.01)
Dominant	172/90	1.09(0.86,1.37)	1.09(0.86,1.39)	31/6	1.53(0.88,2.66)	1.52(0.82,2.81)
Recessive	33/21	0.93(0.65,1.34)	0.92(0.63,1.35)	7/1	1.69(0.76,3.75)	1.40(0.57,3.45)
IL6R rs4072391						
CC	182/105	1.00	1.00	34/13	1.00	1.00
CT	101/57	1.00(0.79,1.28)	1.01(0.79,1.30)	15/2	1.26(0.69,2.32)	1.56(0.79,3.08)
TT	11/5	1.03(0.56,1.90)	1.02(0.55,1.90)	4/0	1.56(0.54,4.44)	4.02(0.86,18.80)
Missing	52/23			7/0		
Log-additive		1.01(0.82,1.24)	1.01(0.82,1.25)		1.25(0.81,1.93)	1.72(0.96,3.09)
Dominant	112/62	1.01(0.80,1.27)	1.01(0.79,1.29)	19/2	1.31(0.75,2.31)	1.64(0.85,3.19)
Recessive	11/5	1.03(0.56,1.88)	1.02(0.55,1.88)	4/0	1.46(0.52,4.09)	3.07(0.67,14.08)
HIF1A						
HIF1A rs2057482						
CC	196/107	1.00	1.00	39/12	1.00	1.00
CT	89/49	1.06(0.83,1.37)	1.11(0.85,1.45)	11/1	1.30(0.67,2.55)	0.70(0.29,1.68)
TT	13/10	0.85(0.49,1.50)	0.81(0.46,1.45)	1/2	0.34(0.05,2.48)	0.45(0.04,4.84)
Missing	48/24			9/0		
Log-additive		1.00(0.82,1.21)	1.00(0.82,1.23)		0.91(0.54,1.52)	0.69(0.34,1.41)
Dominant	102/59	1.03(0.81,1.31)	1.06(0.82,1.37)	12/3	1.05(0.55,2.01)	0.67(0.29,1.52)
Recessive	13/10	0.84(0.48,1.46)	0.79(0.45,1.39)	1/2	0.32(0.04,2.34)	0.47(0.04,4.98)
HIF1A rs2301113						
AA	130/75	1.00	1.00	24/9	1.00	1.00
AC	112/58	1.14(0.88,1.46)	1.20(0.92,1.57)	16/4	1.08(0.57,2.03)	1.23(0.52,2.92)
CC	42/30	0.94(0.66,1.33)	1.05(0.70,1.56)	8/2	1.21(0.54,2.69)	1.27(0.47,3.41)
Missing	62/27			12/0		
Log-additive		1.00(0.86,1.18)	1.07(0.89,1.28)		1.09(0.75,1.60)	1.14(0.71,1.84)

SNP	NSCLC			SCLC		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Dominant	154/88	1.07(0.85,1.36)	1.17(0.91,1.50)	24/6	1.12(0.63,1.97)	1.25(0.59,2.65)
Recessive	42/30	0.89(0.64,1.23)	0.95(0.65,1.38)	8/2	1.17(0.55,2.51)	1.17(0.46,2.94)
miRNAs						
MIR-26A1 rs7372209						
CC	162/91	1.00	1.00	24/10	1.00	1.00
CT	107/64	0.93(0.73,1.19)	0.94(0.73,1.23)	22/4	1.26(0.70,2.24)	0.80(0.40,1.59)
TT	27/13	1.08(0.72,1.63)	1.10(0.71,1.69)	7/0	***3.23(1.38,7.59)***	***3.84(1.35,10.90)***
Missing	50/22			7/1		
Log-additive		0.99(0.83,1.19)	1.01(0.83,1.22)		***1.60(1.05,2.43)***	1.41(0.84,2.36)
Dominant	134/77	0.96(0.76,1.20)	0.97(0.76,1.24)	29/4	1.47(0.86,2.53)	1.06(0.56,2.01)
Recessive	27/13	1.12(0.75,1.66)	1.13(0.75,1.71)	7/0	***2.92(1.30,6.55)***	***4.23(1.54,11.60)***
MIR-27 rs895819						
TT	148/69	1.00	1.00	25/5	1.00	1.00
TC	107/73	0.80(0.63,1.03)	0.80(0.62,1.03)	21/6	0.92(0.51,1.64)	1.23(0.57,2.67)
CC	30/19	0.92(0.62,1.36)	0.93(0.62,1.38)	5/3	0.59(0.23,1.55)	0.85(0.30,2.40)
Missing	61/29			9/1		
Log-additive		0.90(0.75,1.07)	0.90(0.75,1.08)		0.82(0.55,1.22)	0.97(0.61,1.56)
Dominant	137/92	0.83(0.65,1.04)	0.82(0.65,1.05)	26/9	0.83(0.48,1.44)	1.09(0.54,2.22)
Recessive	30/19	1.01(0.70,1.48)	1.03(0.70,1.51)	5/3	0.62(0.25,1.56)	0.77(0.29,2.05)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college and pathology types, including squamous carcinoma, adenocarcinoma and large cell carcinoma, if applicable.

Table 2.1.4 Crude and adjusted associations between selected SNPs and NSCLC survival, stratified by NSCLC subtypes

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Micro RNA processing and maturation									
XPO5 rs11077									
AA	14/12	1.00	1.00	64/30	1.00	1.00	25/10	1.00	1.00
AC	25/11	1.21 (0.63,2.33)	1.07 (0.49,2.35)	68/49	0.79 (0.56,1.11)	0.72 (0.49,1.06)	40/7	1.36 (0.82,2.24)	1.15 (0.62,2.14)
CC	8/14	0.53 (0.22,1.25)	0.39 (0.13,1.14)	27/22	0.71 (0.45,1.11)	***0.57 (0.35,0.94)***	7/7	0.53 (0.23,1.22)	0.42 (0.13,1.37)
Missing	6/5			27/10			13/6		
Log-additive		0.77 (0.53,1.12)	0.67 (0.41,1.10)		0.83 (0.67,1.03)	***0.75 (0.58,0.96)***		0.87 (0.63,1.19)	0.82 (0.51,1.34)
Dominant	33/25	0.92 (0.49,1.72)	0.84 (0.38,1.83)	95/71	0.76 (0.55,1.05)	***0.67 (0.46,0.97)***	47/14	1.10 (0.68,1.78)	1.05 (0.57,1.94)
Recessive	8/14	0.47 (0.22,1.00)	***0.37 (0.15,0.94)***	27/22	0.81 (0.53,1.22)	0.71 (0.46,1.10)	7/7	***0.44 (0.20,0.97)***	0.37 (0.13,1.11)
RAN rs14035									
CC	26/15	1.00	1.00	83/39	1.00	1.00	29/9	1.00	1.00
CT	16/18	0.64 (0.35,1.20)	0.65 (0.33,1.28)	67/51	***0.72 (0.52,1.00)***	***0.71 (0.51,1.00)***	33/12	0.88 (0.54,1.46)	0.99 (0.57,1.71)
TT	4/4	0.73 (0.25,2.09)	0.82 (0.24,2.79)	9/9	0.64 (0.32,1.28)	0.64 (0.32,1.30)	9/3	0.84 (0.40,1.77)	0.79 (0.34,1.86)
Missing	7/5			27/12			14/6		
Log-additive		0.75 (0.47,1.20)	0.77 (0.46,1.30)		***0.75 (0.58,0.98)***	***0.75 (0.57,0.99)***		0.91 (0.64,1.28)	0.92 (0.63,1.35)
Dominant	20/22	0.66 (0.37,1.18)	0.68 (0.36,1.28)	76/60	***0.71 (0.52,0.97)***	***0.70 (0.51,0.98)***	42/15	0.87 (0.54,1.40)	0.95 0.56,1.59)
Recessive	4/4	0.88 (0.32,2.46)	0.98 (0.30,3.25)	9/9	0.75 (0.38,1.48)	0.76 (0.38,1.52)	9/3	0.90 (0.44,1.80)	0.80 (0.36,1.78)

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
DICER1 rs3742330									
AA	40/31	1.00	1.00	123/80	1.00	1.00	56/22	1.00	1.00
AG	8/5	0.99 (0.46,2.11)	1.15 (0.51,2.60)	29/18	1.04 (0.69,1.57)	1.10 (0.70,1.72)	18/2	1.52 (0.89,2.60)	1.50 (0.77,2.89)
GG	0/1			8/2	1.33 (0.65,2.71)	1.29 (0.59,2.80)	0/0	-	-
Missing	5/5			26/11			11/6		
Log-additive		0.83 (0.41,1.67)	0.99 (0.47,2.11)		1.10 (0.83,1.47)	1.12 (0.81,1.54)		1.52 (0.89,2.60)	1.50 (0.77,2.89)
Dominant	8/6	0.89 (0.42,1.91)	1.06 (0.48,2.37)	37/20	1.10 (0.76,1.59)	1.14 (0.75,1.72)	18/2	1.52 (0.89,2.60)	1.50 (0.77,2.89)
Recessive	0/1			8/2	1.32 (0.65,2.68)	1.25 (0.58,2.69)	0/0	-	-
AGO2 rs4961280									
CC	30/27	1.00	1.00	105/65	1.00	1.00	49/21	1.00	1.00
CA	12/10	1.01 (0.51,1.96)	1.22 (0.53,2.78)	48/28	1.01 (0.72,1.42)	1.05 (0.74,1.49)	20/3	1.19 (0.70,2.00)	1.10 (0.61,2.00)
AA	1/0	1.78 (0.24,13.12)	1.97 (0.22,17.68)	5/5	0.74 (0.30,1.82)	0.81 (0.32,2.04)	3/0	***3.93 (1.20,12.89)***	3.23 (0.73,14.27)
Missing	10/5			28/13			13/6		
Log-additive		1.08 (0.59,1.96)	1.28 (0.64,2.55)		0.95 (0.72,1.26)	0.99 (0.74,1.32)		1.41 (0.90,2.20)	1.29 (0.77,2.16)
Dominant	13/10	1.04 (0.54,2.00)	1.27 (0.58,2.81)	53/33	0.98 (0.70,1.36)	1.02 (0.73,1.44)	23/3	1.30 (0.79,2.14)	1.19 (0.67,2.12)
Recessive	1/0	1.78 (0.24,12.98)	1.92 (0.21,17.11)	5/5	0.74 (0.30,1.81)	0.79 (0.32,1.99)	3/0	***3.74 (1.15,12.15)***	3.11 (0.72,13.45)
GEMIN3 rs197412									
TT	16/10	1.00	1.00	53/32	1.00	1.00	22/6	1.00	1.00
TC	21/17	0.90 (0.47,1.73)	1.35 (0.65,2.80)	76/50	1.00 (0.70,1.42)	1.06 (0.74,1.52)	33/16	0.82 (0.48,1.40)	0.79 (0.44,1.41)

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
CC	10/10	0.79 (0.36,1.74)	1.08 (0.43,2.74)	30/17	1.03 (0.66,1.62)	1.32 (0.80,2.19)	17/1	1.62 (0.86,3.05)	1.38 (0.64,2.99)
Missing	6/5			27/12			13/7		
Log-additive		0.89 (0.60,1.31)	1.07 (0.68,1.66)		1.01 (0.81,1.26)	1.13 (0.88,1.45)		1.23 (0.86,1.75)	1.12 (0.75,1.68)
Dominant	31/27	0.86 (0.47,1.58)	1.27 (0.63,2.54)	106/67	1.01 (0.72,1.40)	1.11 (0.78,1.57)	50/17	0.98 (0.60,1.62)	0.88 (0.50,1.53)
Recessive	10/10	0.84 (0.42,1.69)	0.90 (0.40,1.99)	30/17	1.04 (0.70,1.54)	1.28 (0.82,1.99)	17/1	***1.83 (1.06,3.16)***	1.64 (0.86,3.13)
GEMIN4 rs7813									
CC	22/17	1.00	1.00	78/45	1.00	1.00	31/12	1.00	1.00
CT	16/16	0.83 (0.43,1.58)	0.97 (0.46,2.05)	62/37	0.97 (0.70,1.36)	0.83 (0.57,1.20)	26/7	1.13 (0.67,1.91)	1.23 (0.70,2.17)
TT	7/2	1.14 (0.49,2.67)	1.21 (0.49,2.94)	15/17	0.62 (0.36,1.08)	***0.53 (0.30,0.94)***	13/2	***1.97 (1.03,3.77)***	***3.43 (1.48,7.95)***
Missing	8/7			31/12			15/9		
Log-additive		1.00 (0.66,1.53)	1.07 (0.70,1.65)		0.85 (0.67,1.06)	***0.76 (0.59,0.97)***		1.35 (0.97,1.87)	***1.63 (1.10,2.42)***
Dominant	23/18	0.90 (0.50,1.62)	1.05 (0.55,2.02)	77/54	0.87 (0.64,1.20)	0.74 (0.52,1.05)	39/9	1.32 (0.82,2.11)	1.52 (0.90,2.55)
Recessive	7/2	1.24 (0.55,2.78)	1.22 (0.52,2.87)	15/17	0.63 (0.37,1.07)	0.58 (0.34,1.00)	13/2	***1.87 (1.02,3.42)***	***3.14 (1.41,6.99)***
GEMIN4 rs2740348									
CC	30/31	1.00	1.00	114/76	1.00	1.00	50/17	1.00	1.00
CG	11/5	1.48 (0.74,2.96)	1.14 (0.52,2.50)	38/20	1.29 (0.90,1.87)	1.14 (0.77,1.68)	18/5	1.16 (0.67,1.98)	1.52 (0.78,2.95)
GG	2/0	2.90 (0.69,12.19)	1.16 (0.20,6.72)	3/4	0.62 (0.20,1.95)	0.68 (0.21,2.19)	2/0	3.17 (0.75,13.35)	3.35 (0.68,16.49)
Missing	10/6			31/11			15/8		
Log-additive		1.58	1.11		1.08	1.02		1.30	1.63

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.92,2.71)	(0.62,2.01)		(0.80,1.45)	(0.74,1.41)		(0.81,2.09)	(0.95,2.78)
Dominant	13/5	1.60 (0.84,3.07)	1.15 (0.56,2.36)	41/24	1.20 (0.84,1.71)	1.09 (0.74,1.58)	20/5	1.23 (0.73,2.07)	1.65 (0.88,3.09)
Recessive	2/0	2.64 (0.64,10.98)	1.16 (0.20,6.67)	3/4	0.58 (0.19,1.83)	0.66 (0.21,2.10)	2/0	3.05 (0.73,12.78)	3.17 (0.65,15.46)
miRNA downstream									
CDK6 rs42031									
AA	38/28	1.00	1.00	108/73	1.00	1.00	53/18	1.00	1.00
AT	8/7	0.77 (0.36,1.65)	0.70 (0.31,1.56)	42/24	1.07 (0.75,1.52)	1.04 (0.72,1.50)	16/5	0.88 (0.50,1.54)	0.81 (0.44,1.49)
TT	0/1	-	-	7/0	1.94 (0.85,4.42)	2.01 (0.85,4.77)	4/0	1.15 (0.41,3.18)	1.15 (0.38,3.42)
Missing	7/6			29/14			12/7		
Log-additive		0.68 (0.33,1.40)	***0.48 (0.24,0.97)***		1.18 (0.87,1.58)	1.16 (0.85,1.58)		0.97 (0.64,1.47)	0.93 (0.60,1.47)
Dominant	8/8	0.71 (0.33,1.52)	0.51 (0.23,1.15)	49/24	1.13 (0.80,1.59)	1.10 (0.77,1.56)	20/5	0.92 (0.55,1.54)	0.86 (0.49,1.51)
Recessive	0/1	-	-	7/0	1.90 (0.84,4.32)	1.99 (0.85,4.67)	4/0	1.18 (0.43,3.25)	1.21 (0.41,3.57)
TP53INP1 rs896849									
TT	26/22	1.00	1.00	106/60	1.00	1.00	52/16	1.00	1.00
TC	19/14	1.11 (0.61,2.00)	0.93 (0.48,1.79)	43/35	0.82 (0.57,1.17)	0.96 (0.66,1.40)	20/5	1.19 (0.71,2.00)	1.40 (0.77,2.53)
CC	1/1	1.20 (0.16,8.86)	0.74 (0.07,7.77)	11/6	0.93 (0.50,1.73)	1.06 (0.53,2.12)	1/4	0.18 (0.03,1.31)	0.15 (0.02,1.20)
Missing	7/5			26/10			12/5		
Log-additive		1.11 (0.65,1.89)	0.91 (0.50,1.68)		0.90 (0.69,1.16)	1.00 (0.75,1.33)		0.81 (0.54,1.22)	0.85 (0.52,1.40)
Dominant	20/15	1.11 (0.62,1.99)	0.92 (0.48,1.77)	54/41	0.84 (0.60,1.17)	0.97 (0.68,1.40)	21/9	0.94 (0.57,1.56)	1.13 (0.62,2.05)

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Recessive	1/1	1.15 (0.16,8.37)	0.77 (0.08,7.87)	11/6	0.99 (0.54,1.82)	1.08 (0.55,2.11)	1/4	0.17 (0.02,1.25)	0.13 (0.02,1.00)
CXCL12 rs1804429									
TT	43/31	1.00	1.00	145/97	1.00	1.00	66/22	1.00	1.00
TG	3/5	0.58 (0.18,1.85)	0.94 (0.22,4.12)	14/5	1.34 (0.77,2.32)	***1.85 (1.04,3.29)***	7/1	1.11 (0.51,2.43)	1.01 (0.40,2.56)
GG	1/1	0.93 (0.13,6.72)	1.16 (0.13,10.67)	0/0	-	-	0/0	-	-
Missing	6/5			27/9			12/7		
Log-additive		0.74 (0.32,1.69)	1.02 (0.40,2.60)		1.34 (0.77,2.32)	***1.85 (1.04,3.29)***		1.11 (0.51,2.43)	1.01 (0.40,2.56)
Dominant	4/6	0.64 (0.23,1.77)	1.00 (0.28,3.55)	14/5	1.34 (0.77,2.32)	***1.85 (1.04,3.29)***	7/1	1.11 (0.51,2.43)	1.01 (0.40,2.56)
Recessive	1/1	0.97 (0.13,7.04)	1.16 (0.13,10.68)	0/0	-	-	0/0	-	-
E2F2 rs2075993									
GG	17/15	1.00	1.00	58/34	1.00	1.00	20/9	1.00	1.00
GA	17/15	1.08 (0.55,2.11)	2.18 (0.96,4.93)	66/42	0.93 (0.65,1.32)	0.92 (0.62,1.36)	34/11	1.23 (0.71,2.14)	1.40 (0.72,2.69)
AA	10/7	1.32 (0.60,2.88)	***2.93 (1.05,8.20)***	36/25	0.80 (0.53,1.22)	0.83 (0.52,1.31)	19/4	1.52 (0.81,2.86)	1.92 (0.93,3.95)
Missing	9/5			26/10			12/6		
Log-additive		1.14 (0.77,1.68)	***1.74 (1.06,2.88)***		0.90 (0.73,1.10)	0.91 (0.72,1.14)		1.23 (0.90,1.69)	1.39 (0.97,1.99)
Dominant	27/22	1.15 (0.63,2.12)	***2.35 (1.08,5.10)***	102/67	0.88 (0.64,1.22)	0.89 (0.62,1.28)	53/15	1.32 (0.79,2.21)	1.57 (0.86,2.87)
Recessive	10/7	1.27 (0.63,2.57)	1.82 (0.77,4.32)	36/25	0.83 (0.57,1.21)	0.87 (0.59,1.29)	19/4	1.34 (0.80,2.27)	1.57 (0.87,2.84)
DOCK4 rs3801790									
AA	20/15	1.00	1.00	65/47	1.00	1.00	30/14	1.00	1.00

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AG	21/19	0.88 (0.48,1.63)	0.82 (0.41,1.65)	77/37	1.25 (0.90,1.74)	1.34 (0.94,1.91)	34/11	1.13 (0.69,1.85)	1.03 (0.61,1.74)
GG	6/3	1.11 (0.44,2.76)	1.11 (0.43,2.85)	17/16	0.90 (0.53,1.53)	0.82 (0.47,1.44)	10/0	1.98 (0.96,4.07)	2.13 (0.95,4.75)
Missing	6/5			27/11			11/5		
Log-additive		1.00 (0.64,1.54)	0.99 (0.63,1.55)		1.03 (0.82,1.29)	1.01 (0.80,1.28)		1.32 (0.93,1.87)	1.29 (0.88,1.91)
Dominant	27/22	0.92 (0.52,1.65)	0.90 (0.48,1.68)	94/53	1.17 (0.85,1.60)	1.21 (0.86,1.70)	44/11	1.25 (0.79,1.99)	1.17 (0.71,1.93)
Recessive	6/3	1.18 (0.50,2.79)	1.20 (0.48,2.97)	17/16	0.80 (0.48,1.33)	0.70 (0.42,1.18)	10/0	1.86 (0.95,3.64)	2.10 (0.98,4.49)
IL6R rs4072391									
CC	26/26	1.00	1.00	95/58	1.00	1.00	46/17	1.00	1.00
CT	17/9	1.49 (0.81,2.76)	1.28 (0.66,2.47)	53/41	0.81 (0.58,1.14)	0.80 (0.56,1.14)	27/5	1.61 (1.00,2.61)	***1.89 (1.11,3.22)***
TT	2/2	1.32 (0.31,5.58)	1.07 (0.24,4.79)	8/1	1.39 (0.68,2.87)	1.36 (0.64,2.90)	1/2	0.32 (0.04,2.29)	0.29 (0.04,2.12)
Missing	8/5			30/11			11/6		
Log-additive		1.33 (0.82,2.14)	1.16 (0.69,1.96)		0.94 (0.71,1.24)	0.93 (0.69,1.25)		1.12 (0.77,1.65)	1.16 (0.78,1.73)
Dominant	19/11	1.47 (0.81,2.66)	1.25 (0.66,2.38)	61/42	0.86 (0.62,1.19)	0.85 (0.60,1.19)	28/7	1.40 (0.87,2.25)	1.53 (0.92,2.53)
Recessive	2/2	1.15 (0.28,4.76)	0.96 (0.22,4.16)	8/1	1.51 (0.74,3.08)	1.49 (0.71,3.13)	1/2	0.27 (0.04,1.96)	0.25 (0.03,1.82)
HIF1A									
HIF1A rs2057482									
CC	26/25	1.00	1.00	108/63	1.00	1.00	50/17	1.00	1.00
CT	19/9	1.52 (0.84,2.77)	1.21 (0.63,2.32)	45/30	0.93 (0.66,1.32)	0.93 (0.64,1.34)	20/7	1.35 (0.81,2.28)	1.64 (0.91,2.93)
TT	1/2	0.66	0.92	7/7	0.70	0.66	3/0	1.66	1.38

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.09,4.85)	(0.09,9.37)		(0.33,1.50)	(0.30,1.45)		(0.52,5.35)	(0.38,4.95)
Missing	7/6			26/11			12/6		
Log-additive		1.23 (0.75,2.00)	1.14 (0.63,2.06)		0.89 (0.68,1.16)	0.87 (0.66,1.15)		1.32 (0.88,1.99)	1.39 (0.91,2.13)
Dominant	20/11	1.43 (0.80,2.57)	1.19 (0.62,2.27)	52/37	0.89 (0.64,1.24)	0.88 (0.62,1.24)	23/7	1.39 (0.85,2.28)	1.59 (0.93,2.73)
Recessive	1/2	0.56 (0.08,4.09)	0.85 (0.09,8.56)	7/7	0.72 (0.34,1.53)	0.68 (0.31,1.47)	3/0	1.54 (0.48,4.92)	1.31 (0.37,4.73)
HIF1A rs2301113									
AA	15/17	1.00	1.00	71/44	1.00	1.00	36/12	1.00	1.00
AC	23/11	1.81 (0.94,3.48)	1.72 (0.78,3.79)	58/36	1.06 (0.75,1.51)	1.16 (0.81,1.66)	27/8	1.20 (0.73,1.98)	1.24 (0.72,2.14)
CC	6/7	1.15 (0.44,2.95)	1.16 (0.32,4.26)	24/17	0.92 (0.58,1.47)	1.03 (0.61,1.73)	7/5	0.76 (0.34,1.70)	1.10 (0.40,3.03)
Missing	9/7			33/14			15/5		
Log-additive		1.18 (0.80,1.76)	1.24 (0.69,2.23)		0.98 (0.79,1.22)	1.05 (0.83,1.33)		0.96 (0.69,1.34)	1.13 (0.75,1.71)
Dominant	29/18	1.61 (0.86,3.01)	1.65 (0.76,3.61)	82/53	1.02 (0.74,1.40)	1.13 (0.80,1.58)	34/13	1.07 (0.67,1.71)	1.22 (0.72,2.07)
Recessive	6/7	0.84 (0.35,1.98)	0.75 (0.24,2.38)	24/17	0.90 (0.58,1.39)	0.95 (0.58,1.55)	7/5	0.70 (0.32,1.54)	0.98 (0.37,2.60)
miRNAs									
MIR-26A1 rs7372209									
CC	25/24	1.00	1.00	86/50	1.00	1.00	38/13	1.00	1.00
CT	17/12	1.15 (0.62,2.13)	0.92 (0.46,1.85)	53/42	0.80 (0.56,1.12)	0.78 (0.54,1.12)	33/8	1.13 (0.71,1.80)	0.95 (0.56,1.61)
TT	5/1	1.72 (0.65,4.50)	1.86 (0.55,6.22)	19/8	1.24 (0.76,2.04)	1.25 (0.74,2.11)	2/4	0.31 (0.08,1.30)	0.24 (0.05,1.11)
Missing	6/5			28/11			12/5		
Log-additive		1.25	1.15		0.99	0.99		0.85	0.74

SNP	SQC			ADC			LCL		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.81,1.93)	(0.66,1.98)		(0.78,1.26)	(0.77,1.28)		(0.59,1.23)	(0.48,1.15)
Dominant	22/13	1.24 (0.70,2.21)	1.00 (0.51,1.95)	72/50	0.88 (0.64,1.21)	0.87 (0.62,1.21)	35/12	0.98 (0.62,1.55)	0.85 (0.50,1.45)
Recessive	5/1	1.62 (0.64,4.12)	1.95 (0.63,6.09)	19/8	1.36 (0.84,2.20)	1.39 (0.84,2.30)	2/4	0.30 (0.07,1.21)	0.25 (0.06,1.11)
MIR-27 rs895819									
TT	23/14	1.00	1.00	79/42	1.00	1.00	35/9	1.00	1.00
TC	16/17	0.68 (0.36,1.28)	0.61 (0.30,1.25)	57/45	0.76 (0.54,1.08)	0.73 (0.51,1.04)	30/10	1.05 (0.65,1.72)	1.17 (0.68,2.03)
CC	4/5	0.76 (0.26,2.20)	0.91 (0.27,3.05)	17/10	0.97 (0.57,1.63)	1.01 (0.59,1.73)	6/4	0.70 (0.30,1.67)	0.75 (0.29,1.97)
Missing	10/6			33/14			14/7		
Log-additive		0.78 (0.48,1.26)	0.78 (0.45,1.37)		0.90 (0.70,1.15)	0.90 (0.69,1.17)		0.91 (0.65,1.29)	0.97 (0.65,1.44)
Dominant	20/22	0.69 (0.38,1.26)	0.65 0.33,1.28)	74/55	0.80 (0.58,1.10)	0.78 (0.56,1.09)	36/14	0.97 (0.61,1.55)	1.10 (0.64,1.87)
Recessive	4/5	0.91 (0.32,2.55)	1.22 (0.39,3.82)	17/10	1.09 (0.66,1.81)	1.18 (0.70,1.96)	6/4	0.69 (0.30,1.59)	0.68 (0.28,1.68)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college.

Table 2.1.5a Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung cancer survival, in the overall population

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	130(37.4)	63(34.6)	1.00	1.00	1.00	1.00
AC	160(46.0)	71(39.0)	1.02(0.81,1.29)	1.04(0.83,1.29)	1.09(0.85,1.41)	1.11(0.88,1.40)
CC	58(16.7)	48(26.4)	***0.69(0.51,0.94)***	***0.73(0.56,0.97)***	***0.66(0.47,0.93)***	***0.71(0.52,0.96)***
Log-additive			***0.86(0.75,0.99)***	***0.87(0.75,1.00)***	***0.85(0.73,1.00)***	0.86(0.74,1.00)
Dominant	218(62.6)	119(65.4)	0.91(0.73,1.13)	0.91(0.74,1.12)	0.95(0.75,1.21)	0.95(0.76,1.20)
Recessive	58(16.7)	48(26.4)	***0.69(0.52,0.91)***	***0.72(0.56,0.93)***	***0.62(0.46,0.85)***	***0.67(0.51,0.89)***
RAN rs14035						
CC	171(49.7)	73(40.3)	1.00	1.00	1.00	1.00
CT	145(42.2)	88(48.6)	0.81(0.65,1.01)	0.83(0.67,1.02)	0.84(0.67,1.05)	0.86(0.69,1.07)
TT	28(8.1)	20(11.1)	0.74(0.50,1.11)	0.80(0.57,1.13)	0.74(0.49,1.12)	0.80(0.57,1.14)
Log-additive			***0.84(0.71,0.99)***	***0.85(0.72,1.00)***	0.85(0.71,1.01)	0.86(0.72,1.01)
Dominant	173(50.3)	108(59.7)	***0.80(0.64,0.98)***	***0.81(0.66,0.99)***	0.82(0.66,1.02)	0.83(0.68,1.03)
Recessive	28(8.1)	20(11.1)	0.82(0.56,1.21)	0.86(0.62,1.20)	0.81(0.54,1.21)	0.85(0.60,1.20)
GEMIN4 rs2740348						
CC	241(71.5)	141(78.8)	1.00	1.00	1.00	1.00
CG	88(26.1)	34(19.0)	***1.38(1.08,1.76)***	***1.33(1.05,1.67)***	***1.33(1.03,1.71)***	***1.28(1.00,1.62)***
GG	8(2.4)	4(2.2)	1.12(0.56,2.27)	1.05(0.64,1.74)	1.27(0.62,2.59)	1.11(0.67,1.85)
Log-additive			***1.25(1.03,1.54)***	***1.23(1.01,1.50)***	***1.25(1.01,1.55)***	***1.23(1.00,1.51)***
Dominant	96(28.5)	38(21.2)	***1.35(1.07,1.72)***	***1.31(1.05,1.64)***	***1.32(1.03,1.69)***	***1.28(1.01,1.62)***
Recessive	8(2.4)	4(2.2)	1.04(0.52,2.10)	1.02(0.62,1.67)	1.18(0.58,2.40)	1.08(0.65,1.79)
miRNA						

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
downstream						
TP53INP1 rs896849						
TT	233(66.8)	113(61.4)	1.00	1.00	1.00	1.00
TC	103(29.5)	57(31.0)	0.96(0.76,1.21)	0.98(0.78,1.22)	1.05(0.82,1.35)	1.07(0.84,1.35)
CC	13(3.7)	14(7.6)	0.59(0.34,1.03)	0.72(0.48,1.09)	***0.53(0.29,0.98)***	0.69(0.45,1.06)
Log-additive			0.87(0.73,1.05)	0.88(0.74,1.05)	0.89(0.73,1.10)	0.90(0.74,1.10)
Dominant	116(33.2)	71(38.6)	0.90(0.72,1.12)	0.91(0.73,1.12)	0.97(0.76,1.25)	0.98(0.77,1.23)
Recessive	13(3.7)	14(7.6)	0.60(0.34,1.04)	0.72(0.48,1.09)	***0.52(0.29,0.94)***	0.68(0.44,1.04)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college and pathology types, including squamous carcinoma, adenocarcinoma and large cell carcinoma and small cell carcinoma.

Table 2.1.5b Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung cancer survival, in the Caucasians

SNP	Death/Survival	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation					
XPO5 rs11077					
AA+AC	179/79	1.00	1.00	1.00	1.00
CC	30/24	0.69(0.47,1.02)	0.76(0.54,1.05)	***0.60(0.40,0.90)***	***0.68(0.49,0.96)***
AGO2 rs4961280					
CC+CA	194/98	1.00	1.00	1.00	1.00
AA	8/2	1.44(0.71,2.92)	1.19(0.71,1.99)	***2.13(1.02,4.44)***	1.38(0.80,2.38)
GEMIN4 rs2740348					
CC	135/79	1.00	1.00	1.00	1.00
CG+GG	66/22	***1.50(1.11,2.01)***	***1.40(1.07,1.85)***	***1.66(1.21,2.28)***	***1.52(1.14,2.03)***
miRNA downstream					
CXCL12 rs1804429					
TT	190/99	1.00	1.00	1.00	1.00
TG+GG	19/2	***1.71(1.06,2.74)***	1.43(0.95,2.15)	***2.12(1.27,3.56)***	***1.60(1.03,2.48)***
HIF1A					
HIF1A rs2301113					
AA+AC	178/95	1.00	1.00	1.00	1.00
CC	21/5	***1.61(1.02,2.53)***	1.39(0.94,2.06)	***1.84(1.15,2.94)***	***1.51(1.00,2.26)***

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college and pathology types, including squamous carcinoma, adenocarcinoma and large cell carcinoma and small cell carcinoma.

Table 2.1.6 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and NSCLC survival

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	112(37.7)	57(33.9)	1.00	1.00	1.00	1.00
AC	139(46.8)	68(40.5)	0.99(0.77,1.27)	1.01(0.80,1.27)	1.06(0.80,1.39)	1.08(0.84,1.39)
CC	46(15.5)	43(25.6)	***0.65(0.46,0.91)***	***0.70(0.52,0.95)***	***0.65(0.44,0.95)***	***0.71(0.51,0.99)***
Log-additive			***0.84(0.72,0.98)***	***0.84(0.72,0.98)***	0.85(0.71,1.01)	0.85(0.72,1.01)
Dominant	185(62.3)	111(66.1)	0.87(0.69,1.10)	0.88(0.71,1.11)	0.93(0.72,1.21)	0.94(0.73,1.20)
Recessive	46(15.5)	43(25.6)	***0.65(0.48,0.90)***	***0.70(0.53,0.93)***	***0.63(0.45,0.88)***	***0.68(0.51,0.92)***
RAN rs14035						
CC	148(50.2)	64(38.6)	1.00	1.00	1.00	1.00
CT	122(41.4)	85(51.2)	***0.73(0.58,0.93)***	***0.76(0.61,0.96)***	***0.71(0.56,0.91)***	***0.75(0.59,0.95)***
TT	25(8.5)	17(10.2)	0.78(0.51,1.19)	0.84(0.59,1.20)	0.72(0.46,1.11)	0.80(0.55,1.15)
Log-additive			***0.81(0.67,0.98)***	***0.82(0.69,0.98)***	***0.78(0.65,0.95)***	***0.80(0.66,0.96)***
Dominant	147(49.8)	102(61.4)	***0.74(0.59,0.93)***	***0.76(0.61,0.95)***	***0.71(0.56,0.91)***	***0.74(0.59,0.93)***
Recessive	25(8.5)	17(10.2)	0.91(0.60,1.36)	0.93(0.66,1.32)	0.85(0.55,1.30)	0.89(0.62,1.27)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college and pathology types, including squamous carcinoma, adenocarcinoma and large cell carcinoma.

Table 2.1.7 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and SCLC survival

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
RAN rs14035						
CC	23(46.9)	9(60.0)	1.00	1.00	1.00	1.00
CT	23(46.9)	3(20.0)	1.78(0.99,3.18)	1.46(0.93,2.27)	***2.12(1.11,4.05)***	1.51(0.95,2.42)
TT	3(6.1)	3(20.0)	0.54(0.16,1.81)	0.81(0.46,1.42)	0.90(0.24,3.37)	0.94(0.51,1.72)
Log-additive			1.03(0.69,1.52)	1.02(0.72,1.43)	1.33(0.84,2.11)	1.22(0.83,1.79)
Dominant	26(53.1)	6(40.0)	1.40(0.80,2.46)	1.23(0.79,1.90)	1.85(0.99,3.47)	1.41(0.88,2.23)
Recessive	3(6.1)	3(20.0)	0.43(0.13,1.38)	0.77(0.44,1.33)	0.65(0.18,2.39)	0.90(0.50,1.64)
AGO2 rs4961280						
CC	33(66.0)	13(92.9)	1.00	1.00	1.00	1.00
CA	16(32.0)	1(7.1)	1.50(0.83,2.73)	1.24(0.78,1.97)	2.00(0.92,4.35)	1.32(0.79,2.21)
AA	1(2.0)	0	7.29(0.92,58.14)	1.11(0.56,2.20)	15.77(1.54,161.49)	1.12(0.56,2.22)
Log-additive			1.65(0.94,2.89)	1.35(0.86,2.10)	***2.29(1.10,4.75)***	1.48(0.89,2.45)
Dominant	17(34.0)	1(7.1)	1.58(0.88,2.83)	1.30(0.82,2.05)	2.11(0.99,4.52)	1.40(0.84,2.35)
Recessive	1(2.0)	0	6.49(0.82,51.21)	1.11(0.56,2.20)	11.42(1.14,114.04)	1.11(0.56,2.22)
GEMIN3 rs197412						
TT	24(46.2)	7(50.0)	1.00	1.00	1.00	1.00
TC	21(40.4)	3(21.4)	***1.96(1.08,3.53)***	1.52(0.97,2.39)	***2.40(1.23,4.66)***	1.58(0.98,2.55)
CC	7(13.5)	4(28.6)	0.71(0.31,1.66)	0.82(0.49,1.36)	1.11(0.41,2.97)	0.98(0.56,1.71)
Log-additive			0.99(0.70,1.38)	0.99(0.73,1.34)	1.29(0.86,1.95)	1.21(0.85,1.72)
Dominant	28(53.8)	7(50.0)	1.36(0.79,2.34)	1.21(0.79,1.85)	***1.92(1.04,3.56)***	1.44(0.91,2.28)
Recessive	7(13.5)	4(28.6)	0.55(0.25,1.23)	0.76(0.46,1.26)	0.81(0.32,2.09)	0.93(0.53,1.62)
GEMIN4 rs2740348						
CC	33(64.7)	14(93.3)	1.00	1.00	1.00	1.00

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
CG	17(33.3)	1(6.7)	***2.57(1.40,4.73)***	***1.66(1.04,2.67)***	***2.58(1.29,5.18)***	1.58(0.96,2.61)
GG	1(2.0)	0	2.67(0.36,20.03)	1.07(0.54,2.09)	3.08(0.12,76.67)	1.04(0.53,2.06)
Log-additive			***2.23(1.33,3.75)***	***1.65(1.06,2.55)***	***2.45(1.27,4.70)***	1.60(0.99,2.59)
Dominant	18(35.3)	1(6.7)	***2.58(1.42,4.69)***	***1.70(1.06,2.71)***	***2.60(1.31,5.16)***	1.61(0.98,2.64)
Recessive	1(2.0)	0	1.96(0.27,14.43)	1.06(0.54,2.07)	2.48(0.10,62.87)	1.04(0.53,2.05)
miRNAs						
MIR-26A1 rs7372209						
CC	24(45.3)	10(71.4)	1.00	1.00	1.00	1.00
CT	22(41.5)	4(28.6)	1.26(0.70,2.24)	1.06(0.69,1.64)	0.80(0.40,1.59)	0.82(0.51,1.33)
TT	7(13.2)	0	***3.23(1.38,7.59)***	1.49(0.83,2.67)	***3.84(1.35,10.90)***	1.48(0.81,2.71)
Log-additive			***1.60(1.05,2.43)***	1.40(0.97,2.02)	1.41(0.84,2.36)	1.25(0.82,1.89)
Dominant	29(54.7)	4(28.6)	1.47(0.86,2.53)	1.27(0.83,1.95)	1.06(0.56,2.01)	1.03(0.65,1.65)
Recessive	7(13.2)	0	***2.92(1.30,6.55)***	1.48(0.83,2.64)	***4.23(1.54,11.60)***	1.51(0.83,2.76)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college.

Table 2.1.8 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung SQC survival

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	14(29.8)	12(32.4)	1.00	1.00	1.00	1.00
AC	25(53.2)	11(29.7)	1.21(0.63,2.33)	1.21(0.76,1.92)	1.07(0.49,2.35)	1.18(0.71,1.94)
CC	8(17.0)	14(37.8)	0.53(0.22,1.25)	0.74(0.44,1.23)	0.39(0.13,1.14)	0.72(0.41,1.26)
Log-additive			0.77(0.53,1.12)	0.82(0.59,1.14)	0.67(0.41,1.10)	0.77(0.51,1.15)
Dominant	33(70.2)	25(67.6)	0.92(0.49,1.72)	0.95(0.60,1.52)	0.84(0.38,1.83)	0.92(0.55,1.56)
Recessive	8(17.0)	14(37.8)	0.47(0.22,1.00)	0.69(0.43,1.12)	***0.37(0.15,0.94)***	0.69(0.40,1.18)
miRNA downstream						
CDK6 rs42031						
AA	38(82.6)	28(77.8)	1.00	1.00	1.00	1.00
AT	8(17.4)	7(19.4)	0.77(0.36,1.65)	0.90(0.54,1.48)	0.70(0.31,1.56)	0.87(0.52,1.46)
TT	0	1(2.8)	-	0.91(0.47,1.76)		0.75(0.40,1.42)
Log-additive			0.68(0.33,1.40)	0.83(0.51,1.33)	***0.48(0.24,0.97)***	0.68(0.43,1.08)
Dominant	8(17.4)	8(22.2)	0.71(0.33,1.52)	0.86(0.52,1.41)	0.51(0.23,1.15)	0.74(0.45,1.23)
Recessive	0	1(2.8)				
E2F2 rs2075993						
GG	17(38.6)	15(40.5)	1.00	1.00	1.00	1.00
GA	17(38.6)	15(40.5)	1.08(0.55,2.11)	1.01(0.63,1.61)	2.18(0.96,4.93)	1.26(0.77,2.09)
AA	10(22.7)	7(18.9)	1.32(0.60,2.88)	1.13(0.67,1.88)	***2.93(1.05,8.20)***	1.32(0.75,2.32)
Log-additive			1.14(0.77,1.68)	1.11(0.79,1.55)	***1.74(1.06,2.88)***	1.44(0.97,2.16)
Dominant	27(61.4)	22(59.5)	1.15(0.63,2.12)	1.08(0.69,1.71)	***2.35(1.08,5.10)***	1.47(0.89,2.45)
Recessive	10(22.7)	7(18.9)	1.27(0.63,2.57)	1.13(0.68,1.86)	1.82(0.77,4.32)	1.26(0.73,2.18)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college.

Table 2.1.9 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and lung ADC cancer

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	64(40.3)	30(29.7)	1.00	1.00	1.00	1.00
AC	68(42.8)	49(48.5)	0.79(0.56,1.11)	0.84(0.62,1.14)	0.72(0.49,1.06)	0.82(0.59,1.14)
CC	27(17.0)	22(21.8)	0.71(0.45,1.11)	0.80(0.55,1.15)	***0.57(0.35,0.94)***	0.71(0.48,1.05)
Log-additive			0.83(0.67,1.03)	0.84(0.68,1.04)	***0.75(0.58,0.96)***	***0.78(0.61,0.98)***
Dominant	95(59.7)	71(70.3)	0.76(0.55,1.05)	0.80(0.60,1.07)	***0.67(0.46,0.97)***	0.73(0.53,1.02)
Recessive	27(17.0)	22(21.8)	0.81(0.53,1.22)	0.85(0.60,1.21)	0.71(0.46,1.10)	0.78(0.54,1.13)
RAN rs14035						
CC	83(52.2)	39(39.4)	1.00	1.00	1.00	1.00
CT	67(42.1)	51(51.5)	***0.72(0.52,1.00)***	0.78(0.58,1.04)	***0.71(0.51,1.00)***	0.78(0.57,1.05)
TT	9(5.7)	9(9.1)	0.64(0.32,1.28)	0.80(0.50,1.28)	0.64(0.32,1.30)	0.81(0.50,1.31)
Log-additive			***0.75(0.58,0.98)***	***0.78(0.61,1.00)***	***0.75(0.57,0.99)***	0.78(0.60,1.01)
Dominant	76(47.8)	60(60.6)	***0.71(0.52,0.97)***	***0.75(0.57,1.00)***	***0.70(0.51,0.98)***	0.75(0.56,1.01)
Recessive	9(5.7)	9(9.1)	0.75(0.38,1.48)	0.86(0.54,1.37)	0.76(0.38,1.52)	0.87(0.54,1.40)
GEMIN4 rs7813						
CC	78(50.3)	45(45.5)	1.00	1.00	1.00	1.00
CT	62(40.0)	37(37.4)	0.97(0.70,1.36)	1.00(0.74,1.35)	0.83(0.57,1.20)	0.90(0.65,1.24)
TT	15(9.7)	17(17.2)	0.62(0.36,1.08)	0.74(0.49,1.12)	***0.53(0.30,0.94)***	0.68(0.45,1.04)
Log-additive			0.85(0.67,1.06)	0.86(0.69,1.07)	***0.76(0.59,0.97)***	***0.78(0.62,0.99)***
Dominant	77(49.7)	54(54.5)	0.87(0.64,1.20)	0.89(0.67,1.19)	0.74(0.52,1.05)	0.79(0.58,1.08)
Recessive	15(9.7)	17(17.2)	0.63(0.37,1.07)	0.74(0.50,1.11)	0.58(0.34,1.00)	0.71(0.47,1.07)
miRNA downstream						
CXCL12 rs1804429						
TT	145(91.2)	97(95.1)	1.00	1.00	1.00	1.00

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
TG	14(8.8)	5(4.9)	1.34(0.77,2.32)	1.19(0.77,1.86)	***1.85(1.04,3.29)***	1.42(0.89,2.26)
GG	0	0	-	1.00(0.50,2.00)		
Log-additive			1.34(0.77,2.32)	1.19(0.77,1.86)	***1.85(1.04,3.29)***	1.42(0.89,2.26)
Dominant	14(8.8)	5(4.9)	1.34(0.77,2.32)	1.19(0.77,1.86)	***1.85(1.04,3.29)***	1.42(0.89,2.26)
Recessive	0	0				

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college.

Table 2.1.10 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and LCL survival

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	25(34.7)	10(41.7)	1.00	1.00	1.00	1.00
AC	40(55.6)	7(29.2)	1.36(0.82,2.24)	1.30(0.88,1.94)	1.15(0.62,2.14)	1.18(0.76,1.85)
CC	7(9.7)	7(29.2)	0.53(0.23,1.22)	0.73(0.44,1.21)	0.42(0.13,1.37)	0.77(0.43,1.37)
Log-additive			0.87(0.63,1.19)	0.89(0.66,1.19)	0.82(0.51,1.34)	0.88(0.59,1.30)
Dominant	47(65.3)	14(58.3)	1.10(0.68,1.78)	1.06(0.72,1.58)	1.05(0.57,1.94)	1.03(0.65,1.63)
Recessive	7(9.7)	7(29.2)	***0.44(0.20,0.97)***	0.68(0.42,1.09)	0.37(0.13,1.11)	0.74(0.42,1.30)
AGO2 rs4961280						
CC	49(68.1)	21(87.5)	1.00	1.00	1.00	1.00
CA	20(27.8)	3(12.5)	1.19(0.70,2.00)	1.09(0.72,1.65)	1.10(0.61,2.00)	1.03(0.66,1.61)
AA	3(4.2)	0	***3.93(1.20,12.89)***	1.28(0.67,2.45)	3.23(0.73,14.27)	1.19(0.62,2.28)
Log-additive			1.41(0.90,2.20)	1.27(0.87,1.86)	1.29(0.77,2.16)	1.18(0.78,1.79)
Dominant	23(31.9)	3(12.5)	1.30(0.79,2.14)	1.19(0.79,1.79)	1.19(0.67,2.12)	1.11(0.71,1.73)
Recessive	3(4.2)	0	***3.74(1.15,12.15)***	1.28(0.66,2.45)	3.11(0.72,13.45)	1.19(0.62,2.28)
GEMIN3 rs197412						
TT	22(30.6)	6(26.1)	1.00	1.00	1.00	1.00
TC	33(45.8)	16(69.6)	0.82(0.48,1.40)	0.83(0.55,1.24)	0.79(0.44,1.41)	0.82(0.54,1.25)
CC	17(23.6)	1(4.4)	1.62(0.86,3.05)	1.34(0.84,2.14)	1.38(0.64,2.99)	1.21(0.73,2.00)
Log-additive			1.23(0.86,1.75)	1.18(0.86,1.61)	1.12(0.75,1.68)	1.09(0.77,1.54)
Dominant	50(69.4)	17(73.9)	0.98(0.60,1.62)	0.99(0.66,1.49)	0.88(0.50,1.53)	0.92(0.60,1.43)
Recessive	17(23.6)	1(4.4)	***1.83(1.06,3.16)***	1.44(0.92,2.25)	1.64(0.86,3.13)	1.30(0.81,2.10)
GEMIN4 rs7813						
CC	31(44.3)	12(57.1)	1.00	1.00	1.00	1.00
CT	26(37.1)	7(33.3)	1.13(0.67,1.91)	1.02(0.68,1.54)	1.23(0.70,2.17)	1.05(0.68,1.60)

SNP	Death N (%)	Survival N (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
TT	13(18.6)	2(9.5)	***1.97(1.03,3.77)***	1.41(0.87,2.30)	***3.43(1.48,7.95)***	1.61(0.93,2.78)
Log-additive			1.35(0.97,1.87)	1.28(0.95,1.72)	***1.63(1.10,2.42)***	***1.45(1.03,2.04)***
Dominant	39(55.7)	9(42.9)	1.32(0.82,2.11)	1.21(0.82,1.78)	1.52(0.90,2.55)	1.31(0.86,1.98)
Recessive	13(18.6)	2(9.5)	***1.87(1.02,3.42)***	1.41(0.87,2.27)	***3.14(1.41,6.99)***	1.60(0.93,2.75)
miRNA downstream						
IL6R rs4072391						
CC	46(62.2)	17(70.8)	1.00	1.00	1.00	1.00
CT	27(36.5)	5(20.8)	1.61(1.00,2.61)	1.41(0.94,2.10)	***1.89(1.11,3.22)***	1.52(0.99,2.33)
TT	1(1.4)	2(8.3)	0.32(0.04,2.29)	0.81(0.44,1.49)	0.29(0.04,2.12)	0.80(0.44,1.47)
Log-additive			1.12(0.77,1.65)	1.10(0.78,1.54)	1.16(0.78,1.73)	1.12(0.79,1.59)
Dominant	28(37.8)	7(29.2)	1.40(0.87,2.25)	1.25(0.84,1.86)	1.53(0.92,2.53)	1.32(0.87,1.99)
Recessive	1(1.4)	2(8.3)	0.27(0.04,1.96)	0.79(0.44,1.45)	0.25(0.03,1.82)	0.78(0.43,1.43)

* Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, and education level as high school, college and beyond college.

Section IV

Table 2.2.1 Crude and adjusted associations between selected SNPs and UADT cancer survival

SNP	Death* (%)	Survival* (%)	Crude HR (95% CI)	Adjusted** HR (95% CI)
Micro RNA processing and maturation				
XPO5 rs11077				
AA	72(37.9)	112(41.8)	1.00	1.00
AC	82(43.2)	110(41.0)	1.14(0.83,1.57)	1.14(0.82,1.59)
CC	36(19.0)	46(17.2)	1.20(0.81,1.80)	1.27(0.82,1.97)
Missing	58(23)	85(24)		
Log-additive			1.10(0.91,1.34)	1.13(0.92,1.40)
Dominant	118(62.1)	156(58.2)	1.16(0.86,1.56)	1.18(0.86,1.60)
Recessive	36(19.0)	46(17.2)	1.12(0.78,1.61)	1.18(0.80,1.75)
RAN rs14035				
CC	88(47.1)	130(48.3)	1.00	1.00
CT	83(44.4)	108(40.2)	1.08(0.80,1.46)	0.95(0.70,1.29)
TT	16(8.6)	31(11.5)	0.78(0.46,1.33)	0.78(0.45,1.34)
Missing	61(25)	84(24)		
Log-additive			0.95(0.77,1.18)	0.91(0.72,1.14)
Dominant	99(52.9)	139(51.7)	1.02(0.76,1.36)	0.92(0.68,1.23)
Recessive	16(8.6)	31(11.5)	0.75(0.45,1.26)	0.80(0.47,1.34)
DICER1 rs3742330				
AA	150(79.4)	217(79.5)	1.00	1.00
AG	39(20.6)	52(19.1)	0.98(0.69,1.41)	0.85(0.57,1.27)
GG	0	4(1.5)		
Missing	59(24)	80(23)		
Log-additive			0.89(0.63,1.24)	0.76(0.52,1.11)
Dominant	39(20.6)	56(20.5)	0.93(0.65,1.33)	0.81(0.54,1.20)
Recessive	0	4(1.5)		
AGO2 rs4961280				
CC	124(66.0)	183(68.0)	1.00	1.00
CA	59(31.4)	77(28.6)	1.07(0.78,1.46)	1.07(0.77,1.47)
AA	5(2.7)	9(3.4)	0.96(0.39,2.35)	1.10(0.43,2.77)

SNP	Death* (%)	Survival* (%)	Crude HR (95% CI)	Adjusted** HR (95% CI)
Missing	60(24)	84(24)		
Log-additive			1.04(0.80,1.35)	1.06(0.80,1.40)
Dominant	64(34.0)	86(32.0)	1.06(0.78,1.43)	1.07(0.78,1.46)
Recessive	5(2.7)	9(3.4)	0.94(0.39,2.28)	1.07(0.43,2.68)
GEMIN3 rs197412				
TT	59(31.1)	80(29.4)	1.00	1.00
TC	89(46.8)	129(47.4)	0.95(0.68,1.33)	0.83(0.59,1.17)
CC	42(22.1)	63(23.2)	0.94(0.63,1.40)	0.80(0.53,1.21)
Missing	58(23)	81(23)		
Log-additive			0.97(0.79,1.18)	0.89(0.72,1.10)
Dominant	131(68.9)	192(70.6)	0.95(0.70,1.29)	0.82(0.59,1.13)
Recessive	42(22.1)	63(23.2)	0.97(0.69,1.37)	0.90(0.63,1.29)
GEMIN4 rs7813				
CC	81(43.6)	112(41.8)	1.00	1.00
CT	80(43.0)	118(44.0)	0.99(0.72,1.34)	1.10(0.80,1.53)
TT	25(13.4)	38(14.2)	0.92(0.59,1.44)	1.07(0.67,1.72)
Missing	62(25)	85(24)		
Log-additive			0.97(0.79,1.19)	1.05(0.84,1.31)
Dominant	105(56.5)	156(58.2)	0.97(0.72,1.30)	1.10(0.80,1.49)
Recessive	25(13.4)	38(14.2)	0.93(0.61,1.41)	1.02(0.66,1.57)
GEMIN4 rs2740348				
CC	142(75.1)	194(72.9)	1.00	1.00
CG	42(22.2)	67(25.2)	0.90(0.64,1.28)	1.01(0.71,1.44)
GG	5(2.7)	5(1.9)	1.24(0.51,3.03)	1.37(0.55,3.41)
Missing	59(24)	87(25)		
Log-additive			0.97(0.72,1.29)	1.06(0.79,1.43)
Dominant	47(24.9)	72(27.1)	0.93(0.67,1.29)	1.04(0.74,1.46)
Recessive	5(2.7)	5(1.9)	1.27(0.52,3.10)	1.36(0.55,3.39)
miRNA downstream				
CDK6 rs42031				
AA	139(72.4)	187(69.5)	1.00	1.00
AT	47(24.5)	73(27.1)	0.90(0.65,1.26)	0.87(0.62,1.23)
TT	6(3.1)	9(3.4)	0.88(0.39,2.00)	0.88(0.38,2.01)

SNP	Death* (%)	Survival* (%)	Crude HR (95% CI)	Adjusted** HR (95% CI)
Missing	56(22)	84(24)		
Log-additive			0.92(0.70,1.20)	0.89(0.67,1.19)
Dominant	53(27.6)	82(30.5)	0.90(0.66,1.24)	0.87(0.63,1.21)
Recessive	6(3.1)	9(3.4)	0.91(0.40,2.05)	0.91(0.40,2.09)
TP53INP1 rs896849				
TT	122(64.6)	182(66.4)	1.00	1.00
TC	54(28.6)	78(28.5)	1.03(0.75,1.42)	1.05(0.75,1.47)
CC	13(6.9)	14(5.1)	1.24(0.70,2.20)	1.05(0.56,1.98)
Missing	59(24)	79(22)		
Log-additive			1.08(0.85,1.36)	1.04(0.81,1.33)
Dominant	67(35.4)	92(33.6)	1.07(0.79,1.44)	1.05(0.77,1.44)
Recessive	13(6.9)	14(5.1)	1.23(0.70,2.16)	1.03(0.55,1.92)
CXCL12 rs1804429				
TT	173(90.6)	249(91.9)	1.00	1.00
TG	18(9.4)	21(7.8)	1.18(0.72,1.91)	1.17(0.71,1.94)
GG	0	1(0.4)		
Missing	57(23)	82(23)		
Log-additive			1.09(0.68,1.75)	1.10(0.67,1.79)
Dominant	18(9.4)	22(8.1)	1.14(0.70,1.85)	1.14(0.69,1.89)
Recessive	0	1(0.4)		
E2F2 rs2075993				
GG	67(35.6)	84(31.0)	1.00	1.00
GA	83(44.2)	131(48.3)	0.82(0.60,1.14)	0.89(0.63,1.27)
AA	38(20.2)	56(20.7)	0.86(0.57,1.28)	0.96(0.62,1.50)
Missing	60(24)	82(23)		
Log-additive			0.91(0.74,1.11)	0.97(0.78,1.22)
Dominant	121(64.4)	187(69.0)	0.83(0.62,1.12)	0.91(0.65,1.27)
Recessive	38(20.2)	56(20.7)	0.96(0.67,1.38)	1.04(0.71,1.52)
DOCK4 rs3801790				
AA	73(38.4)	114(41.6)	1.00	1.00
AG	95(50.0)	113(41.2)	1.25(0.92,1.70)	1.21(0.88,1.66)
GG	22(11.6)	47(17.2)	0.76(0.47,1.23)	0.66(0.40,1.09)
Missing	58(23)	79(22)		

SNP	Death* (%)	Survival* (%)	Crude HR (95% CI)	Adjusted** HR (95% CI)
Log-additive			0.96(0.79,1.17)	0.91(0.73,1.12)
Dominant	117(61.6)	160(58.4)	1.12(0.83,1.50)	1.06(0.78,1.44)
Recessive	22(11.6)	47(17.2)	0.68(0.43,1.06)	***0.60(0.38,0.95)***
IL6R rs4072391				
CC	112(60.2)	161(60.1)	1.00	1.00
CT	63(33.9)	89(33.2)	1.02(0.75,1.39)	1.08(0.79,1.49)
TT	11(5.9)	18(6.7)	0.89(0.48,1.66)	0.96(0.51,1.81)
Missing	62(25)	85(24)		
Log-additive			0.98(0.78,1.24)	1.03(0.81,1.31)
Dominant	74(39.8)	107(39.9)	1.00(0.74,1.34)	1.06(0.78,1.44)
Recessive	11(5.9)	18(6.7)	0.88(0.48,1.63)	0.93(0.50,1.74)
HIF1A				
HIF1A rs2057482				
CC	138(73.4)	183(68.0)	1.00	1.00
CT	44(23.4)	77(28.6)	0.82(0.59,1.16)	0.77(0.54,1.09)
TT	6(3.2)	9(3.4)	1.02(0.45,2.30)	1.09(0.47,2.50)
Missing	60(24)	84(24)		
Log-additive			0.89(0.67,1.17)	0.85(0.64,1.14)
Dominant	50(26.6)	86(32.0)	0.84(0.61,1.17)	0.80(0.57,1.11)
Recessive	6(3.2)	9(3.4)	1.07(0.47,2.41)	1.16(0.51,2.66)
HIF1A rs2301113				
AA	92(50.8)	127(49.8)	1.00	1.00
AC	63(34.8)	89(34.9)	1.02(0.74,1.41)	0.89(0.64,1.25)
CC	26(14.4)	39(15.3)	0.93(0.60,1.44)	0.73(0.45,1.19)
Missing	67(27)	98(28)		
Log-additive			0.98(0.80,1.20)	0.86(0.69,1.08)
Dominant	89(49.2)	128(50.2)	0.99(0.74,1.33)	0.85(0.62,1.16)
Recessive	26(14.4)	39(15.3)	0.92(0.61,1.40)	0.77(0.48,1.23)
miRNAs				
MIR-26A1 rs7372209				
CC	103(54.5)	155(57.4)	1.00	1.00
CT	74(39.2)	90(33.3)	1.21(0.90,1.63)	1.18(0.85,1.64)
TT	12(6.4)	25(9.3)	0.79(0.43,1.44)	0.77(0.41,1.45)

SNP	Death* (%)	Survival* (%)	Crude HR (95% CI)	Adjusted** HR (95% CI)
Missing	59(24)	83(24)		
Log-additive			1.02(0.82,1.27)	1.00(0.78,1.27)
Dominant	86(45.5)	115(42.6)	1.13(0.85,1.50)	1.10(0.80,1.51)
Recessive	12(6.4)	25(9.3)	0.73(0.41,1.31)	0.71(0.39,1.32)
MIR-27 rs895819				
TT	72(38.9)	121(45.2)	1.00	1.00
TC	88(47.6)	116(43.3)	1.21(0.88,1.65)	1.23(0.89,1.70)
CC	25(13.5)	31(11.6)	1.27(0.81,2.01)	1.37(0.84,2.23)
Missing	63(25)	85(24)		
Log-additive			1.15(0.93,1.42)	1.18(0.95,1.49)
Dominant	113(61.1)	147(54.9)	1.22(0.91,1.64)	1.25(0.92,1.72)
Recessive	25(13.5)	31(11.6)	1.15(0.76,1.76)	1.21(0.77,1.90)

*The proportions of genotypes were among nonmissing only.

**Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college and pathology types, including squamous carcinoma and adenocarcinoma.

Table 2.2.2a Crude and adjusted associations between selected SNPs and UADT SQC survival, both in the overall population and in the Caucasians

SNP	Overall			Caucasians		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	47/95	1.00	1.00	26/53	1.00	1.00
AC	63/91	1.33(0.91,1.94)	1.30(0.88,1.92)	40/55	1.41(0.86,2.31)	1.43(0.87,2.35)
CC	31/41	1.46(0.93,2.30)	1.48(0.91,2.42)	11/25	0.94(0.46,1.90)	1.05(0.51,2.17)
Missing	54/75			26/44		
Log-additive		1.22(0.98,1.52)	1.23(0.96,1.56)		1.04(0.77,1.41)	1.10(0.80,1.52)
Dominant	94/132	1.37(0.97,1.95)	1.35(0.93,1.95)	51/80	1.27(0.79,2.04)	1.33(0.83,2.15)
Recessive	31/41	1.26(0.84,1.87)	1.27(0.83,1.95)	11/25	0.77(0.41,1.46)	0.86(0.44,1.67)
RAN rs14035						
CC	70/110	1.00	1.00	40/68	1.00	1.00
CT	56/91	0.95(0.67,1.35)	0.86(0.60,1.23)	31/53	0.96(0.60,1.54)	0.92(0.57,1.49)
TT	12/27	0.71(0.38,1.30)	0.70(0.37,1.31)	4/13	0.54(0.19,1.50)	0.67(0.23,1.92)
Missing	57/74			28/43		
Log-additive		0.88(0.69,1.13)	0.84(0.65,1.10)		0.84(0.59,1.21)	0.87(0.60,1.28)
Dominant	68/118	0.90(0.64,1.25)	0.83(0.59,1.16)	35/66	0.88(0.56,1.39)	0.89(0.56,1.41)
Recessive	12/27	0.72(0.40,1.30)	0.75(0.41,1.38)	4/13	0.55(0.20,1.50)	0.69(0.24,1.95)
DICER1 rs3742330						
AA	110/187	1.00	1.00	68/117	1.00	1.00
AG	30/41	1.11(0.74,1.67)	0.89(0.57,1.39)	11/19	0.89(0.47,1.68)	0.71(0.36,1.40)
GG	0/4			0/1	-	-
Missing	55/70			24/40		
Log-additive		0.97(0.66,1.41)	0.75(0.49,1.14)		0.83(0.45,1.54)	0.62(0.33,1.17)
Dominant	30/45	1.04(0.70,1.56)	0.82(0.52,1.28)	11/20	0.86(0.45,1.62)	0.65(0.33,1.28)
Recessive	0/4			0/1	-	-
AGO2 rs4961280						
CC	98/155	1.00	1.00	54/95	1.00	1.00
CA	39/65	0.94(0.65,1.37)	1.02(0.69,1.49)	22/34	1.07(0.65,1.75)	0.99(0.60,1.64)

SNP	Overall			Caucasians		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	2/8	0.48(0.12,1.94)	0.57(0.14,2.37)	1/5	0.44(0.06,3.15)	0.32(0.04,2.41)
Missing	56/74			26/43		
Log-additive		0.87(0.63,1.21)	0.94(0.67,1.32)		0.94(0.61,1.45)	0.85(0.55,1.33)
Dominant	41/73	0.90(0.63,1.30)	0.98(0.67,1.43)	23/39	1.00(0.62,1.63)	0.91(0.55,1.50)
Recessive	2/8	0.49(0.12,1.96)	0.56(0.14,2.35)	1/5	0.43(0.06,3.07)	0.32(0.04,2.41)
GEMIN3 rs197412						
TT	42/66	1.00	1.00	31/43	1.00	1.00
TC	65/109	0.96(0.65,1.41)	0.79(0.52,1.18)	36/63	0.81(0.50,1.30)	0.74(0.45,1.21)
CC	34/56	0.97(0.62,1.53)	0.72(0.44,1.15)	11/31	0.54(0.27,1.07)	***0.48(0.24,0.96)***
Missing	54/71			25/40		
Log-additive		0.98(0.78,1.24)	0.84(0.66,1.07)		0.75(0.55,1.03)	***0.70(0.51,0.97)***
Dominant	99/165	0.96(0.67,1.38)	0.76(0.52,1.11)	47/94	0.72(0.46,1.14)	0.66(0.41,1.05)
Recessive	34/56	1.00(0.68,1.47)	0.84(0.56,1.25)	11/31	0.61(0.32,1.15)	0.57(0.30,1.08)
GEMIN4 rs7813						
CC	65/92	1.00	1.00	28/51	1.00	1.00
CT	56/100	0.84(0.59,1.20)	0.97(0.67,1.43)	34/57	1.12(0.68,1.85)	1.14(0.67,1.94)
TT	16/35	0.69(0.40,1.19)	0.74(0.41,1.31)	12/27	0.84(0.43,1.66)	0.80(0.40,1.60)
Missing	58/75			29/42		
Log-additive		0.83(0.65,1.06)	0.89(0.69,1.15)		0.95(0.70,1.30)	0.93(0.67,1.28)
Dominant	72/135	0.80(0.57,1.12)	0.91(0.64,1.31)	46/84	1.03(0.65,1.65)	1.02(0.40,1.68)
Recessive	16/35	0.75(0.45,1.26)	0.75(0.44,1.28)	12/27	0.79(0.43,1.47)	0.74(0.40,1.40)
GEMIN4 rs2740348						
CC	110/166	1.00	1.00	57/95	1.00	1.00
CG	28/54	0.82(0.54,1.24)	0.92(0.60,1.41)	17/34	0.89(0.52,1.52)	0.93(0.54,1.62)
GG	2/5	0.66(0.16,2.66)	0.95(0.23,3.94)	2/3	1.10(0.27,4.51)	1.48(0.35,6.27)
Missing	55/77			27/45		
Log-additive		0.81(0.57,1.17)	0.93(0.64,1.36)		0.94(0.59,1.48)	1.01(0.63,1.63)
Dominant	30/59	0.80(0.54,1.20)	0.92(0.61,1.39)	19/37	0.90(0.54,1.52)	0.97(0.57,1.65)
Recessive	2/5	0.69(0.17,2.77)	0.97(0.23,4.00)	2/3	1.13(0.28,4.62)	1.51(0.36,6.34)
miRNA downstream						
CDK6 rs42031						

SNP	Overall			Caucasians		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	108/160	1.00	1.00	53/88	1.00	1.00
AT	32/60	0.84(0.57,1.25)	0.81(0.54,1.22)	23/40	0.96(0.59,1.56)	0.93(0.56,1.56)
TT	3/8	0.60(0.19,1.87)	0.67(0.21,2.13)	3/7	0.73(0.23,2.33)	0.67(0.21,2.17)
Missing	52/74			24/42		
Log-additive		0.82(0.59,1.14)	0.81(0.57,1.16)		0.91(0.62,1.35)	0.88(0.59,1.32)
Dominant	35/68	0.81(0.56,1.19)	0.80(0.54,1.19)	26/47	0.93(0.58,1.48)	0.89(0.55,1.46)
Recessive	3/8	0.62(0.20,1.95)	0.71(0.22,2.26)	3/7	0.74(0.23,2.34)	0.69(0.22,2.19)
TP53INP1 rs896849						
TT	90/151	1.00	1.00	56/86	1.00	1.00
TC	40/68	0.99(0.68,1.43)	0.96(0.65,1.40)	18/46	0.65(0.38,1.10)	0.64(0.38,1.10)
CC	10/14	1.14(0.59,2.18)	0.84(0.41,1.72)	3/6	0.84(0.26,2.69)	0.71(0.21,2.37)
Missing	55/69			26/39		
Log-additive		1.03(0.79,1.35)	0.93(0.70,1.24)		0.74(0.48,1.14)	0.72(0.46,1.11)
Dominant	50/82	1.01(0.72,1.43)	0.93(0.65,1.34)	21/52	0.67(0.41,1.11)	0.65(0.39,1.08)
Recessive	10/14	1.14(0.60,2.17)	0.85(0.42,1.73)	3/6	0.95(0.30,3.02)	0.81(0.24,2.66)
CXCL12 rs1804429						
TT	130/212	1.00	1.00	75/128	1.00	1.00
TG	12/19	1.08(0.60,1.95)	1.47(0.79,2.73)	3/8	0.68(0.22,2.16)	0.71(0.21,2.36)
GG	0/0			0/0		
Missing	53/71			25/41		
Log-additive		1.08(0.60,1.95)	1.47(0.79,2.73)		0.68(0.22,2.16)	0.71(0.21,2.36)
Dominant	12/19	1.08(0.60,1.95)	1.47(0.79,2.73)	3/8	0.68(0.22,2.16)	0.71(0.21,2.36)
Recessive	0/0			0/0		
E2F2 rs2075993						
GG	55/71	1.00	1.00	20/30	1.00	1.00
GA	63/114	0.76(0.53,1.09)	0.80(0.54,1.20)	43/76	0.85(0.50,1.44)	0.71(0.41,1.24)
AA	21/45	0.67(0.40,1.10)	0.70(0.40,1.23)	13/30	0.69(0.34,1.39)	0.52(0.25,1.08)
Missing	56/72			27/41		
Log-additive		0.80(0.63,1.02)	0.83(0.63,1.09)		0.83(0.59,1.17)	0.72(0.50,1.04)
Dominant	84/159	0.73(0.52,1.03)	0.78(0.53,1.15)	56/106	0.80(0.48,1.34)	0.66(0.38,1.13)
Recessive	21/45	0.78(0.49,1.24)	0.82(0.50,1.33)	13/30	0.78(0.43,1.41)	0.67(0.36,1.24)

SNP	Overall			Caucasians		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
DOCK4 rs3801790						
AA	56/101	1.00	1.00	35/65	1.00	1.00
AG	69/90	1.31(0.92,1.86)	1.32(0.92,1.91)	35/53	1.22(0.77,1.96)	1.17(0.72,1.88)
GG	16/42	0.73(0.42,1.27)	0.70(0.39,1.25)	8/20	0.78(0.36,1.68)	0.73(0.34,1.58)
Missing	54/69			25/39		
Log-additive		0.96(0.76,1.20)	0.94(0.74,1.20)		0.98(0.71,1.34)	0.94(0.68,1.30)
Dominant	85/132	1.14(0.81,1.59)	1.15(0.81,1.64)	43/73	1.11(0.71,1.73)	1.05(0.67,1.65)
Recessive	16/42	0.63(0.38,1.06)	0.60(0.35,1.02)	8/20	0.71(0.34,1.47)	0.68(0.32,1.42)
IL6R rs4072391						
CC	82/136	1.00	1.00	48/81	1.00	1.00
CT	47/76	1.03(0.72,1.47)	1.05(0.73,1.53)	25/43	1.02(0.63,1.65)	0.91(0.56,1.50)
TT	8/15	0.92(0.45,1.90)	0.90(0.43,1.90)	1/11	0.19(0.03,1.40)	0.16(0.02,1.18)
Missing	58/75			29/42		
Log-additive		0.99(0.75,1.30)	1.00(0.75,1.33)		0.79(0.53,1.18)	0.71(0.47,1.07)
Dominant	55/91	1.01(0.72,1.42)	1.03(0.72,1.47)	26/54	0.87(0.54,1.41)	0.78(0.48,1.27)
Recessive	8/15	0.91(0.45,1.86)	0.89(0.43,1.83)	1/11	0.19(0.03,1.38)	0.17(0.02,1.21)
HIF1A						
HIF1A rs2057482						
CC	100/155	1.00	1.00	55/94	1.00	1.00
CT	35/65	0.86(0.58,1.26)	0.81(0.55,1.21)	20/34	0.99(0.59,1.64)	1.07(0.63,1.81)
TT	4/8	0.88(0.33,2.40)	0.81(0.29,2.23)	1/5	0.43(0.06,3.11)	0.45(0.06,3.28)
Missing	56/74			27/44		
Log-additive		0.88(0.64,1.22)	0.84(0.60,1.17)		0.89(0.57,1.39)	0.94(0.60,1.48)
Dominant	39/73	0.86(0.59,1.24)	0.81(0.56,1.19)	21/39	0.93(0.56,1.54)	1.00(0.60,1.68)
Recessive	4/8	0.92(0.34,2.49)	0.86(0.31,2.35)	1/5	0.43(0.06,3.11)	0.44(0.06,3.21)
HIF1A rs2301113						
AA	67/107	1.00	1.00	44/72	1.00	1.00
AC	43/74	0.95(0.65,1.39)	0.86(0.58,1.29)	23/41	0.94(0.57,1.55)	0.90(0.53,1.52)
CC	23/35	1.00(0.62,1.60)	0.73(0.43,1.26)	7/12	0.95(0.43,2.11)	0.90(0.40,2.05)
Missing	62/86			29/52		
Log-additive		0.99(0.79,1.24)	0.86(0.66,1.10)		0.96(0.68,1.36)	0.93(0.65,1.34)

SNP	Overall			Caucasians		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Dominant	66/109	0.96(0.69,1.35)	0.82(0.57,1.18)	30/53	0.94(0.59,1.49)	0.90(0.56,1.46)
Recessive	23/35	1.02(0.65,1.59)	0.78(0.47,1.30)	7/12	0.97(0.45,2.12)	0.94(0.42,2.09)
miRNAs						
MIR-26A1 rs7372209						
CC	77/133	1.00	1.00	36/73	1.00	1.00
CT	55/77	1.21(0.86,1.71)	1.19(0.81,1.76)	36/51	1.39(0.88,2.21)	1.32(0.82,2.13)
TT	8/20	0.79(0.38,1.63)	0.78(0.37,1.67)	4/12	0.75(0.27,2.11)	0.70(0.24,2.00)
Missing	55/72			27/41		
Log-additive		1.03(0.79,1.33)	1.01(0.76,1.34)		1.09(0.77,1.54)	1.04(0.73,1.49)
Dominant	63/97	1.13(0.81,1.58)	1.12(0.77,1.62)	40/63	1.28(0.82,2.01)	1.21(0.76,1.92)
Recessive	8/20	0.73(0.36,1.49)	0.72(0.34,1.51)	4/12	0.65(0.24,1.77)	0.62(0.22,1.72)
MIR-27 rs895819						
TT	52/99	1.00	1.00	34/61	1.00	1.00
TC	64/102	1.12(0.78,1.61)	1.04(0.70,1.52)	34/62	0.96(0.60,1.54)	0.92(0.56,1.52)
CC	20/26	1.35(0.80,2.25)	1.44(0.82,2.51)	7/13	0.99(0.44,2.22)	1.18(0.52,2.70)
Missing	59/75			28/41		
Log-additive		1.15(0.90,1.47)	1.15(0.88,1.52)		0.98(0.69,1.39)	1.02(0.70,1.48)
Dominant	84/128	1.17(0.83,1.65)	1.10(0.76,1.59)	41/75	0.96(0.61,1.52)	0.96(0.60,1.54)
Recessive	20/26	1.27(0.79,2.04)	1.41(0.85,2.34)	7/13	1.01(0.46,2.19)	1.23(0.56,2.71)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.2b Crude and adjusted associations between selected SNPs and esophageal ADC

SNP	Death/ Survival	Esophageal ADC Crude HR (95% CI)	Esophageal ADC Adjusted* HR (95% CI)
Micro RNA processing and maturation			
XPO5 rs11077			
AA	19/10	1.00	1.00
AC	16/13	0.69(0.36,1.35)	0.69(0.32,1.49)
CC	4/5	0.49(0.17,1.43)	0.50(0.15,1.66)
Missing	3/4		
Log-additive		0.70(0.43,1.12)	0.70(0.41,1.19)
Dominant	20/18	0.64(0.34,1.20)	0.64(0.31,1.30)
Recessive	4/5	0.59(0.21,1.65)	0.59(0.19,1.86)
RAN rs14035			
CC	14/13	1.00	1.00
CT	22/13	1.22(0.63,2.39)	1.36(0.59,3.17)
TT	3/2	1.57(0.45,5.49)	2.08(0.48,9.01)
Missing	3/4		
Log-additive		1.24(0.73,2.11)	1.41(0.74,2.67)
Dominant	25/15	1.26(0.65,2.42)	1.45(0.64,3.26)
Recessive	3/2	1.40(0.43,4.55)	1.77(0.44,7.16)
DICER1 rs3742330			
AA	34/21	1.00	1.00
AG	5/7	0.58(0.23,1.47)	0.60(0.18,2.02)
GG	0/0		
Missing	3/4		
Log-additive		0.57(0.22,1.47)	0.60(0.18,2.01)
Dominant	5/7	0.58(0.23,1.47)	0.60(0.18,2.02)
Recessive	0/0		
AGO2 rs4961280			
CC	18/21	1.00	1.00
CA	18/7	1.66(0.86,3.20)	1.86(0.90,3.82)
AA	3/0	8.50(2.31,31.27)	8.75(1.59,48.08)

SNP	Death/ Survival	Esophageal ADC Crude HR (95% CI)	Esophageal ADC Adjusted* HR (95% CI)
Missing	3/4		
Log-additive		***2.10(1.19,3.71)***	***2.19(1.16,4.16)***
Dominant	21/7	1.86(0.98,3.50)	1.98(0.97,4.03)
Recessive	3/0	6.68(1.91,23.39)	5.69(1.11,29.18)
GEMIN3 rs197412			
TT	13/9	1.00	1.00
TC	18/16	0.87(0.43,1.79)	0.66(0.29,1.51)
CC	8/3	1.41(0.58,3.39)	1.19(0.44,3.20)
Missing	3/4		
Log-additive		1.14(0.71,1.82)	1.05(0.62,1.78)
Dominant	26/19	0.99(0.51,1.93)	0.77(0.36,1.69)
Recessive	8/3	1.52(0.70,3.32)	1.57(0.68,3.62)
GEMIN4 rs7813			
CC	12/11	1.00	1.00
CT	20/15	1.25(0.61,2.56)	1.77(0.78,4.01)
TT	7/2	1.68(0.66,4.27)	2.30(0.79,6.71)
Missing	3/4		
Log-additive		1.29(0.81,2.05)	1.55(0.93,2.58)
Dominant	27/17	1.34(0.68,2.64)	1.89(0.87,4.12)
Recessive	7/2	1.47(0.65,3.33)	1.63(0.65,4.10)
GEMIN4 rs2740348			
CC	27/19	1.00	1.00
CG	10/9	0.94(0.46,1.95)	0.98(0.41,2.39)
GG	2/0	1.81(0.43,7.67)	2.69(0.45,16.18)
Missing	3/4		
Log-additive		1.10(0.62,1.96)	1.24(0.64,2.41)
Dominant	12/9	1.02(0.52,2.02)	1.16(0.52,2.60)
Recessive	2/0	1.84(0.44,7.70)	2.69(0.45,16.19)
miRNA downstream			
CDK6 rs42031			
AA	26/16	1.00	1.00

SNP	Death/ Survival	Esophageal ADC Crude HR (95% CI)	Adjusted* HR (95% CI)
AT	11/11	0.67(0.33,1.37)	0.70(0.32,1.55)
TT	2/1	1.14(0.27,4.83)	1.24(0.25,6.16)
Missing	3/4		
Log-additive		0.81(0.45,1.45)	0.86(0.46,1.61)
Dominant	13/12	0.72(0.37,1.40)	0.76(0.36,1.60)
Recessive	2/1	1.31(0.32,5.44)	1.38(0.28,6.71)
TP53INP1 rs896849			
TT	25/22	1.00	1.00
TC	12/6	1.42(0.71,2.83)	1.47(0.69,3.13)
CC	2/0	2.80(0.65,12.10)	1.80(0.30,10.91)
Missing	3/4		
Log-additive		1.52(0.87,2.66)	1.42(0.76,2.65)
Dominant	14/6	1.52(0.79,2.94)	1.50(0.72,3.11)
Recessive	2/0	2.51(0.59,10.64)	1.56(0.27,9.13)
CXCL12 rs1804429			
TT	35/25	1.00	1.00
TG	4/2	1.02(0.36,2.87)	0.71(0.21,2.42)
GG	0/1		
Missing	3/4		
Log-additive		0.75(0.30,1.88)	0.58(0.19,1.78)
Dominant	4/3	0.83(0.30,2.35)	0.61(0.18,2.05)
Recessive	0/1		
E2F2 rs2075993			
GG	10/11	1.00	1.00
GA	16/9	1.41(0.64,3.11)	1.24(0.53,2.90)
AA	13/8	1.44(0.63,3.29)	1.72(0.67,4.43)
Missing	3/4		
Log-additive		1.19(0.80,1.77)	1.31(0.82,2.11)
Dominant	29/17	1.43(0.69,2.93)	1.40(0.65,3.03)
Recessive	13/8	1.18(0.61,2.30)	1.53(0.68,3.44)
DOCK4 rs3801790			

SNP	Death/ Survival	Esophageal ADC Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	13/10	1.00	1.00
AG	22/15	1.09(0.55,2.17)	1.39(0.60,3.22)
GG	4/3	0.87(0.28,2.67)	0.80(0.24,2.73)
Missing	3/4		
Log-additive		0.98(0.60,1.60)	0.97(0.56,1.68)
Dominant	26/18	1.05(0.54,2.05)	1.23(0.55,2.76)
Recessive	4/3	0.82(0.29,2.32)	0.65(0.22,1.95)
IL6R rs4072391			
CC	25/19	1.00	1.00
CT	12/8	1.02(0.51,2.03)	0.92(0.44,1.91)
TT	2/1	1.01(0.24,4.25)	1.01(0.21,4.78)
Missing	3/4		
Log-additive		1.01(0.59,1.73)	0.96(0.54,1.71)
Dominant	14/9	1.02(0.53,1.96)	0.93(0.46,1.87)
Recessive	2/1	1.00(0.24,4.15)	1.04(0.23,4.82)
HIF1A			
HIF1A rs2057482			
CC	29/18	1.00	1.00
CT	9/10	0.79(0.37,1.67)	0.75(0.29,1.94)
TT	1/0	1.88(0.25,13.98)	2.39(0.27,20.78)
Missing	3/4		
Log-additive		0.91(0.47,1.76)	0.94(0.40,2.19)
Dominant	10/10	0.84(0.41,1.72)	0.81(0.32,2.06)
Recessive	1/0	2.00(0.27,14.73)	2.70(0.32,22.83)
HIF1A rs2301113			
AA	19/12	1.00	1.00
AC	17/11	1.26(0.65,2.43)	1.13(0.54,2.36)
CC	2/3	0.64(0.15,2.73)	0.67(0.12,3.65)
Missing	4/6		
Log-additive		0.99(0.61,1.62)	0.98(0.54,1.79)
Dominant	19/14	1.14(0.60,2.16)	1.08(0.52,2.24)

SNP	Death/ Survival	Esophageal ADC Crude HR (95% CI)	Adjusted* HR (95% CI)
Recessive	2/3	0.57(0.14,2.39)	0.62(0.12,3.21)
miRNAs			
MIR-26A1 rs7372209			
CC	21/17	1.00	1.00
CT	15/9	1.14(0.59,2.21)	1.21(0.53,2.75)
TT	3/1	1.03(0.31,3.45)	0.89(0.16,5.07)
Missing	3/5		
Log-additive		1.06(0.66,1.73)	1.08(0.53,2.19)
Dominant	18/10	1.12(0.60,2.10)	1.20(0.53,2.74)
Recessive	3/1	0.98(0.30,3.18)	0.75(0.16,3.57)
MIR-27 rs895819			
TT	15/14	1.00	1.00
TC	20/10	1.64(0.84,3.21)	***2.64(1.17,5.99)***
CC	4/4	1.01(0.34,3.05)	2.22(0.62,8.01)
Missing	3/4		
Log-additive		1.16(0.75,1.80)	***1.75(1.02,3.00)***
Dominant	24/14	1.49(0.78,2.84)	***2.56(1.17,5.60)***
Recessive	4/4	0.79(0.28,2.21)	1.37(0.42,4.47)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.3 Crude and adjusted associations between selected SNPs and UADT SQC survival, stratified by cancer sites

	Oral and oropharyngeal			Laryngeal			Esophageal		
SNP	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Micro RNA biogenesis									
XPO5 rs11077									
AA	27/64	1.00	1.00	6/17	1.00	1.00	8/4	1.00	1.00
AC		1.46	***1.76***		1.47	1.32		0.82	0.28
	36/55	(0.89,2.40)	***(1.05,2.97)***	13/23	(0.56,3.88)	(0.38,4.54)	7/5	(0.29,2.27)	(0.04,1.90)
CC		1.37	1.42		3.07	6.02		2.15	2.24
	18/31	(0.76,2.49)	(0.76,2.66)	9/6	(1.09,8.63)	(1.46,24.89)	2/0	(0.43,10.69)	(0.22,22.53)
Missing	45/59			5/11			3/3		
Log-add		1.19	1.23		***1.78***	***2.51***		1.15	1.10
		(0.90,1.58)	(0.92,1.65)		***(1.04,3.04)***	***(1.17,5.39)***		(0.52,2.54)	(0.27,4.51)
Dominant		1.43	***1.63***		1.87	2.03		0.95	0.42
	54/86	(0.90,2.27)	***(1.01,2.65)***	22/29	(0.76,4.61)	(0.65,6.32)	9/5	(0.37,2.47)	(0.07,2.57)
Recessive		1.13	1.07		***2.39***	5.04		2.37	4.80
	18/31	(0.67,1.90)	(0.62,1.86)	9/6	***(1.08,5.30)***	(1.58,16.11)	2/0	(0.51,11.01)	(0.68,33.81)
RAN rs14035									
CC	45/77	1.00	1.00	13/22	1.00	1.00	5/2	1.00	1.00
CT		0.86	0.79		1.03	0.70		0.68	0.82
	30/61	(0.54,1.36)	(0.49,1.28)	9/14	(0.44,2.42)	(0.24,2.08)	10/8	(0.23,1.99)	(0.22,3.04)
TT		0.81	0.69		0.68	0.71		0.85	0.52
	6/12	(0.35,1.89)	(0.28,1.68)	4/10	(0.22,2.10)	(0.18,2.77)	2/1	(0.16,4.38)	(0.07,4.23)
Missing	45/59			7/11			3/1		
Log-add		0.88	0.81		0.87	0.82		0.84	0.75
		(0.62,1.25)	(0.56,1.16)		(0.52,1.44)	(0.42,1.60)		(0.36,1.94)	(0.28,1.99)
Dominant		0.85	0.77		0.89	0.71		0.70	0.79
	36/73	(0.55,1.31)	(0.49,1.21)	13/24	(0.41,1.93)	(0.26,1.91)	12/9	(0.25,2.00)	(0.21,2.91)
Recessive		0.86	0.76		0.68	0.86		1.12	0.62
	6/12	(0.38,1.98)	(0.31,1.81)	4/10	(0.23,1.96)	(0.25,2.97)	2/1	(0.26,4.89)	(0.10,3.69)
DICER1									

	Oral and oropharyngeal			Laryngeal			Esophageal		
SNP	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
rs3742330									
AA	67/126	1.00	1.00	22/39	1.00	1.00	13/10	1.00	1.00
AG		0.98	0.81		1.37	0.79		2.67	21.26
	14/25	(0.55,1.75)	(0.43,1.53)	7/7	(0.58,3.20)	(0.22,2.90)	4/0	(0.83,8.55)	(0.62,734.83)
GG	0/2	-	-	0/1			0/0		
Missing	45/56			4/10			3/2		
Log-add		0.88	0.69		1.11	0.77		2.67	21.26
		(0.51,1.52)	(0.38,1.25)		(0.51,2.40)	(0.21,2.79)		(0.83,8.55)	(0.61,734.83)
Dominant		0.93	0.74		1.25	0.78		2.67	21.26
	14/27	(0.52,1.65)	(0.39,1.40)	7/8	(0.54,2.94)	(0.21,2.88)	4/0	(0.83,8.55)	(0.62,734.83)
Recessive	0/2	-	-	0/1			0/0		
AGO2									
rs4961280									
CC	54/104	1.00	1.00	20/27	1.00	1.00	14/9	1.00	1.00
CA		1.14	1.22		0.65	0.42		1.00	1.33
	26/42	(0.72,1.82)	(0.74,2.02)	7/16	(0.28,1.54)	(0.13,1.30)	3/1	(0.29,3.51)	(0.19,9.48)
AA					0.88	1.98			
	0/5	-	-	1/2	(0.12,6.54)	(0.15,26.37)	0/0		
Missing	46/58			5/12			3/2		
Log-add		0.94	0.99		0.74	0.60		1.00	1.33
		(0.61,1.43)	(0.63,1.56)		(0.36,1.53)	(0.22,1.62)		(0.29,3.51)	(0.19,9.48)
Dominant		1.05	1.11		0.67	0.48		1.00	1.33
	26/47	(0.65,1.67)	(0.67,1.83)	8/18	(0.30,1.53)	(0.16,1.41)	3/1	(0.29,3.51)	(0.19,9.48)
Recessive					1.00	2.73			
	0/5	-	-	1/2	(0.14,7.36)	(0.23,32.07)	0/0		
GEMIN3									
rs197412									
TT	28/39	1.00	1.00	5/13	1.00	1.00	4/4	1.00	1.00
TC		0.74	0.62		1.32	0.70		1.82	2.98
	37/76	(0.45,1.21)	(0.37,1.05)	12/22	(0.47,3.75)	(0.19,2.64)	11/3	(0.58,5.76)	(0.60,14.77)
CC	15/39	0.62	***0.47***	12/12	2.03	2.11	2/1	1.59	2.63

	Oral and oropharyngeal			Laryngeal			Esophageal		
SNP	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.33,1.15)	***(0.24,0.92)***		(0.71,5.76)	(0.51,8.72)		(0.29,8.73)	(0.10,68.13)
Missing	46/55			4/10			3/4		
Log-add		0.78	***0.67***		1.45	1.83		1.35	2.23
		(0.57,1.06)	***(0.48,0.95)***		(0.87,2.41)	(0.88,3.79)		(0.65,2.82)	(0.62,8.04)
Dominant		0.70	***0.57***		1.60	0.97		1.78	2.94
	52/115	(0.44,1.11)	***(0.35,0.94)***	24/34	(0.61,4.20)	(0.28,3.36)	13/4	(0.58,5.50)	(0.62,14.07)
Recessive		0.74	0.64		1.68	2.83		1.06	1.38
	15/39	(0.42,1.30)	(0.35,1.16)	12/12	(0.80,3.52)	(1.13,7.10)	2/1	(0.24,4.65)	(0.06,33.42)
GEMIN4 rs7813									
CC	31/60	1.00	1.00	16/18	1.00	1.00	6/4	1.00	1.00
CT		1.15	1.28		0.62	0.54		0.92	1.60
	37/63	(0.71,1.85)	(0.78,2.11)	11/23	(0.29,1.33)	(0.19,1.55)	7/3	(0.31,2.73)	(0.37,6.94)
TT		0.73	0.81					1.20	1.59
	10/28	(0.36,1.48)	(0.38,1.73)	0/5			4/1	(0.34,4.27)	(0.28,8.90)
Missing	48/58			6/11			3/4		
Log-add		0.92	0.98		***0.50***	***0.36***		1.08	1.28
		(0.67,1.25)	(0.70,1.36)		***(0.25,0.99)***	***(0.14,0.90)***		(0.56,2.07)	(0.55,2.95)
Dominant		1.02	1.15		0.53	0.41		1.00	1.60
	47/91	(0.65,1.61)	(0.71,1.87)	11/28	(0.24,1.13)	(0.14,1.20)	11/4	(0.37,2.72)	(0.41,6.30)
Recessive		0.68	0.71					1.26	1.21
	10/28	(0.35,1.31)	(0.35,1.41)	0/5			4/1	(0.41,3.87)	(0.28,5.23)
GEMIN4 rs2740348									
CC	60/106	1.00	1.00	23/35	1.00	1.00	14/8	1.00	1.00
CG		0.89	1.00		0.75	0.41		1.01	1.10
	18/37	(0.53,1.51)	(0.58,1.72)	5/11	(0.29,1.98)	(0.12,1.40)	3/1	(0.29,3.52)	(0.20,6.01)
GG		0.91	1.38						
	2/4	(0.22,3.70)	(0.33,5.80)	0/1	-	-	0/0	-	-
Missing	46/62			5/10			3/3		
Log-add		0.91	1.05		0.68	0.41		1.01	1.10

SNP	Oral and oropharyngeal			Laryngeal			Esophageal		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.58,1.42)	(0.66,1.67)		(0.27,1.69)	(0.12,1.36)		(0.29,3.52)	(0.20,6.01)
Dominant		0.89	1.03		0.70	0.41		1.01	1.10
	20/41	(0.54,1.48)	(0.61,1.73)	5/12	(0.27,1.84)	(0.12,1.37)	3/1	(0.29,3.52)	(0.20,6.01)
Recessive		0.93	1.38						
	2/4	(0.23,3.79)	(0.33,5.77)	0/1	-	-	0/0	-	-
miRNA downstream									
CDK6 rs42031									
AA	60/105	1.00	1.00	25/32	1.00	1.00	12/8	1.00	1.00
AT		0.92	0.95		0.46	0.20		1.19	1.39
	20/38	(0.56,1.53)	(0.56,1.62)	4/14	(0.16,1.32)	(0.06,0.73)	5/3	(0.42,3.39)	(0.35,5.51)
TT		0.65	0.63						
	2/6	(0.16,2.68)	(0.15,2.64)	0/0	-	-	0/0	-	-
Missing	44/60			4/11			3/1		
Log-add		0.88	0.89		0.46	0.20		1.19	1.39
		(0.58,1.34)	(0.57,1.38)		(0.16,1.32)	(0.06,0.73)		(0.42,3.39)	(0.35,5.51)
Dominant		0.89	0.91		0.46	0.20		1.19	1.39
	22/44	(0.55,1.45)	(0.54,1.52)	4/14	(0.16,1.32)	(0.06,0.73)	5/3	(0.42,3.39)	(0.35,5.51)
Recessive		0.67	0.64						
	2/6	(0.16,2.72)	(0.15,2.66)	0/0	-	-	0/0	-	-
TP53INP1 rs896849									
TT	51/101	1.00	1.00	18/28	1.00	1.00	9/9	1.00	1.00
TC		1.15	1.12		0.79	0.95		1.55	1.59
	27/44	(0.72,1.84)	(0.69,1.82)	6/14	(0.31,1.98)	(0.33,2.74)	6/2	(0.55,4.36)	(0.35,7.26)
CC		0.70	0.50		1.35	1.11		3.17	14.30
	3/9	(0.22,2.24)	(0.15,1.69)	4/4	(0.46,4.00)	(0.24,5.22)	1/0	(0.38,26.41)	(0.91,223.95)
Missing	45/55			5/11			4/1		
Log-add		1.00	0.91		1.06	1.02		1.65	2.46
		(0.69,1.45)	(0.62,1.33)		(0.62,1.81)	(0.50,2.09)		(0.72,3.77)	(0.77,7.84)
Dominant	30/53	1.08	1.00	10/18	0.95	0.98	7/2	1.67	2.14

SNP	Oral and oropharyngeal			Laryngeal			Esophageal		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
		(0.69,1.70)	(0.63,1.60)		(0.44,2.05)	(0.37,2.63)		(0.62,4.49)	(0.54,8.56)
Recessive		0.67	0.48		1.45	1.14		2.73	13.05
	3/9	(0.21,2.11)	(0.15,1.61)	4/4	(0.50,4.17)	(0.26,4.93)	1/0	(0.34,21.85)	(0.87,196.34)
CXCL12 rs1804429									
TT	78/140	1.00	1.00	27/41	1.00	1.00	14/10	1.00	1.00
TG		0.51	0.74		0.63	0.84		2.56	2.33
	3/12	(0.16,1.61)	(0.23,2.41)	2/6	(0.15,2.63)	(0.17,4.29)	3/0	(0.71,9.24)	(0.31,17.51)
GG	0/0	-	-	0/0	-	-	0/0	-	-
Missing				4/10			3/2		
Log-add		0.51	0.74		0.63	0.84		2.56	2.33
	45/57	(0.16,1.61)	(0.23,2.41)		(0.15,2.63)	(0.16,4.29)		(0.71,9.24)	(0.31,17.51)
Dominant		0.51	0.74		0.63	0.84		2.56	2.33
	3/12	(0.16,1.61)	(0.23,2.41)	2/6	(0.15,2.63)	(0.17,4.29)	3/0	(0.71,9.24)	(0.31,17.51)
Recessive	0/0	-	-	0/0	-	-	0/0	-	-
E2F2 rs2075993									
GG	33/39	1.00	1.00	11/22	1.00	1.00	9/3	1.00	1.00
GA		0.63	0.71		1.01	0.82		0.72	0.53
	39/83	(0.40,1.01)	(0.42,1.19)	11/20	(0.44,2.32)	(0.25,2.71)	5/4	(0.24,2.16)	(0.11,2.48)
AA		***0.45***	0.53		1.30	1.12		0.77	0.54
	9/29	***(0.22,0.94)***	(0.24,1.19)	5/6	(0.45,3.73)	(0.23,5.45)	3/2	(0.21,2.84)	(0.10,2.82)
Missing	45/58			6/9			3/3		
Log-add		***0.66***	0.72		1.11	1.05		0.84	0.72
		(0.47,0.92)	(0.50,1.05)		(0.66,1.88)	(0.47,2.35)		(0.44,1.61)	(0.30,1.70)
Dominant		***0.59***	0.67		1.08	0.86		0.74	0.53
	48/112	***(0.38,0.92)***	(0.41,1.11)	16/26	(0.50,2.33)	(0.27,2.74)	8/6	(0.29,1.92)	(0.14,2.07)
Recessive		0.59	0.68		1.29	1.33		0.87	0.75
	9/29	(0.30,1.19)	(0.33,1.40)	5/6	(0.49,3.42)	(0.40,4.46)	3/2	(0.25,3.05)	(0.17,3.38)
DOCK4 rs3801790									

	Oral and oropharyngeal			Laryngeal			Esophageal		
SNP	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
AA	30/64	1.00	1.00	11/25	1.00	1.00	8/4	1.00	1.00
AG		1.31	1.28		1.62	1.48		1.53	5.06
	41/64	(0.82,2.10)	(0.79,2.08)	13/16	(0.72,3.61)	(0.56,3.93)	8/3	(0.57,4.10)	(0.78,32.81)
GG		0.84	0.71		1.35	2.03		0.34	0.09
	10/26	(0.41,1.72)	(0.34,1.48)	4/6	(0.43,4.22)	(0.51,8.14)	1/3	(0.04,2.75)	(0.01,1.46)
Missing	45/55			5/10			3/2		
Log-add		1.00	0.93		1.24	1.44		0.84	0.71
		(0.74,1.36)	(0.68,1.27)		(0.75,2.05)	(0.76,2.72)		(0.44,1.62)	(0.23,2.17)
Dominant		1.18	1.11		1.54	1.60		1.11	1.47
	51/90	(0.75,1.85)	(0.69,1.77)	17/22	(0.72,3.29)	(0.65,3.95)	9/6	(0.43,2.87)	(0.34,6.35)
Recessive		0.73	0.62		1.07	1.73		0.29	0.07
	10/26	(0.37,1.41)	(0.31,1.22)	4/6	(0.37,3.08)	(0.47,6.39)	1/3	(0.04,2.16)	(0.00,1.14)
IL6R rs4072391									
CC	51/97	1.00	1.00	13/25	1.00	1.00	10/5	1.00	1.00
CT		1.04	1.07		1.29	1.14		0.64	0.39
	24/45	(0.64,1.69)	(0.65,1.78)	14/18	(0.61,2.75)	(0.49,2.69)	4/3	(0.20,2.04)	(0.10,1.59)
TT		0.96	1.34					1.01	0.50
	5/10	(0.38,2.41)	(0.50,3.56)	0/3	-	-	2/0	(0.22,4.66)	(0.07,3.91)
Missing	46/57			6/11			4/4		
Log-add		1.01	1.11		0.96	0.82		0.87	0.57
		(0.71,1.44)	(0.76,1.64)		(0.50,1.82)	(0.39,1.73)		(0.41,1.86)	(0.22,1.46)
Dominant		1.03	1.11		1.15	1.02		0.73	0.42
	29/55	(0.65,1.62)	(0.69,1.79)	14/21	(0.54,2.46)	(0.43,2.42)	6/3	(0.26,2.01)	(0.12,1.46)
Recessive		0.95	1.30					1.18	0.67
	5/10	(0.38,2.35)	(0.50,3.41)	0/3	-	-	2/0	(0.27,5.22)	(0.08,5.39)
HIF1A									
HIF1A rs2057482									
CC	60/100	1.00	1.00	20/28	1.00	1.00	10/9	1.00	1.00
CT		0.72	0.76		0.76	0.68		1.75	1.06
	18/44	(0.43,1.22)	(0.44,1.32)	8/16	(0.33,1.73)	(0.27,1.72)	5/1	(0.59,5.15)	(0.25,4.44)

SNP	Oral and oropharyngeal			Laryngeal			Esophageal		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
TT		0.61	0.50					8.07	16.02
	2/6	(0.15,2.51)	(0.12,2.11)	0/2	-	-	2/0	(1.54,42.37)	(1.66,154.74)
Missing	46/59			5/11			3/2		
Log-add		0.74	0.74		0.66	0.65		***2.35***	2.39
		(0.47,1.15)	(0.47,1.16)		(0.31,1.40)	(0.27,1.57)		***(1.08,5.10)***	(0.85,6.68)
Dominant		0.71	0.72		0.69	0.66		2.20	1.87
	20/50	(0.43,1.17)	(0.42,1.22)	8/18	(0.30,1.57)	(0.26,1.64)	7/1	(0.83,5.85)	(0.49,7.10)
Recessive		0.67	0.53					6.77	15.78
	2/6	(0.16,2.72)	(0.13,2.23)	0/2	-	-	2/0	(1.36,33.81)	(1.69,147.27)
HIF1A rs2301113									
AA	42/74	1.00	1.00	11/17	1.00	1.00	6/4	1.00	1.00
AC		0.84	0.85		1.05	1.33		1.25	0.14
	23/49	(0.50,1.39)	(0.50,1.44)	10/16	(0.44,2.47)	(0.46,3.88)	5/3	(0.38,4.10)	(0.01,1.38)
CC		0.89	0.69		0.73	0.63		2.65	6.44
	12/23	(0.47,1.69)	(0.33,1.43)	5/11	(0.25,2.09)	(0.16,2.45)	5/0	(0.79,8.85)	(0.83,49.76)
Missing	49/63			7/13			4/5		
Log-add		0.92	0.84		0.88	0.87		1.61	1.99
		(0.68,1.25)	(0.60,1.17)		(0.54,1.44)	(0.47,1.63)		(0.86,3.03)	(0.66,5.96)
Dominant		0.86	0.80		0.91	1.02		1.68	1.04
	35/72	(0.55,1.34)	(0.50,1.29)	15/27	(0.42,1.99)	(0.39,2.68)	10/3	(0.61,4.67)	(0.21,5.27)
Recessive		0.95	0.73		0.71	0.56		2.41	12.10
	12/23	(0.51,1.76)	(0.36,1.48)	5/11	(0.27,1.89)	(0.16,2.02)	5/0	(0.82,7.04)	(1.62,90.41)
miRNAs									
MIR-26A1 rs7372209									
CC	38/89	1.00	1.00	18/28	1.00	1.00	12/5	1.00	1.00
CT		1.51	1.49		1.31	3.09		0.68	0.74
	35/52	(0.95,2.38)	(0.88,2.52)	10/12	(0.60,2.83)	(0.99,9.64)	5/4	(0.24,1.93)	(0.18,3.00)
TT		1.56	1.77						
	7/11	(0.70,3.49)	(0.74,4.20)	0/6	-	-	0/1	-	-

SNP	Oral and oropharyngeal			Laryngeal			Esophageal		
	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)	Death/ Survival	Crude HR (95% CI)	Adjusted* HR (95% CI)
Missing	46/57			5/11			3/2		
Log-add		1.34	1.38		0.76	0.81		0.56	0.74
		(0.97,1.86)	(0.95,2.01)		(0.41,1.40)	(0.41,1.57)		(0.22,1.44)	(0.18,3.00)
Dominant		1.51	1.53		0.95	1.25		0.59	0.74
	42/63	(0.98,2.35)	(0.93,2.54)	10/18	(0.44,2.06)	(0.48,3.26)	5/5	(0.21,1.67)	(0.18,3.00)
Recessive		1.31	1.44						
	7/11	(0.60,2.84)	(0.64,3.26)	0/6	-	-	0/1	-	-
MIR-27 rs895819									
TT	32/65	1.00	1.00	7/22	1.00	1.00	9/3	1.00	1.00
TC		0.99	0.86		2.14	1.70		0.73	1.14
	34/69	(0.61,1.60)	(0.52,1.44)	17/19	(0.89,5.18)	(0.62,4.64)	6/4	(0.26,2.07)	(0.22,5.89)
CC		1.52	1.54		1.54	3.18		0.68	0.48
	14/17	(0.81,2.85)	(0.78,3.04)	2/4	(0.32,7.43)	(0.49,20.56)	2/2	(0.15,3.19)	(0.06,3.89)
Missing	46/58			7/12			3/3		
Log-add		1.18	1.15		1.48	1.74		0.80	0.73
		(0.86,1.62)	(0.81,1.64)		(0.82,2.69)	(0.80,3.81)		(0.39,1.62)	(0.28,1.94)
Dominant		1.10	0.98		2.06	1.83		0.72	0.86
	48/86	(0.70,1.72)	(0.60,1.59)	19/23	(0.87,4.90)	(0.69,4.84)	8/6	(0.28,1.88)	(0.18,4.06)
Recessive		1.53	1.68		0.96	2.48		0.79	0.45
	14/17	(0.86,2.72)	(0.91,3.09)	2/4	(0.23,4.06)	(0.41,14.97)	2/2	(0.18,3.45)	(0.07,2.91)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.4 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and UADT cancer survival

SNP	Death (%)	Survival (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
miRNA downstream						
DOCK4 rs3801790						
AA	73(38.4)	114(41.6)	1.00	1.00	1.00	1.00
AG	95(50.0)	113(41.2)	1.25(0.92,1.70)	1.23(0.93,1.62)	1.21(0.88,1.66)	1.20(0.91,1.60)
GG	22(11.6)	47(17.2)	0.76(0.47,1.23)	0.82(0.56,1.20)	0.66(0.40,1.09)	0.75(0.51,1.11)
Log-additive			0.96(0.79,1.17)	0.96(0.80,1.17)	0.91(0.73,1.12)	0.91(0.75,1.12)
Dominant	117(61.6)	160(58.4)	1.12(0.83,1.50)	1.10(0.84,1.44)	1.06(0.78,1.44)	1.05(0.79,1.39)
Recessive	22(11.6)	47(17.2)	0.68(0.43,1.06)	0.76(0.53,1.09)	***0.60(0.38,0.95)***	0.70 (0.48, 1.01)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college and pathology types, including squamous carcinoma and adenocarcinoma.

Table 2.2.5 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and UADT SQC survival, in the Caucasians only

SNP	Death/Survival	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
miRNA downstream					
GEMIN3 rs197412					
TT	31/43	1.00	1.00	1.00	1.00
TC	36/63	0.81(0.50,1.30)	0.92(0.62,1.35)	0.74(0.45,1.21)	0.88(0.59,1.31)
CC	11/31	0.54(0.27,1.07)	0.74(0.46,1.17)	***0.48(0.24,0.96)***	0.70(0.44,1.12)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college and pathology types, including squamous carcinoma and adenocarcinoma.

Table 2.2.6 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and esophageal ADC survival

SNP	Death (%)	Survival (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
AGO2 rs4961280						
CC	18(46.2)	21(75.0)	1.00	1.00	1.00	1.00
CA	18(46.2)	7(25.0)	1.66(0.86,3.20)	1.23(0.77,1.96)	1.86(0.90,3.82)	1.23(0.75,2.02)
AA	3(7.7)	0	8.50(2.31,31.27)	1.34(0.69,2.62)	8.75(1.59,48.08)	1.27(0.66,2.46)
Log-additive			***2.10(1.19,3.71)***	1.55(1.00,2.42)	***2.19(1.16,4.16)***	1.52(0.95,2.45)
Dominant	21(53.8)	7(25.0)	1.86(0.98,3.50)	1.40(0.88,2.24)	1.98(0.97,4.03)	1.39(0.85,2.29)
Recessive	3(7.7)	0	6.68(1.91,23.39)	1.34(0.69,2.60)	5.69(1.11,29.18)	1.25(0.65,2.42)
miRNAs						
MIR-27 rs895819						
TT	15(38.5)	14(50.0)	1.00	1.00	1.00	1.00
TC	20(51.3)	10(35.7)	1.64(0.84,3.21)	1.31(0.82,2.10)	***2.64(1.17,5.99)***	1.47(0.88,2.45)
CC	4(10.3)	4(14.3)	1.01(0.34,3.05)	0.97(0.54,1.72)	2.22(0.62,8.01)	1.12(0.61,2.07)
Log-additive			1.16(0.75,1.80)	1.11(0.77,1.61)	***1.75(1.02,3.00)***	1.41(0.92,2.17)
Dominant	24(61.5)	14(50.0)	1.49(0.78,2.84)	1.24(0.78,1.98)	***2.56(1.17,5.60)***	1.53(0.92,2.54)
Recessive	4(10.3)	4(14.3)	0.79(0.28,2.21)	0.93(0.53,1.63)	1.37(0.42,4.47)	1.08(0.59,1.98)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.7 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and oral and oropharyngeal SQC survival

SNP	Death (%)	Survival (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	27(33.3)	64(42.7)	1.00	1.00	1.00	1.00
AC	36(44.4)	55(36.7)	1.46(0.89,2.40)	1.25(0.85,1.84)	***1.76(1.05,2.97)***	1.40(0.94,2.09)
CC	18(22.2)	31(20.7)	1.37(0.76,2.49)	1.15(0.74,1.80)	1.42(0.76,2.66)	1.15(0.73,1.81)
Log-additive			1.19(0.90,1.58)	1.16(0.89,1.51)	1.23(0.92,1.65)	1.20(0.91,1.56)
Dominant	54(66.7)	86(57.3)	1.43(0.90,2.27)	1.28(0.88,1.87)	***1.63(1.01,2.65)***	1.39(0.94,2.06)
Recessive	18(22.2)	31(20.7)	1.13(0.67,1.90)	1.08(0.71,1.64)	1.07(0.62,1.86)	1.04(0.67,1.61)
GEMIN3 rs197412						
TT	28(35.0)	39(25.3)	1.00	1.00	1.00	1.00
TC	37(46.3)	76(49.4)	0.74(0.45,1.21)	0.86(0.58,1.28)	0.62(0.37,1.05)	0.81(0.54,1.21)
CC	15(18.8)	39(25.3)	0.62(0.33,1.15)	0.78(0.50,1.23)	***0.47(0.24,0.92)***	0.70(0.44,1.12)
Log-additive			0.78(0.57,1.06)	0.81(0.61,1.08)	***0.67(0.48,0.95)***	***0.73(0.54,0.99)***
Dominant	52(65.0)	115(74.7)	0.70(0.44,1.11)	0.78(0.53,1.15)	***0.57(0.35,0.94)***	0.69(0.46,1.05)
Recessive	15(18.8)	39(25.3)	0.74(0.42,1.30)	0.83(0.54,1.27)	0.64(0.35,1.16)	0.77(0.50,1.19)
miRNA downstream						
E2F2 rs2075993						
GG	33(40.7)	39(25.8)	1.00	1.00	1.00	1.00
GA	39(48.2)	83(55.0)	0.63(0.40,1.01)	0.78(0.53,1.14)	0.71(0.42,1.19)	0.85(0.57,1.28)
AA	9(11.1)	29(19.2)	***0.45(0.22,0.94)***	0.70(0.43,1.13)	0.53(0.24,1.19)	0.78(0.47,1.29)
Log-additive			***0.66(0.47,0.92)***	***0.71(0.53,0.96)***	0.72(0.50,1.05)	0.78(0.56,1.08)
Dominant	48(59.3)	112(74.2)	***0.59(0.38,0.92)***	0.69(0.47,1.00)	0.67(0.41,1.11)	0.77(0.51,1.17)
Recessive	9(11.1)	29(19.2)	0.59(0.30,1.19)	0.76(0.48,1.21)	0.68(0.33,1.40)	0.82(0.51,1.34)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.8 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and laryngeal SQC survival

SNP	Death (%)	Survival (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
Micro RNA processing and maturation						
XPO5 rs11077						
AA	6(21.4)	17(37.0)	1.00	1.00	1.00	1.00
AC	13(13.0)	23(23.0)	1.47(0.56,3.88)	1.00(0.60,1.68)	1.32(0.38,4.54)	0.89(0.51,1.57)
CC	9(32.1)	6(13.0)	3.07(1.09,8.63)	1.42(0.81,2.49)	6.02(1.46,24.89)	1.50(0.82,2.75)
Log-additive			***1.78(1.04,3.04)***	1.44(0.94,2.19)	***2.51(1.17,5.39)***	1.54(0.94,2.54)
Dominant	22(78.6)	29(63.0)	1.87(0.76,4.61)	1.28(0.75,2.17)	2.03(0.65,6.32)	1.23(0.69,2.19)
Recessive	9(32.1)	6(13.0)	***2.39(1.08,5.30)***	1.42(0.82,2.46)	5.04(1.58,16.11)	1.52(0.83,2.78)
GEMIN3 rs197412						
TT	5(17.2)	13(27.7)	1.00	1.00	1.00	1.00
TC	12(41.4)	22(46.8)	1.32(0.47,3.75)	0.98(0.58,1.67)	0.70(0.19,2.64)	0.76(0.44,1.34)
CC	12(41.4)	12(25.5)	2.03(0.71,5.76)	1.27(0.74,2.17)	2.11(0.51,8.72)	1.34(0.75,2.40)
Log-additive			1.45(0.87,2.41)	1.27(0.85,1.91)	1.83(0.88,3.79)	1.34(0.81,2.20)
Dominant	24(82.8)	34(72.3)	1.60(0.61,4.20)	1.18(0.69,2.04)	0.97(0.28,3.36)	0.99(0.54,1.82)
Recessive	12(41.4)	12(25.5)	1.68(0.80,3.52)	1.27(0.76,2.12)	2.83(1.13,7.10)	1.46(0.84,2.54)
GEMIN4 rs7813						
CC	16(59.3)	18(39.1)	1.00	1.00	1.00	1.00
CT	11(40.7)	23(50.0)	0.62(0.29,1.33)	0.86(0.51,1.43)	0.54(0.19,1.55)	0.94(0.53,1.65)
TT	0	5(10.9)	-	-	-	-
Log-additive			***0.50(0.25,0.99)***	0.69(0.43,1.11)	***0.36(0.14,0.90)***	0.67(0.39,1.12)
Dominant	11(40.7)	28(60.9)	0.53(0.24,1.13)	0.75(0.45,1.24)	0.41(0.14,1.20)	0.76(0.43,1.36)
Recessive	0	5(10.9)				
miRNA downstream						
CDK6 rs42031						
AA	25(86.2)	32(69.6)	1.00	1.00	1.00	1.00

SNP	Death (%)	Survival (%)	Crude HR (95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
AT	4(13.8)	14(30.4)	0.46(0.16,1.32)	0.77(0.44,1.33)	0.20(0.06,0.73)	0.65(0.37,1.16)
TT	0	0	-	-	-	-
Log-additive			0.46(0.16,1.32)	0.77(0.44,1.33)	***0.20(0.06,0.73)***	0.65(0.37,1.16)
Dominant	4(13.8)	14(30.4)	0.46(0.16,1.32)	0.77(0.44,1.33)	0.20(0.06,0.73)	0.65(0.37,1.16)
Recessive	0	0	-	-	-	-

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Table 2.2.9 Semi-Bayesian shrinkage of crude and adjusted associations between selected SNPs and esophageal SQC survival

SNP	Death (%)	Survival (%)	Crude HR 95% CI)	Bayesian Posterior Crude HR (95% posterior limits)	Adjusted* HR (95% CI)	Bayesian Posterior Adjusted* HR (95% posterior limits)
HIF1A						
HIF1A rs2057482						
CC	10(58.8)	9(90.0)	1.00	1.00	1.00	1.00
CT	5(29.4)	1(10.0)	1.75(0.59,5.15)	1.12(0.62,2.02)	1.06(0.25,4.44)	0.98(0.53,1.82)
TT	2(11.8)	0	8.07(1.54,42.37)	1.22(0.62,2.39)	16.02(1.66,154.74)	1.21(0.62,2.39)
Log-additive			***2.35(1.08,5.10)***	1.43(0.83,2.46)	2.39(0.85,6.68)	1.31(0.73,2.34)
Dominant	7(41.2)	1(10.0)	2.20(0.83,5.85)	1.29(0.72,2.31)	1.87(0.49,7.10)	1.15(0.62,2.11)
Recessive	2(11.8)	0	6.77(1.36,33.81)	1.21(0.62,2.38)	15.78(1.69,147.27)	1.21(0.62,2.39)
HIF1A rs2301113						
AA	6(37.5)	4(57.1)	1.00	1.00	1.00	1.00
AC	5(31.3)	3(42.9)	1.25(0.38,4.10)	0.98(0.55,1.76)	0.14(0.01,1.38)	0.78(0.40,1.50)
CC	5(31.3)	0	2.65(0.79,8.85)	1.27(0.69,2.33)	6.44(0.83,49.76)	1.29(0.67,2.50)
Log-additive			1.61(0.86,3.03)	1.30(0.81,2.08)	1.99(0.66,5.96)	1.23(0.69,2.18)
Dominant	10(62.5)	3(42.9)	1.68(0.61,4.67)	1.18(0.67,2.09)	1.04(0.21,5.27)	1.01(0.53,1.90)
Recessive	5(31.3)	0	2.41(0.82,7.04)	1.27(0.69,2.33)	12.10(1.62,90.41)	1.30(0.67,2.51)

*Adjusted for age, gender, ethnicity, cell differentiation, smoking as pack-years, alcohol drinking as alcoholic drinks per day, and education level as high school, college and beyond college.

Polygenic risk score section

Table 3.1.1 Polygenic risk score and lung cancer development

Score*	Cases/Controls	Adjusted** OR (95% CI)
1 (0-3 risk alleles)	243/394	1.00
2 (4 risk alleles)	123/194	1.05(0.75,1.47)
3 (5 risk alleles)	95/164	1.00(0.70,1.44)
4 (6-10 risk alleles)	77/184	0.70(0.48,1.01)
as continuous	538/936	0.94(0.88,1.02)

*The scores are categorized by their quartiles in the controls.

**Adjusted for age, gender, education level and ethnicity and smoking.

Table 3.2.1 Polygenic risk score and UADT cancer development

Score*	Cases/Controls	Adjusted** OR (95% CI)
1 (0-3 risk alleles)	204/394	1.00
2 (4 risk alleles)	114/194	1.13(0.83,1.55)
3 (5 risk alleles)	78/164	0.94(0.67,1.34)
4 (6-10 risk alleles)	72/184	0.79(0.56,1.12)
as continuous	468/936	0.97(0.91,1.04)

*The scores are categorized by their quartiles in the controls.

**Adjusted for age, gender, education level and ethnicity, smoking and drinking.

Table 4.1.1 Polygenic risk score and lung cancer survival

Score*	Death/All	Adjusted** HR (95% CI)
1 (0-3 risk alleles)	162/243	1.00
2 (4 risk alleles)	89/123	1.19(0.91,1.55)
3 (5 risk alleles)	58/95	0.87(0.64,1.18)
4 (6-9 risk alleles)	46/77	0.87(0.62,1.21)
as continuous	355/538	0.99(0.92,1.05)

*The scores are categorized by their quartiles in the cancer cases.

**Adjusted for age, gender, education level and ethnicity, differential grades, and pathology types, and smoking.

Table 4.2.1 Polygenic risk score and UADT cancer survival

Score*	Death/All	Adjusted** HR (95% CI)
1 (0-3 risk alleles)	81/204	1.00
2 (4 risk alleles)	48/114	0.90(0.63,1.31)
3 (5 risk alleles)	36/78	1.28(0.85,1.91)
4 (6-8 risk alleles)	27/72	0.85(0.55,1.33)
as continuous	192/468	0.99(0.90,1.08)

*The scores are categorized by their quartiles in the cancer cases.

**Adjusted for age, gender, education level and ethnicity, differential grades, and pathology types, and smoking and drinking.

Figure Section I

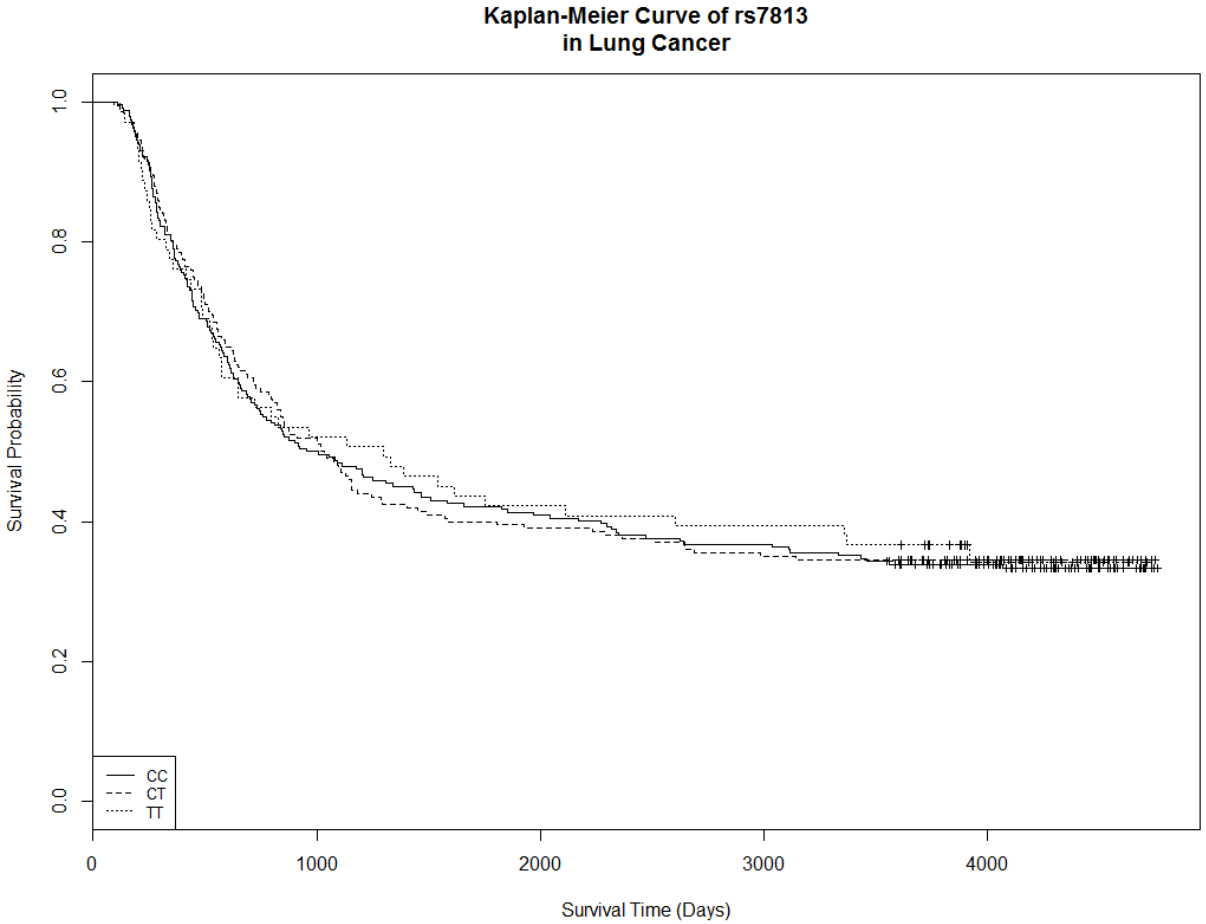

Figure 1.1 Kaplan-Meier curve of *GEMIN4* rs7813 in lung cancer

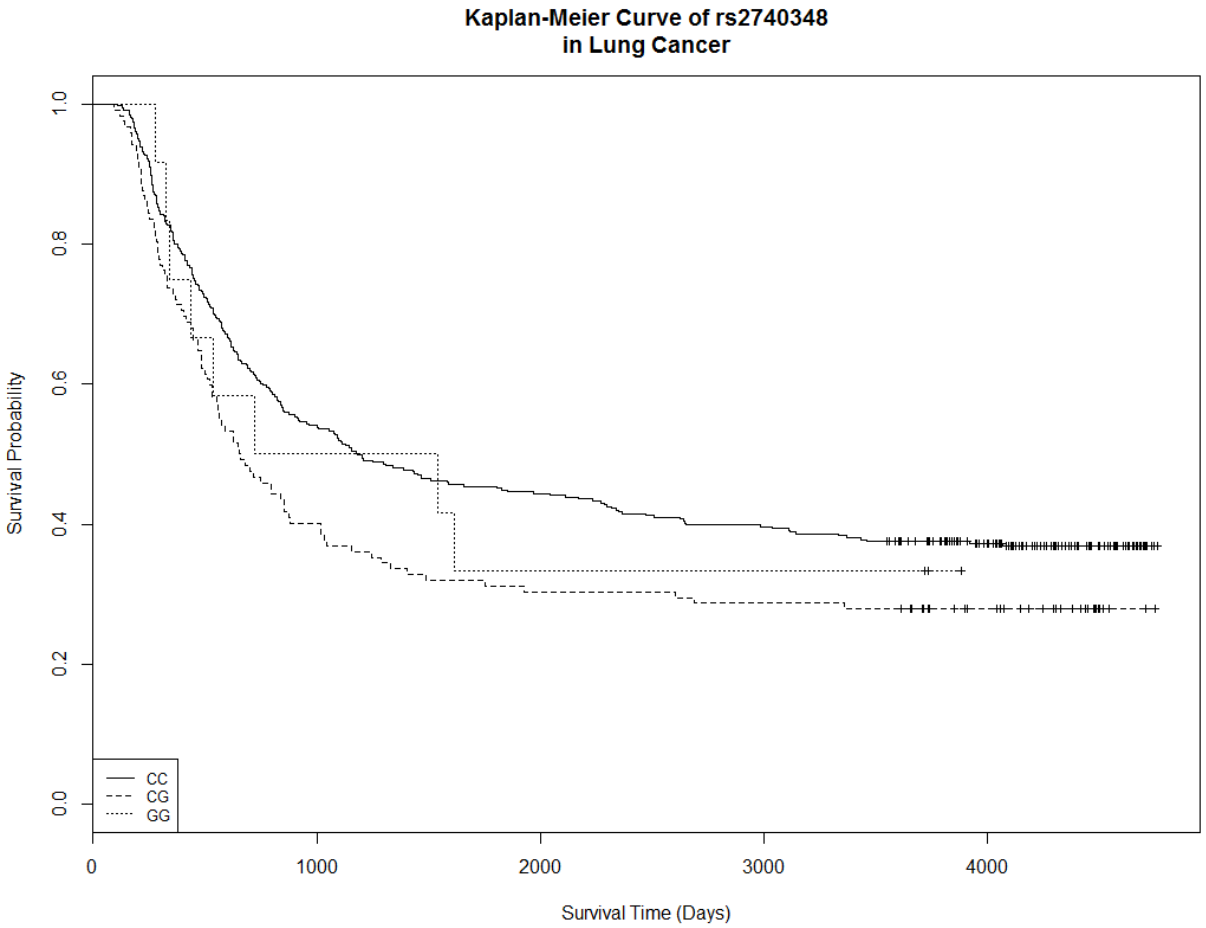

Figure 1.2 Kaplan-Meier curve of *GEMIN4* rs2740348 in lung cancer

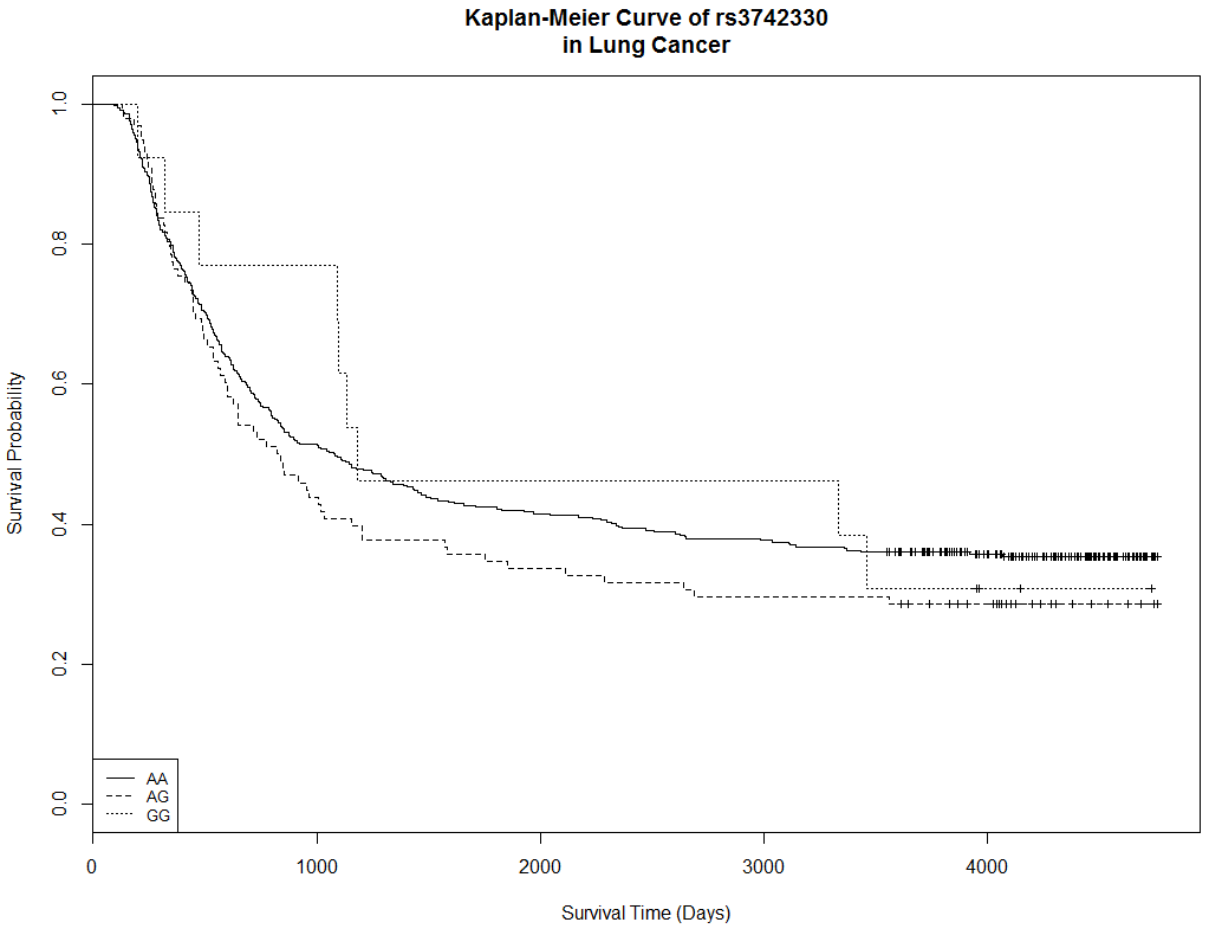

Figure 1.3 Kaplan-Meier curve of *DICER1* rs3742330 in lung cancer

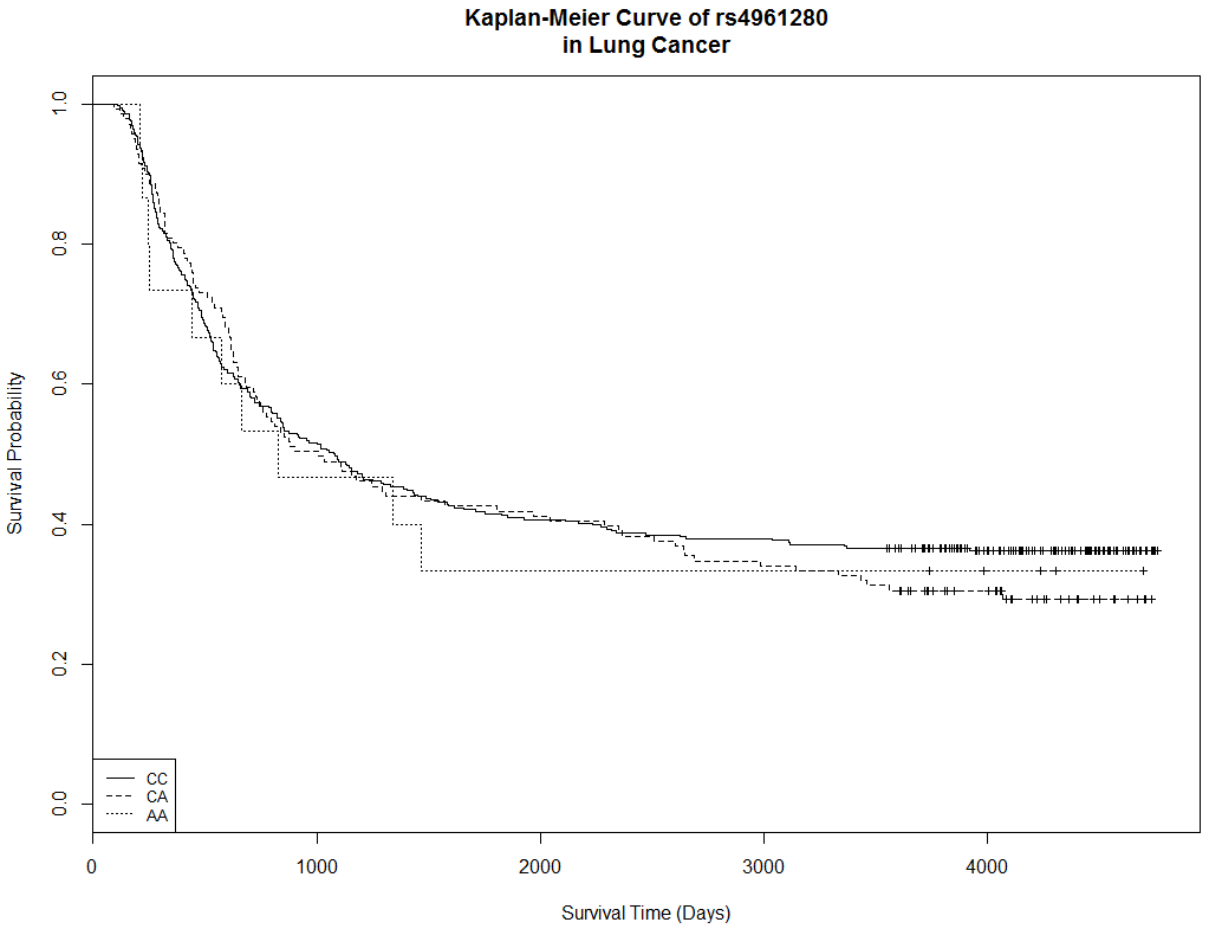

Figure 1.4 Kaplan-Meier curve of *AGO2* rs4961280 in lung cancer

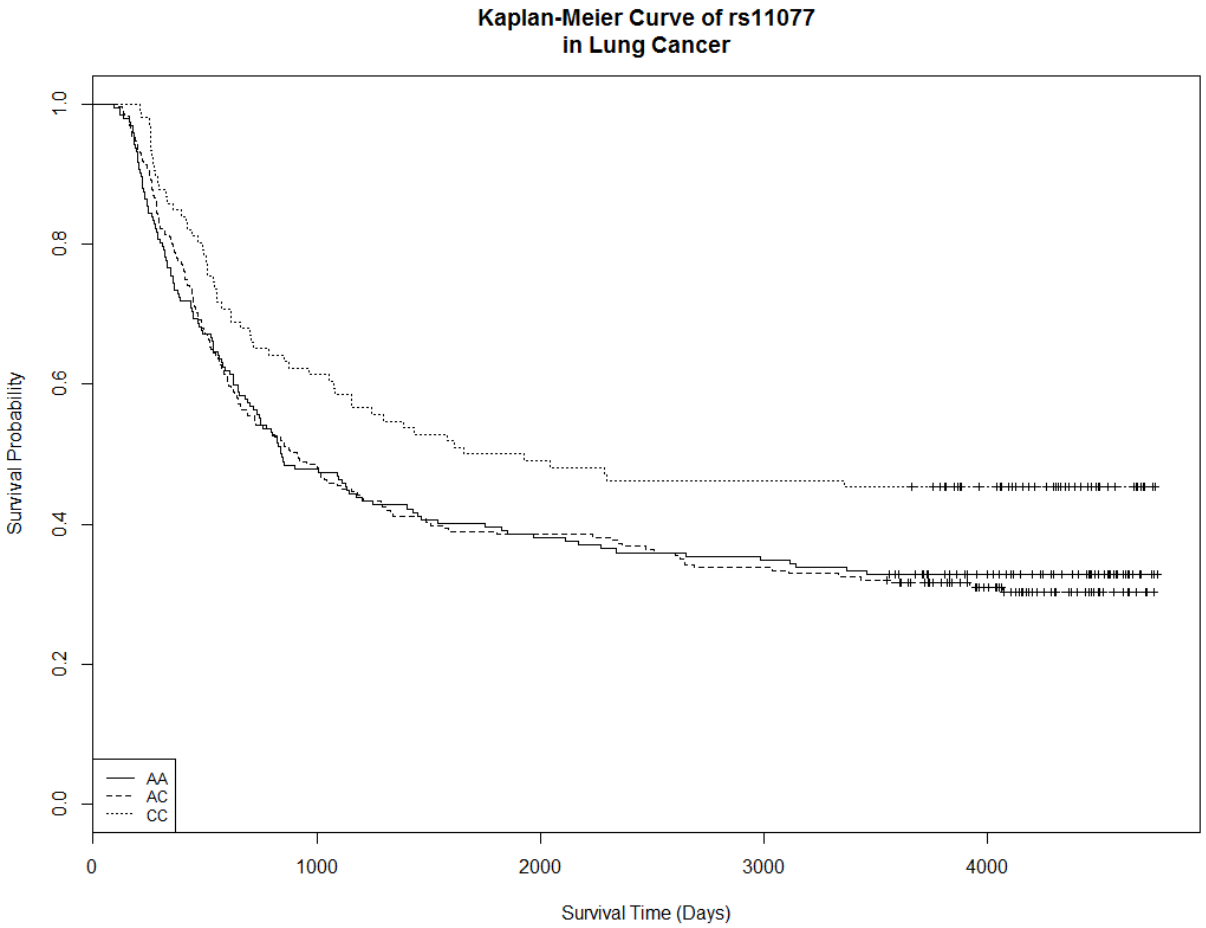

Figure 1.5 Kaplan-Meier curve of *XPO5* rs11077 in lung cancer

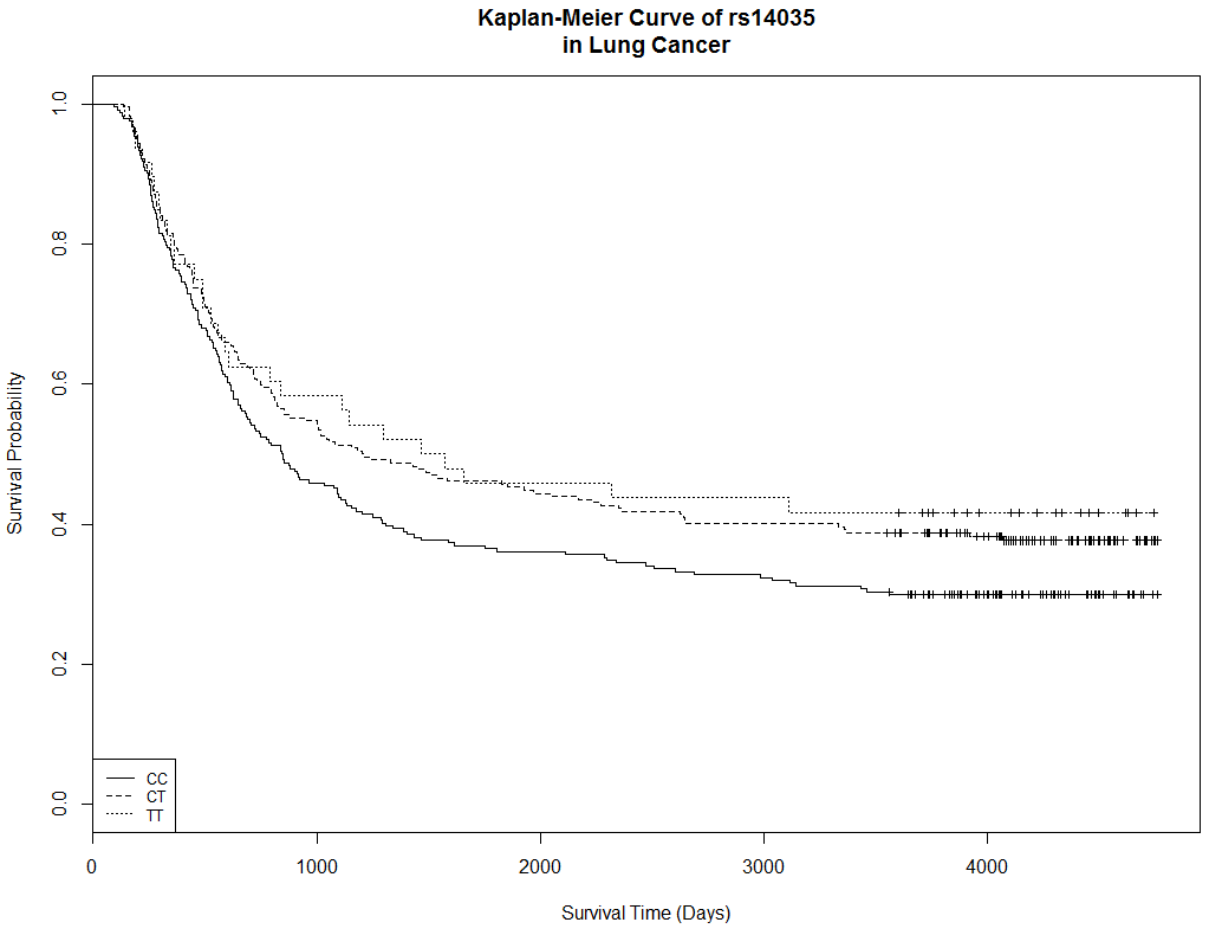

Figure 1.6 Kaplan-Meier curve of *RAN* rs14035 in lung cancer

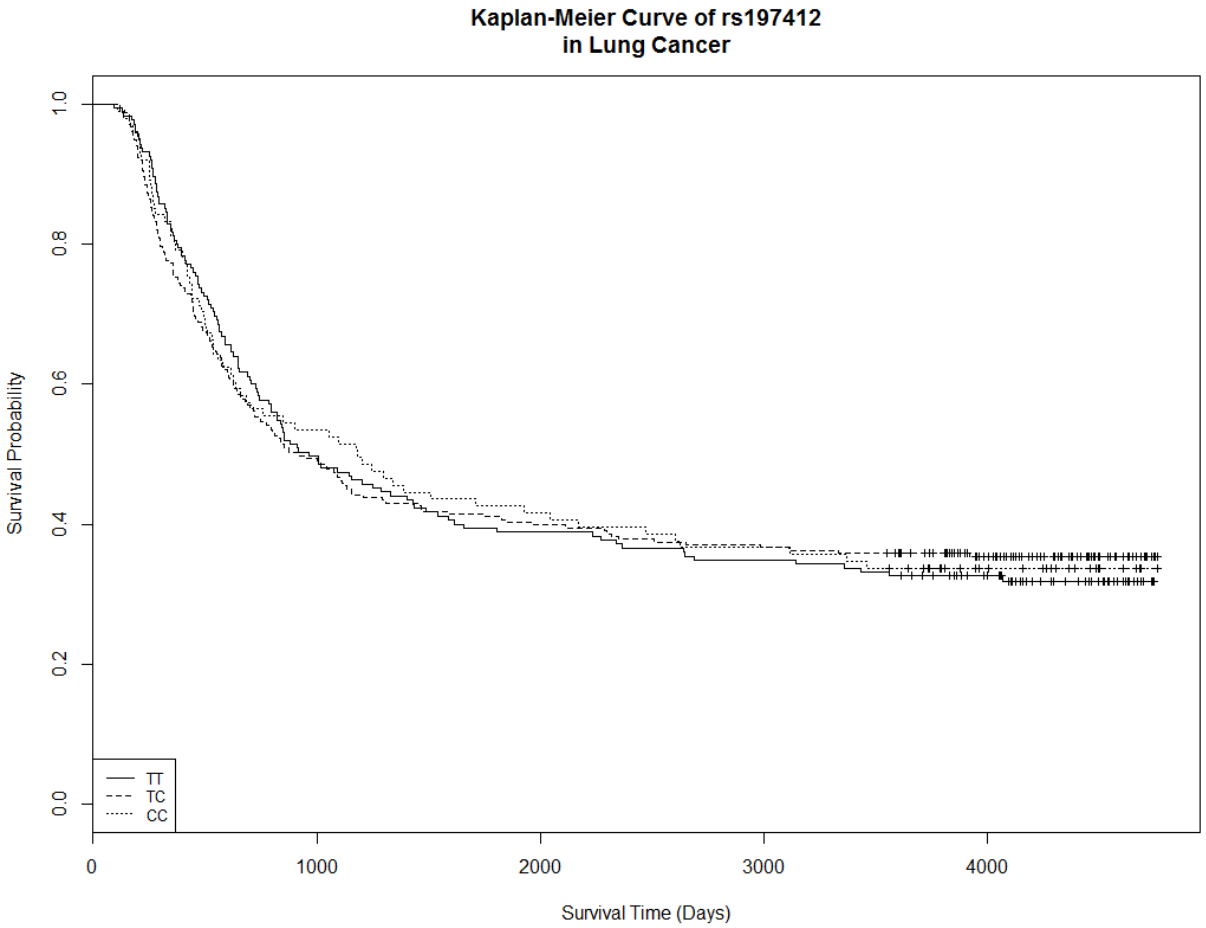

Figure 1.7 Kaplan-Meier curve of *GEMIN3* rs197412 in lung cancer

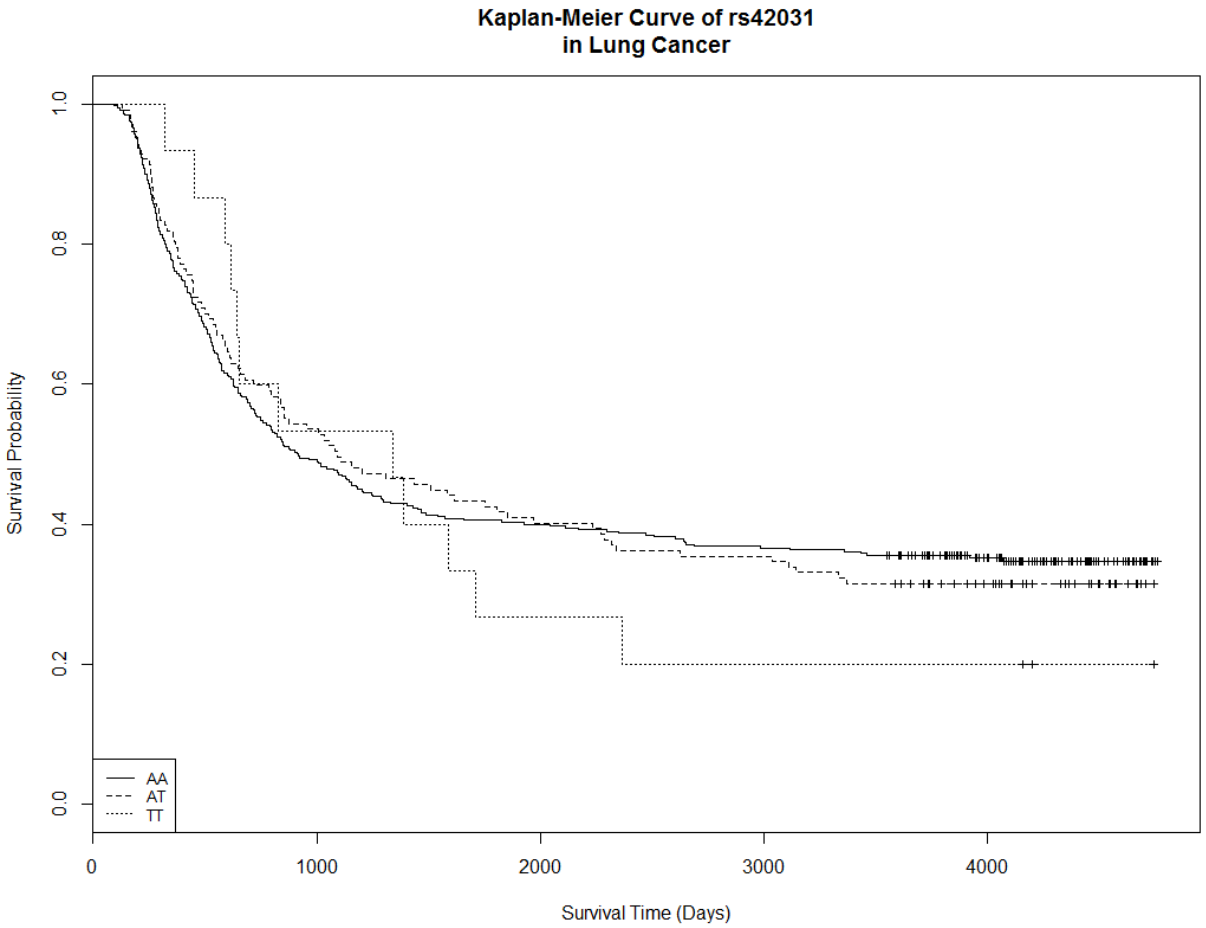

Figure 1.8 Kaplan-Meier curve of *CDK6* rs42031 in lung cancer

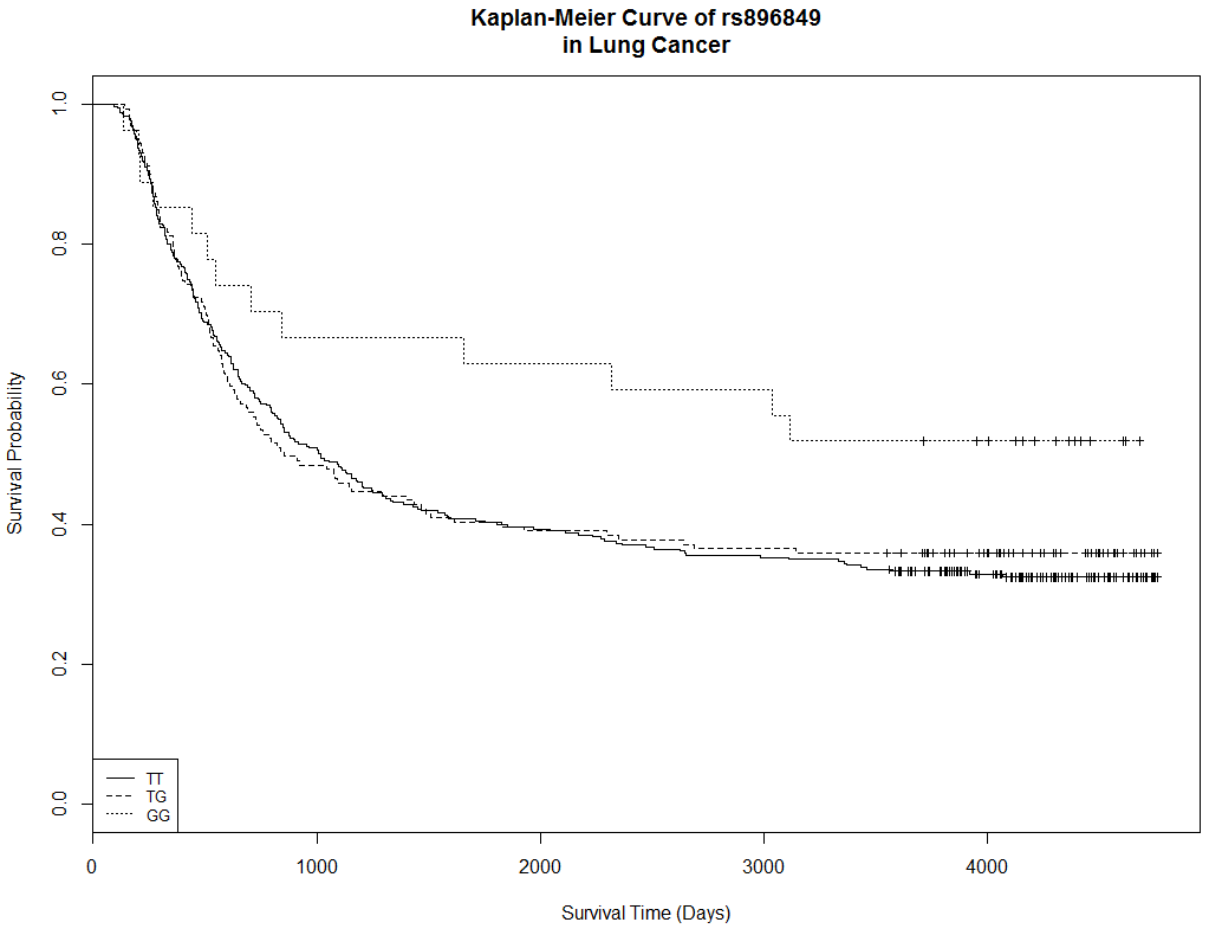

Figure 1.9 Kaplan-Meier curve of *TP53INP1* rs896849 in lung cancer

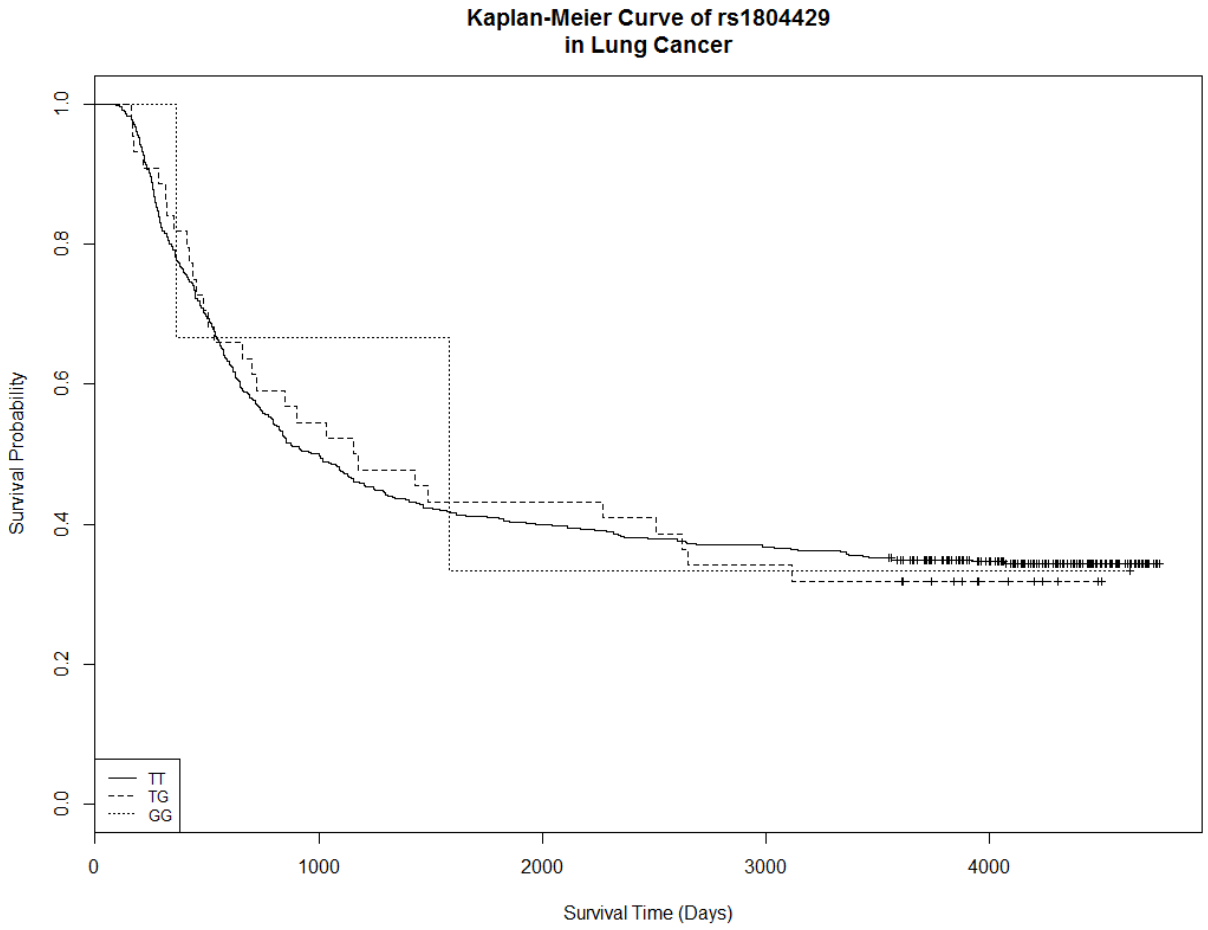

Figure 1.10 Kaplan-Meier curve of *CXCL12* rs1804429 in lung cancer

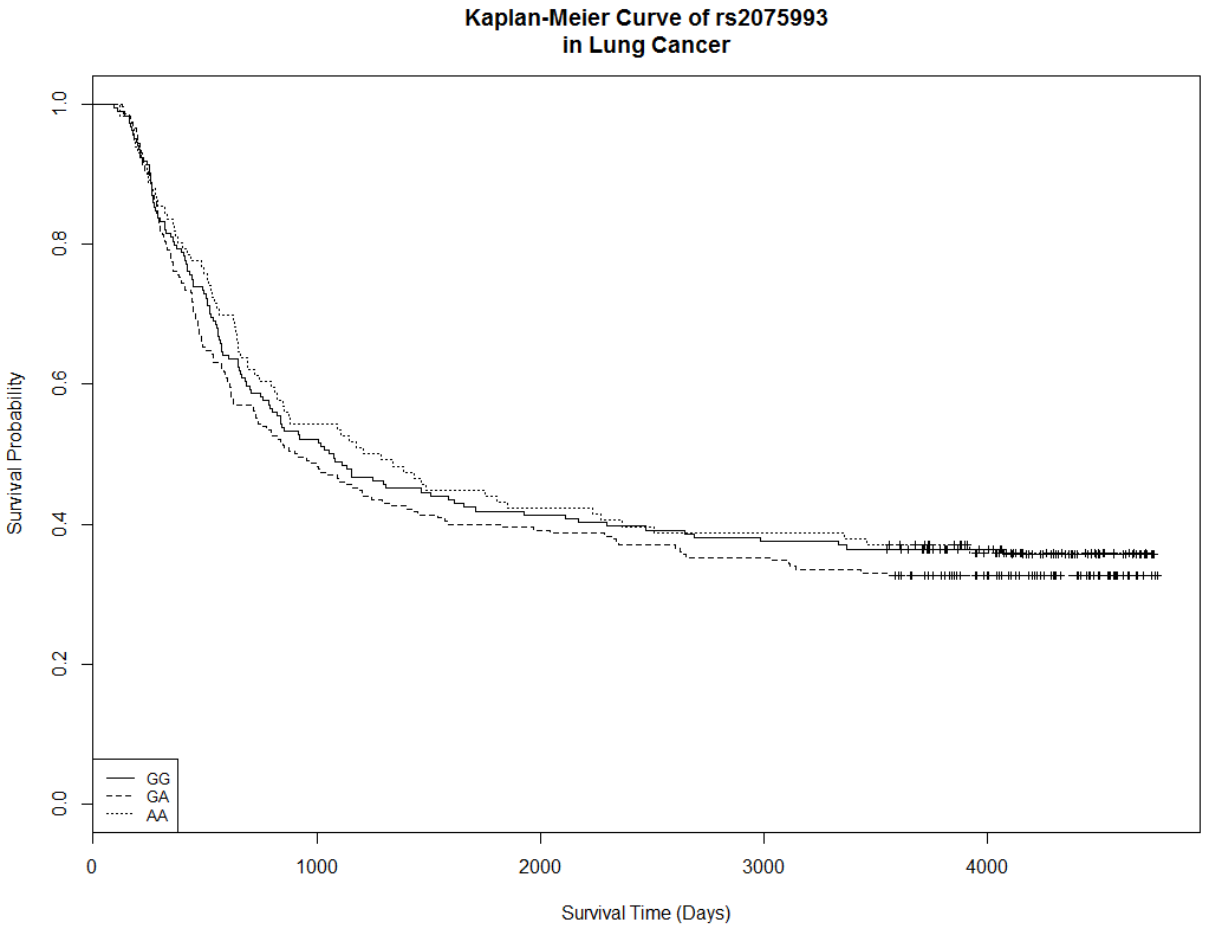

Figure 1.11 Kaplan-Meier curve of *E2F2* rs2075993 in lung cancer

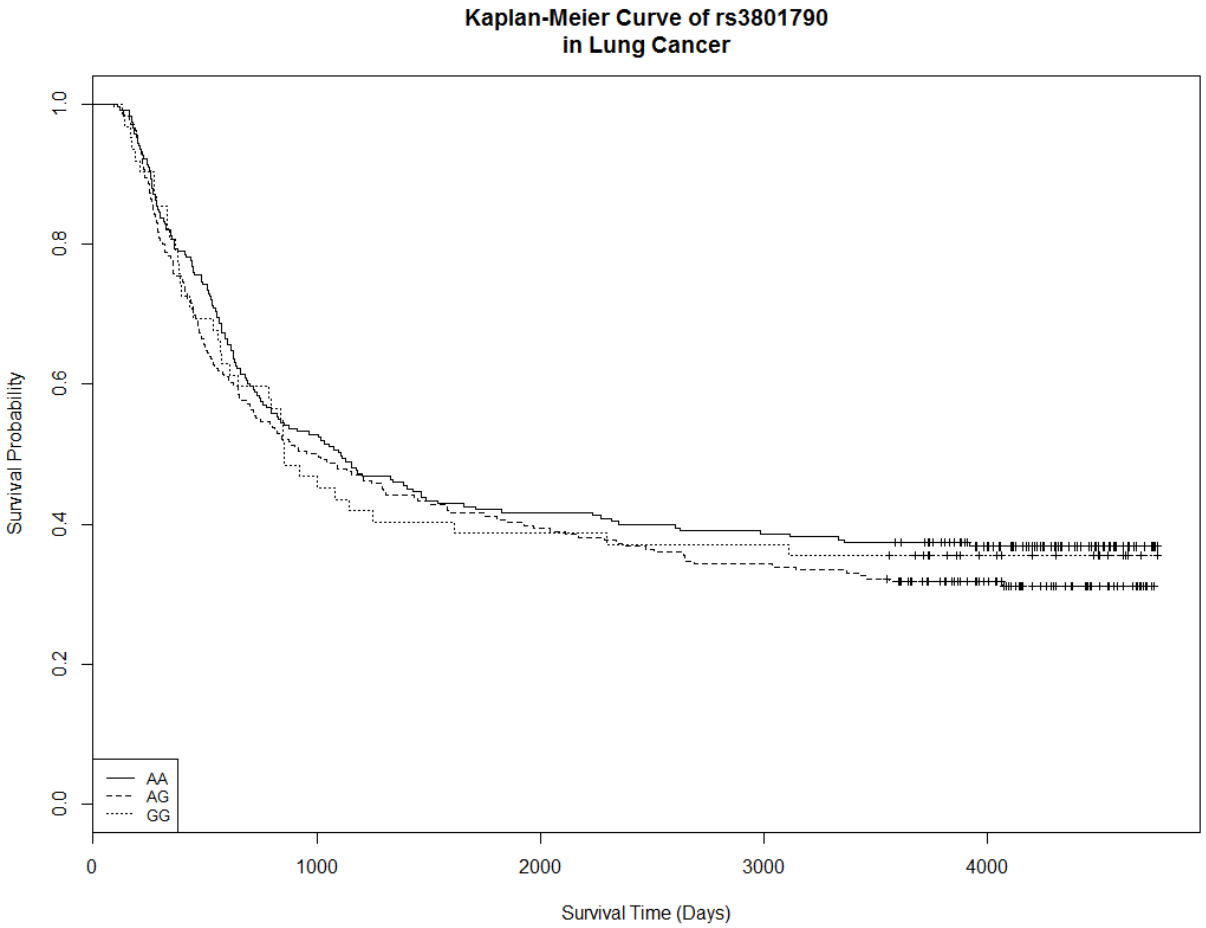

Figure 1.12 Kaplan-Meier curve of *DOCK4* rs3801790 in lung cancer

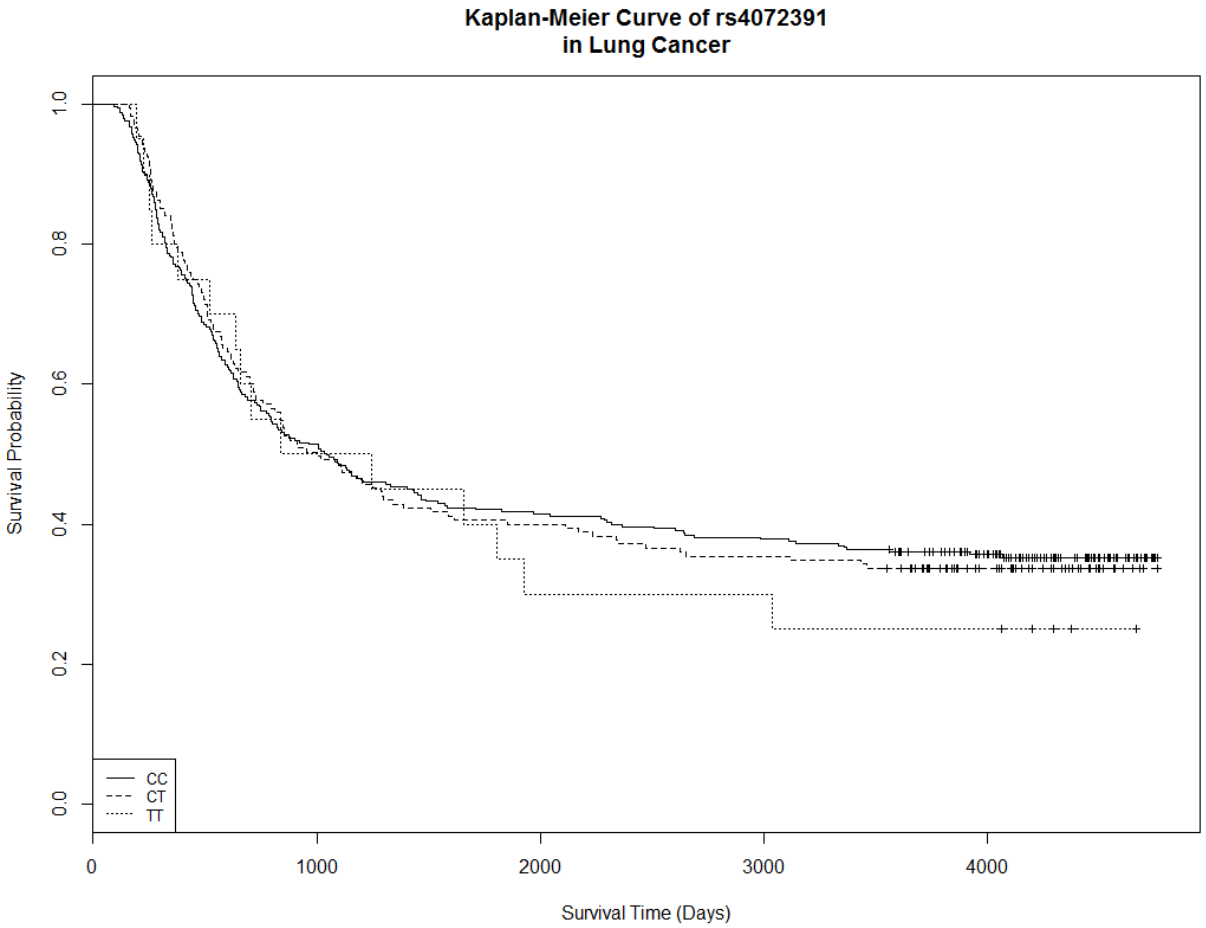

Figure 1.13 Kaplan-Meier curve of *IL6R* rs4072391 in lung cancer

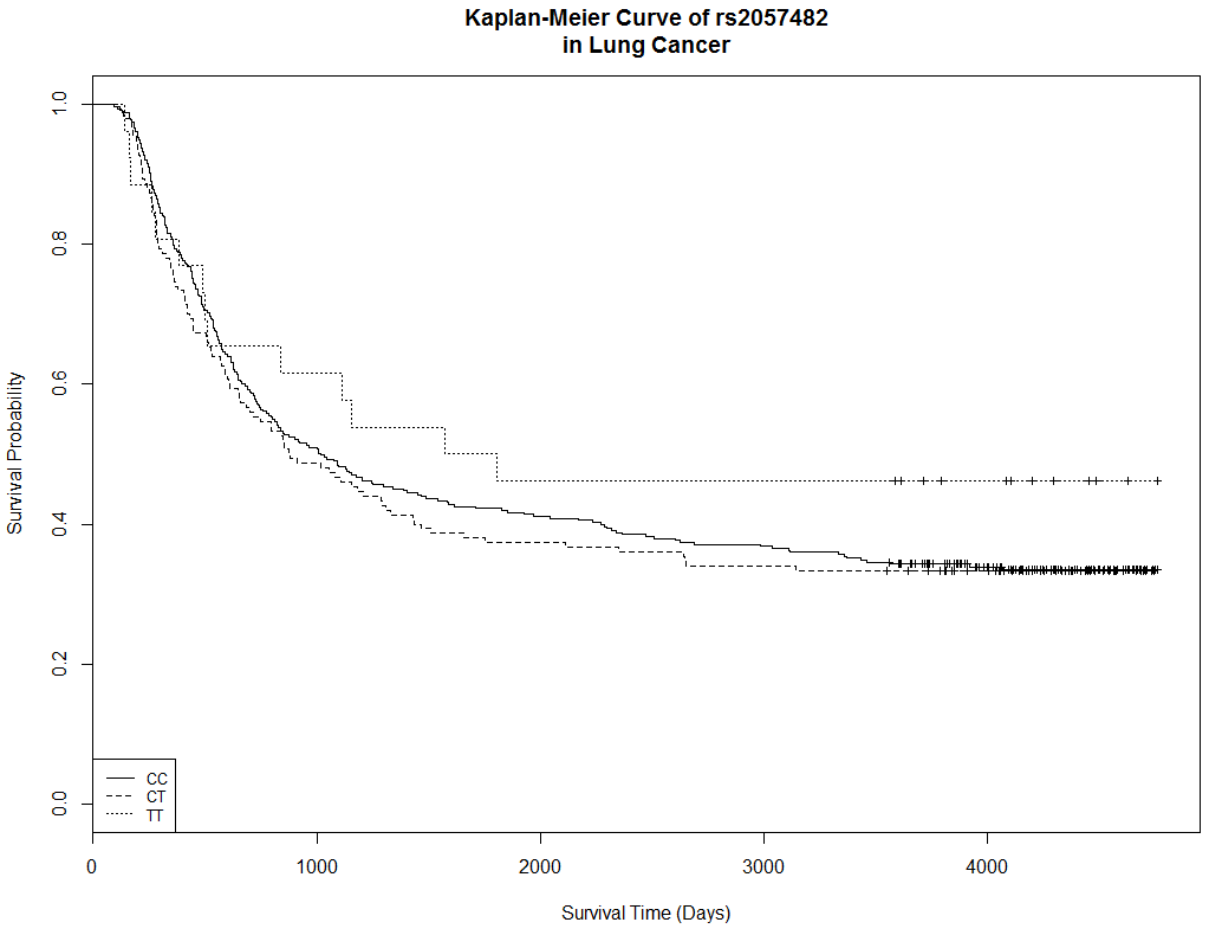

Figure 1.14 Kaplan-Meier curve of *HIF1A* rs2057482 in lung cancer

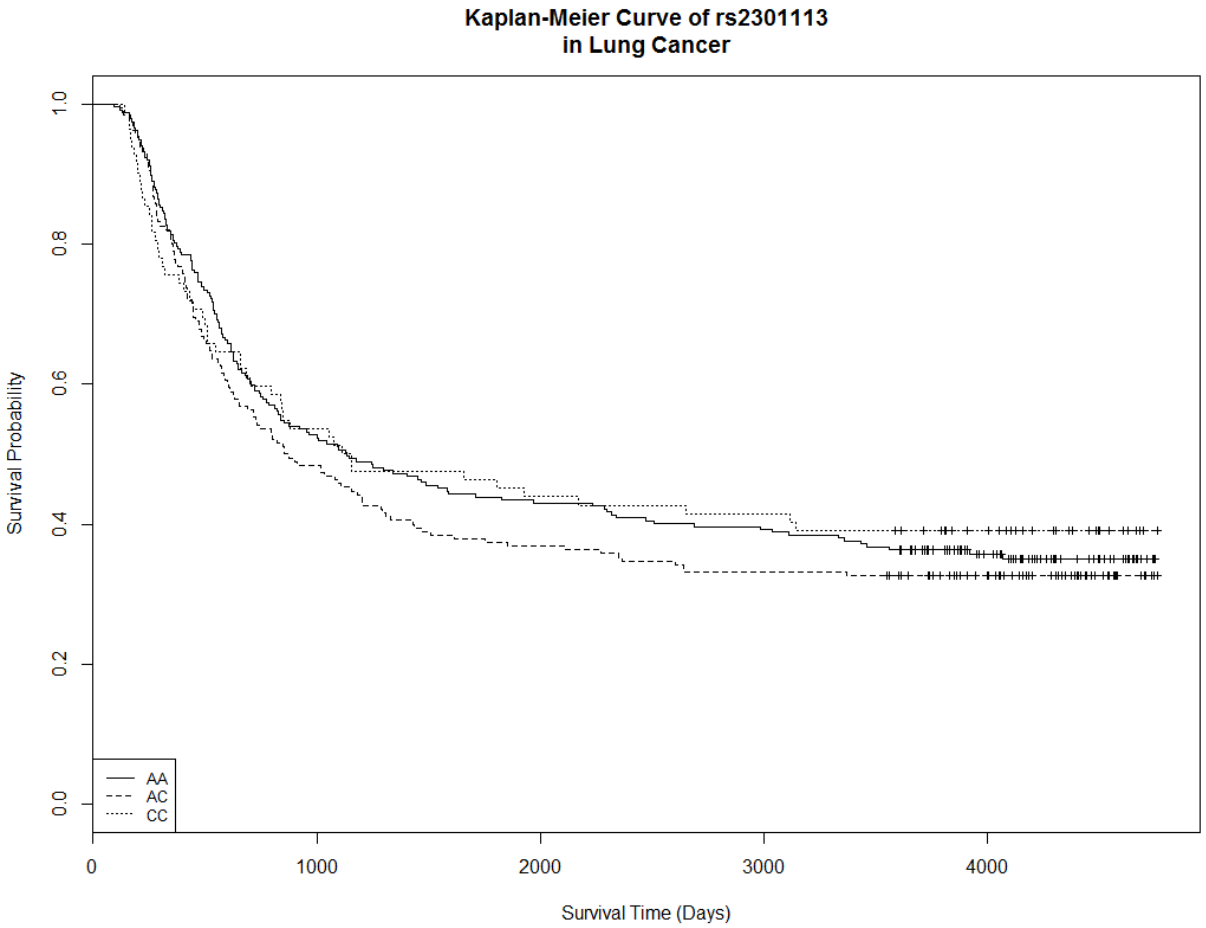

Figure 1.15 Kaplan-Meier curve of *HIF1A* rs2301113 in lung cancer

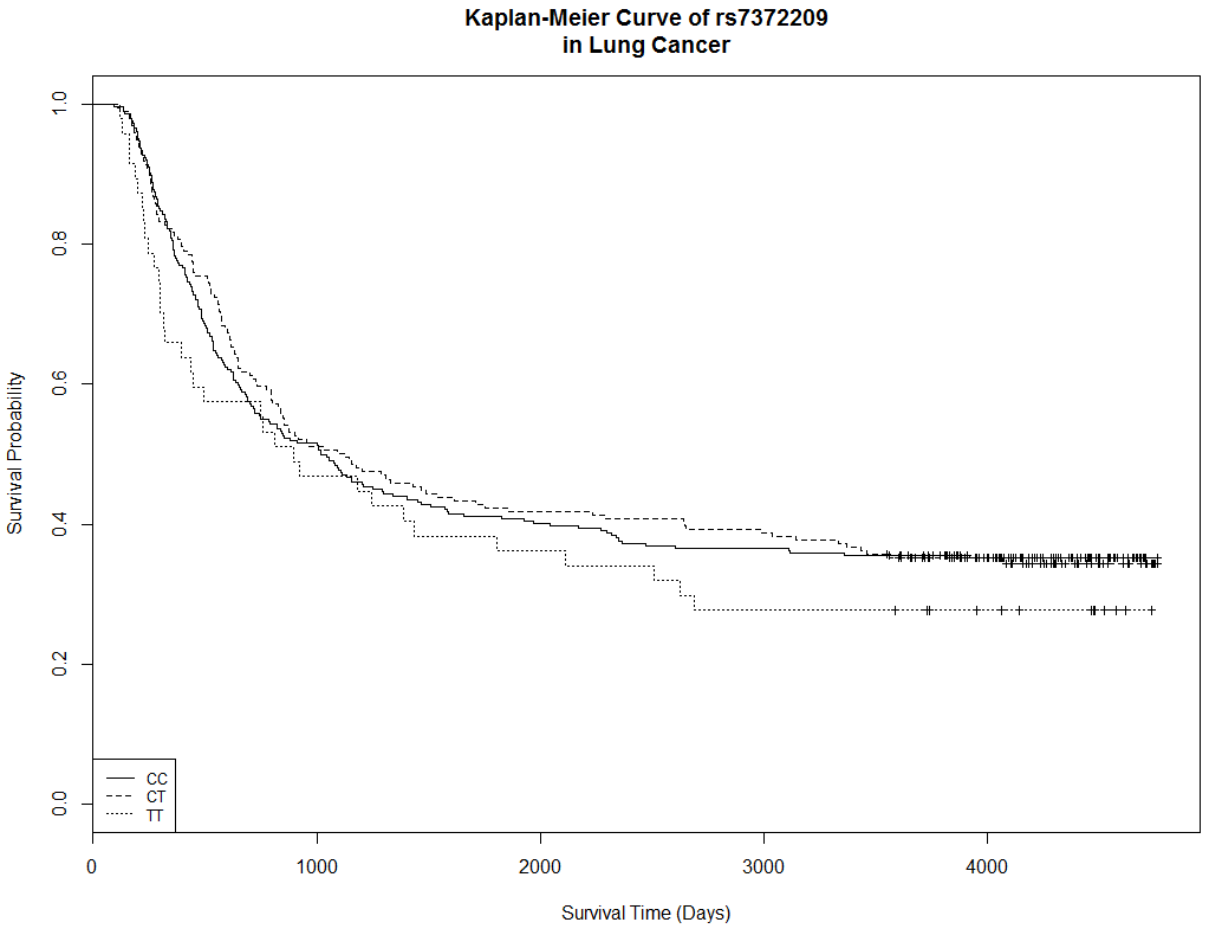

Figure 1.16 Kaplan-Meier curve of *MIR-26A1* rs7372209 in lung cancer

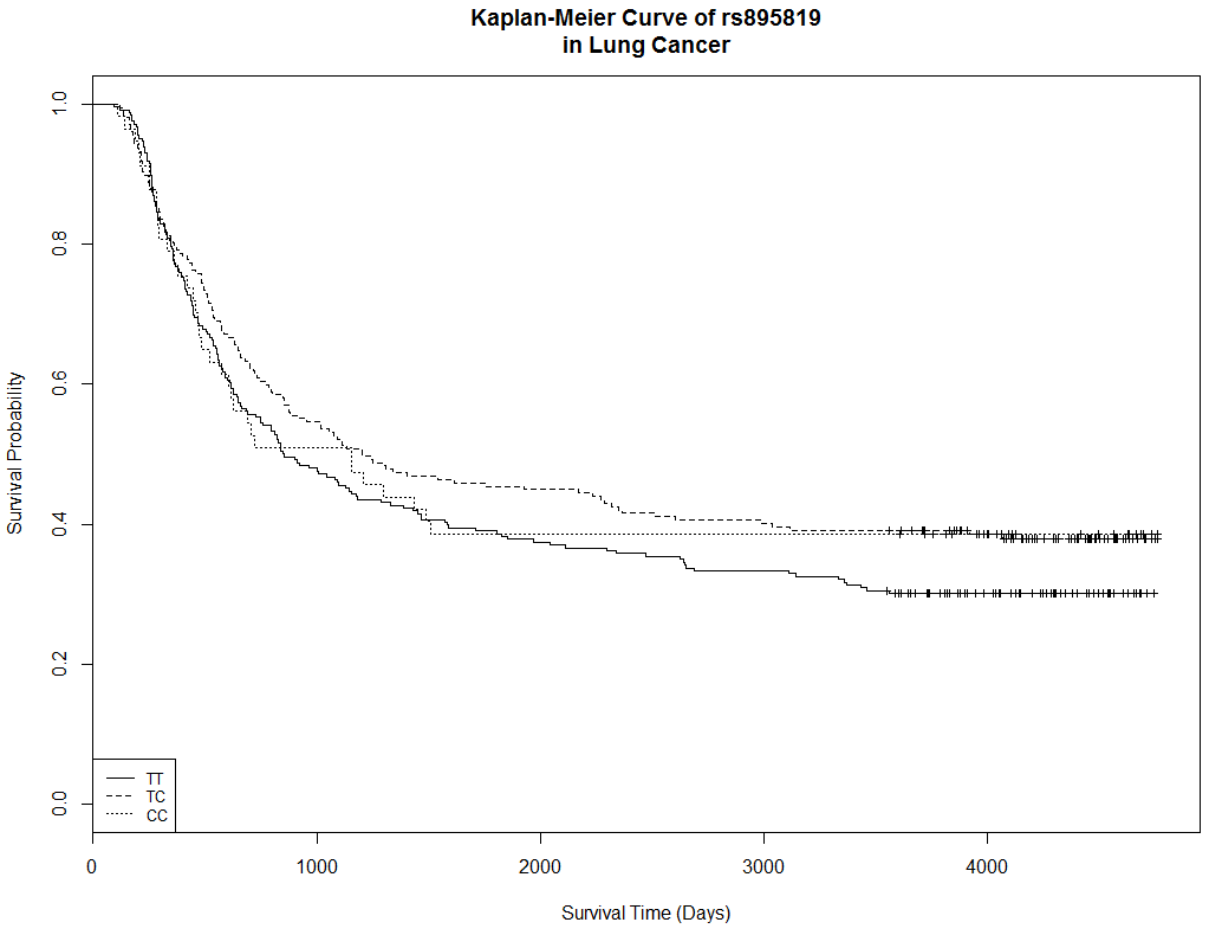

Figure 1.17 Kaplan-Meier curve of *MIR-27* rs895819 in lung cancer

Figure Section II

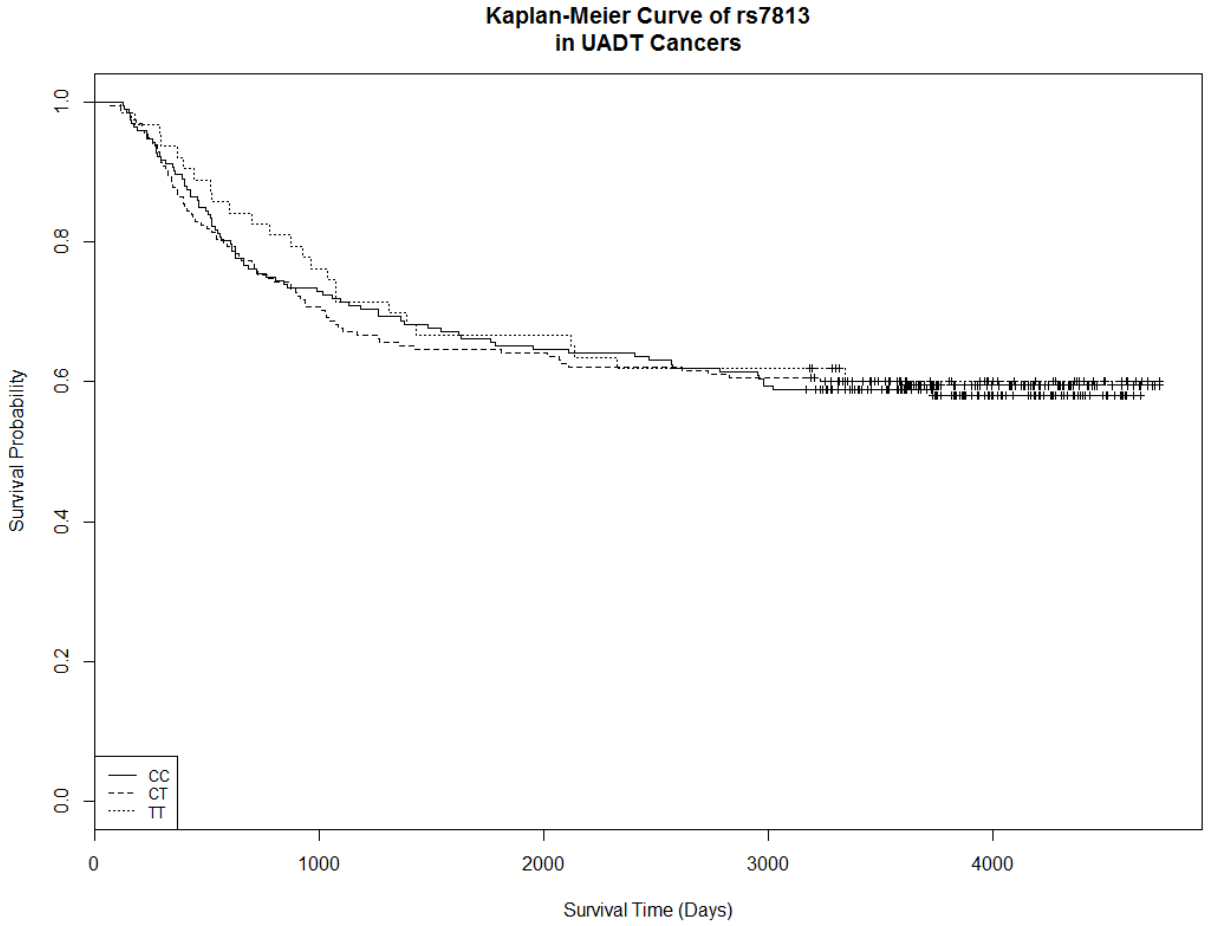

Figure 2.1 Kaplan-Meier curve of *GEMIN4* rs7813 in UADT cancers

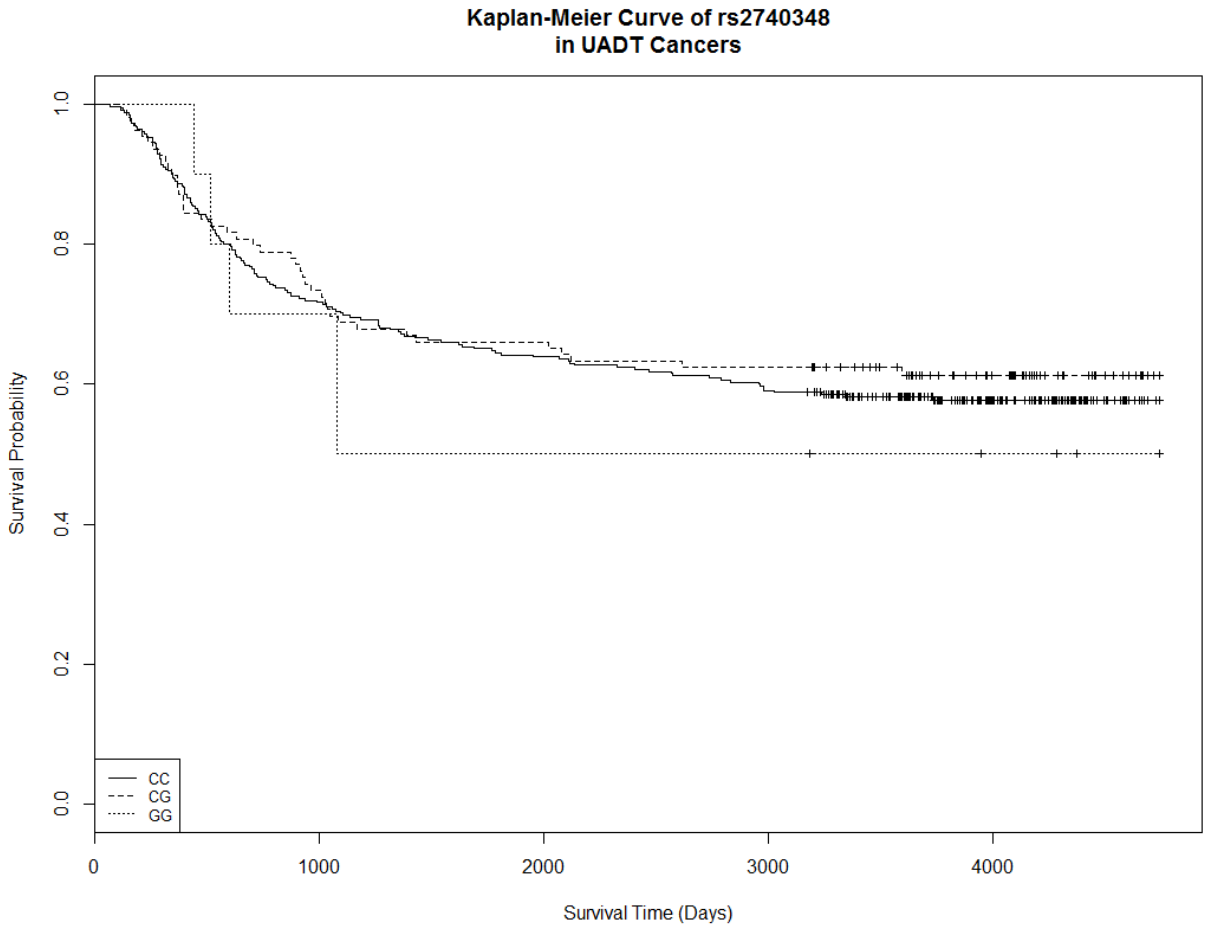

Figure 2.2 Kaplan-Meier curve of *GEMIN4* rs2740348 in UADT cancers

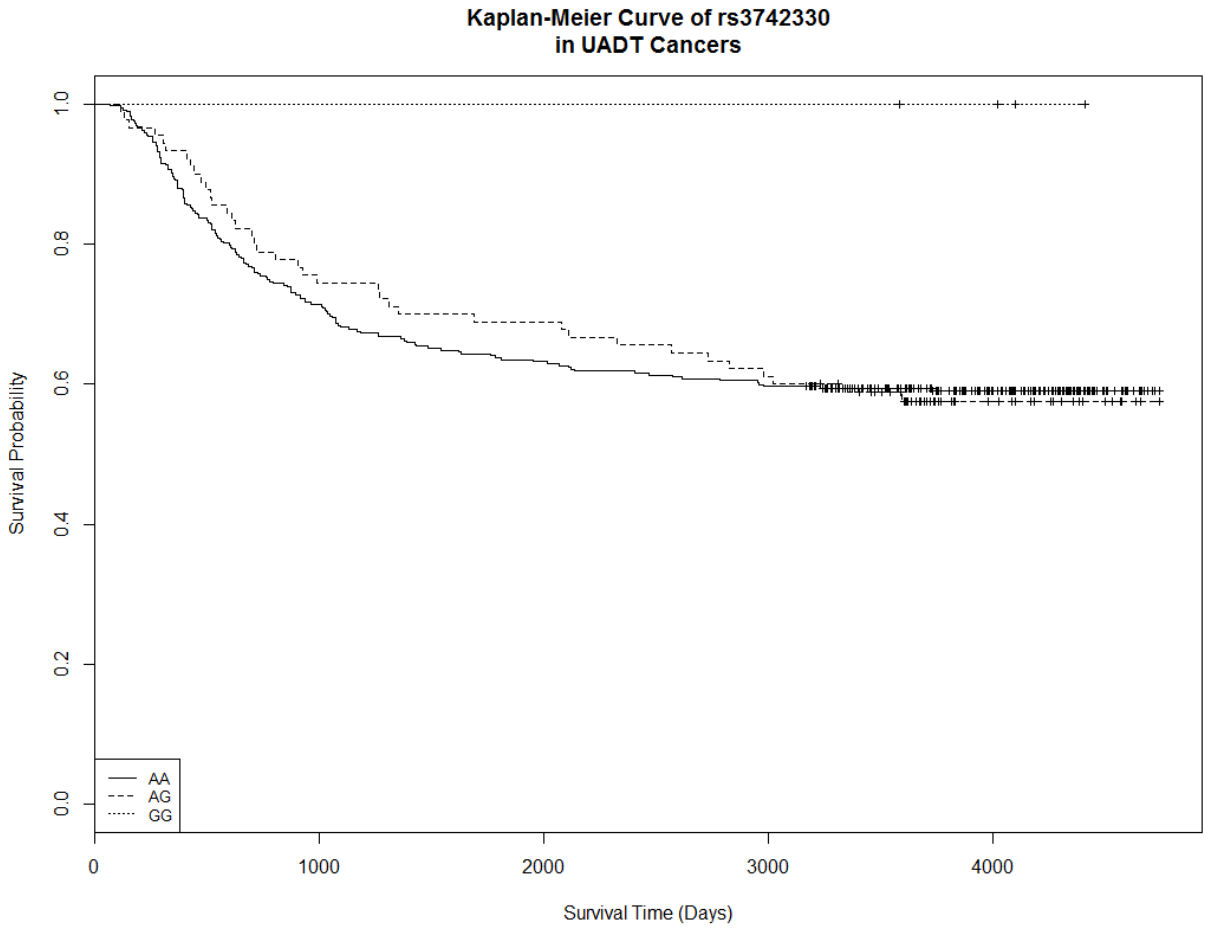

Figure 2.3 Kaplan-Meier curve of *DICER1* rs3742330 in UADT cancers

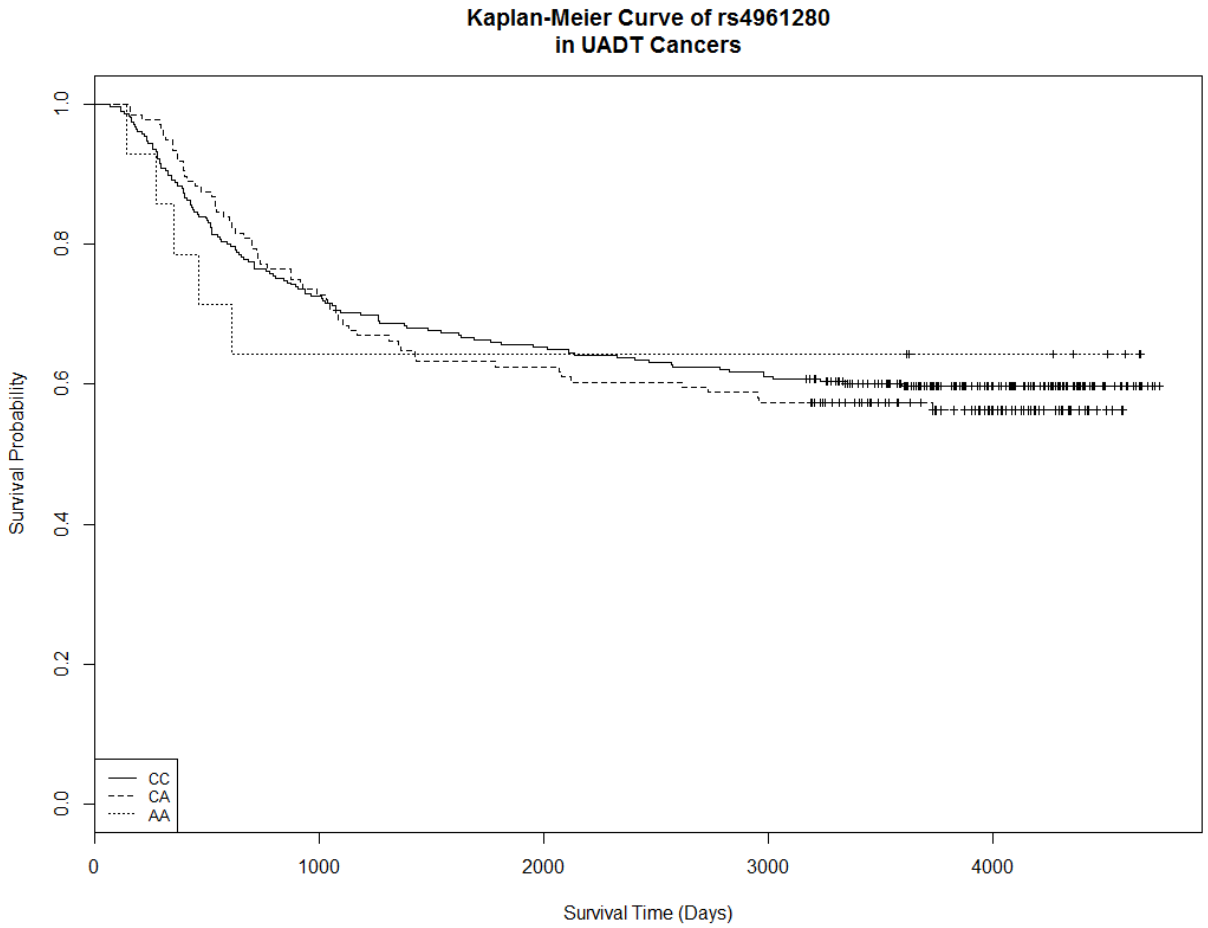

Figure 2.4 Kaplan-Meier curve of *AGO2* rs4961280 in UADT cancers

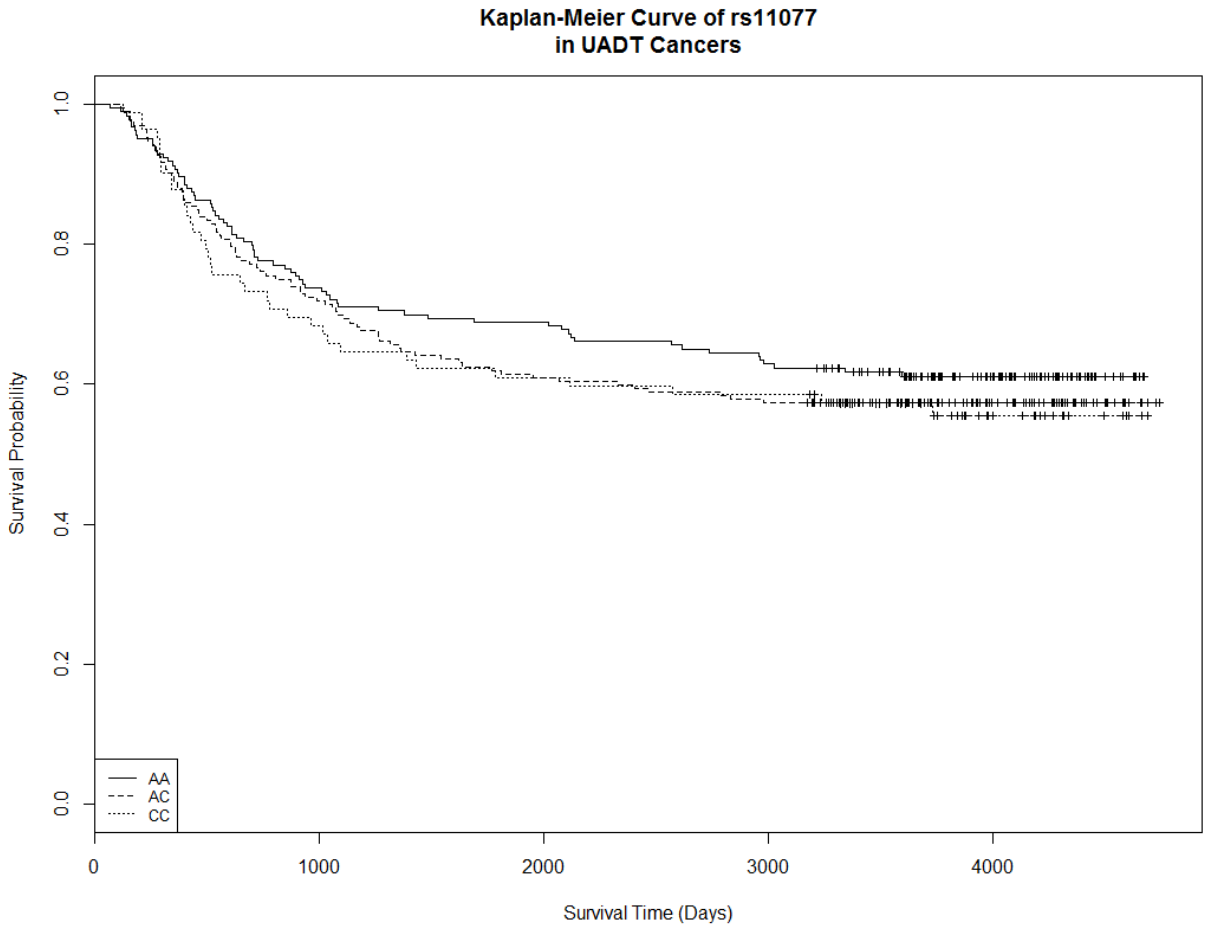

Figure 2.5 Kaplan-Meier curve of *XPO5* rs11077 in UADT cancers

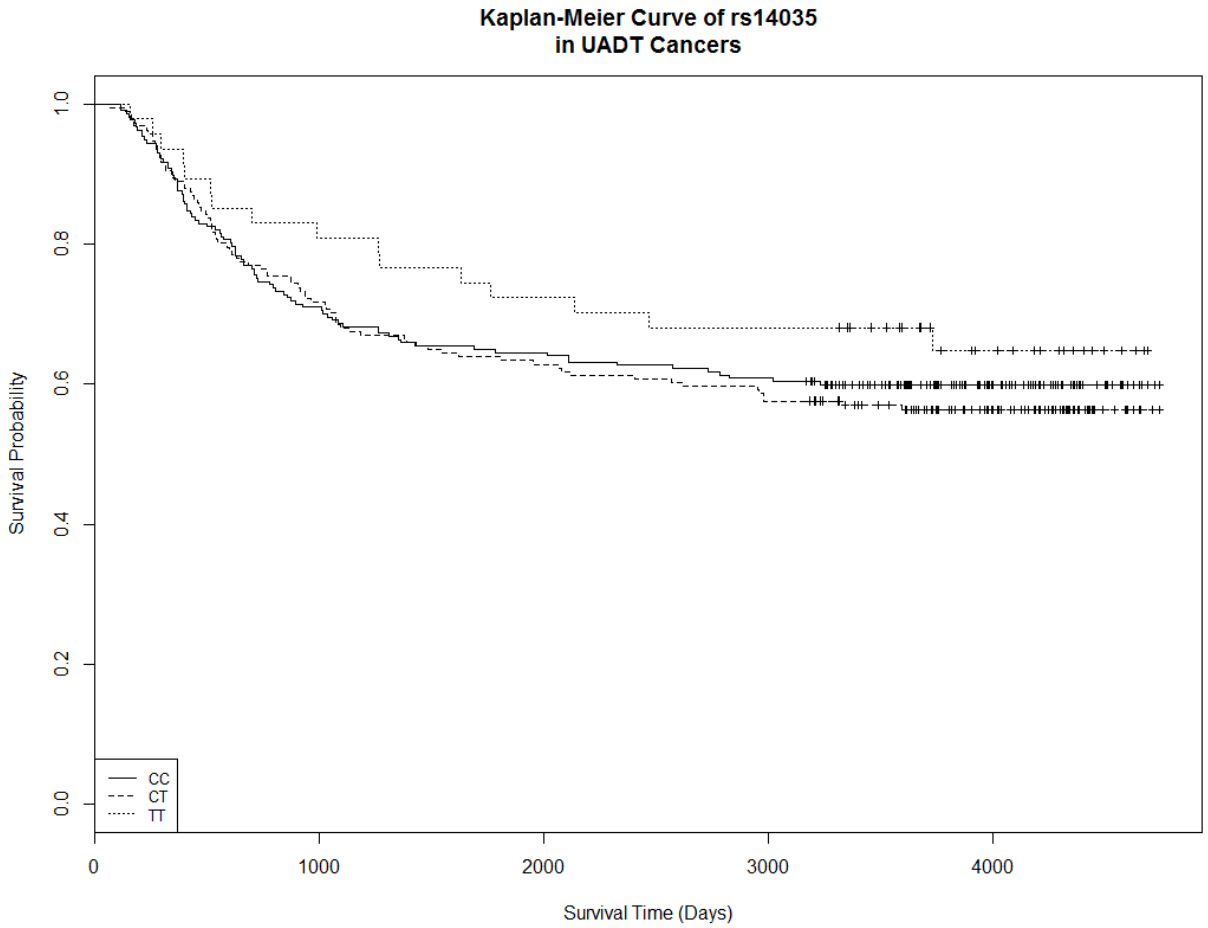

Figure 2.6 Kaplan-Meier curve of *RAN* rs14035 in UADT cancers

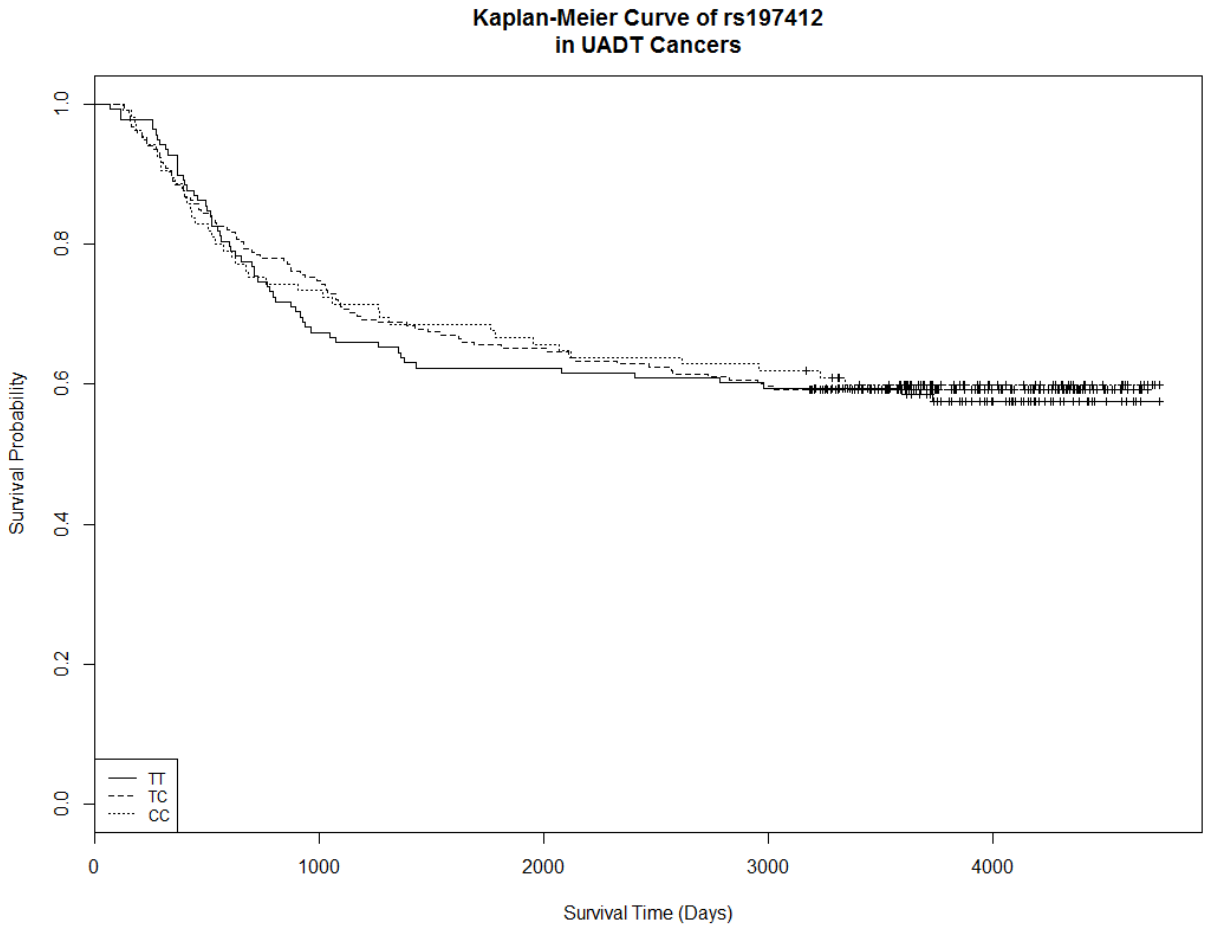

Figure 2.7 Kaplan-Meier curve of *GEMIN3* rs197412 in UADT cancers

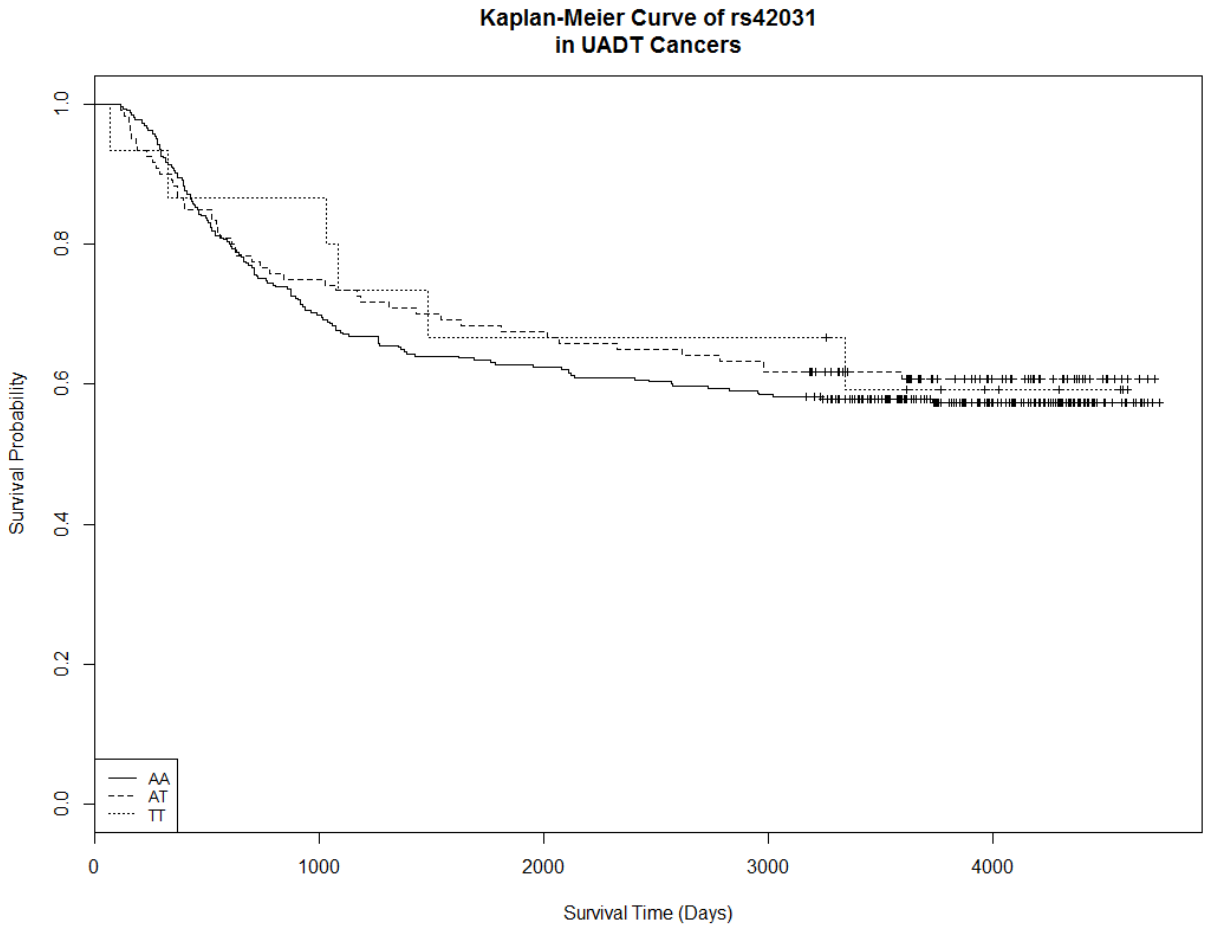

Figure 2.8 Kaplan-Meier curve of *CDK6* rs42031 in UADT cancers

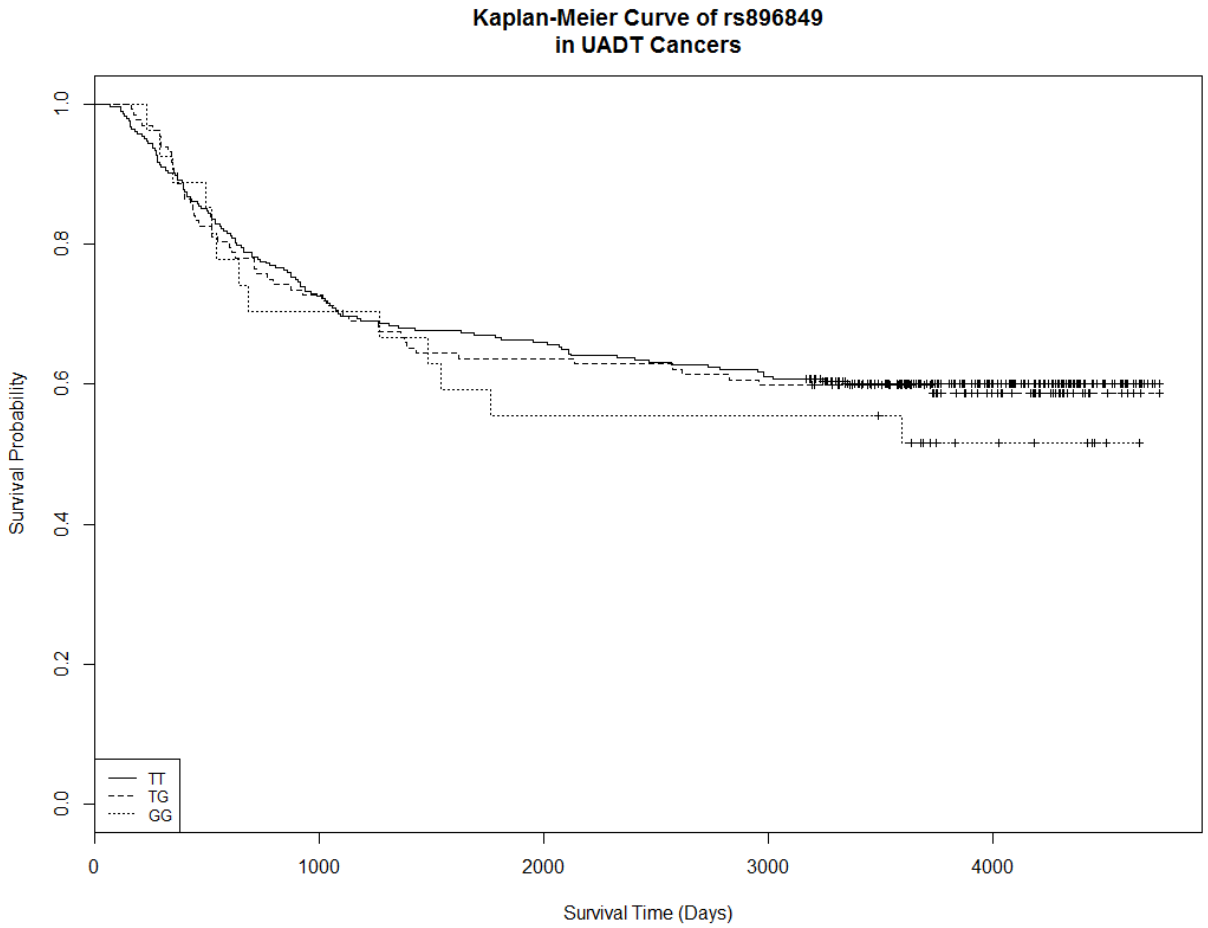

Figure 2.9 Kaplan-Meier curve of *TP53INP1* rs896849 in UADT cancers

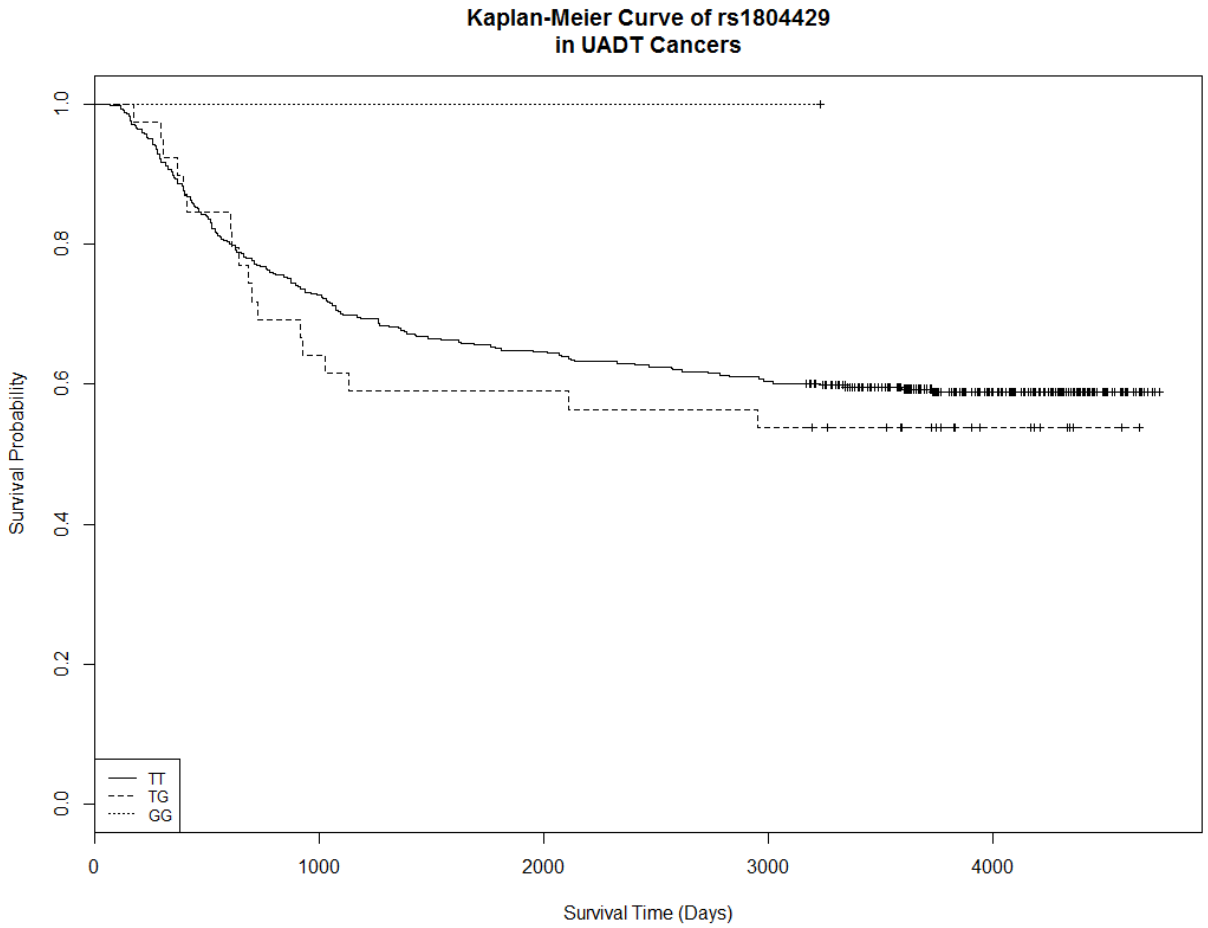

Figure 2.10 Kaplan-Meier curve of *CXCL12* rs1804429 in UADT cancers

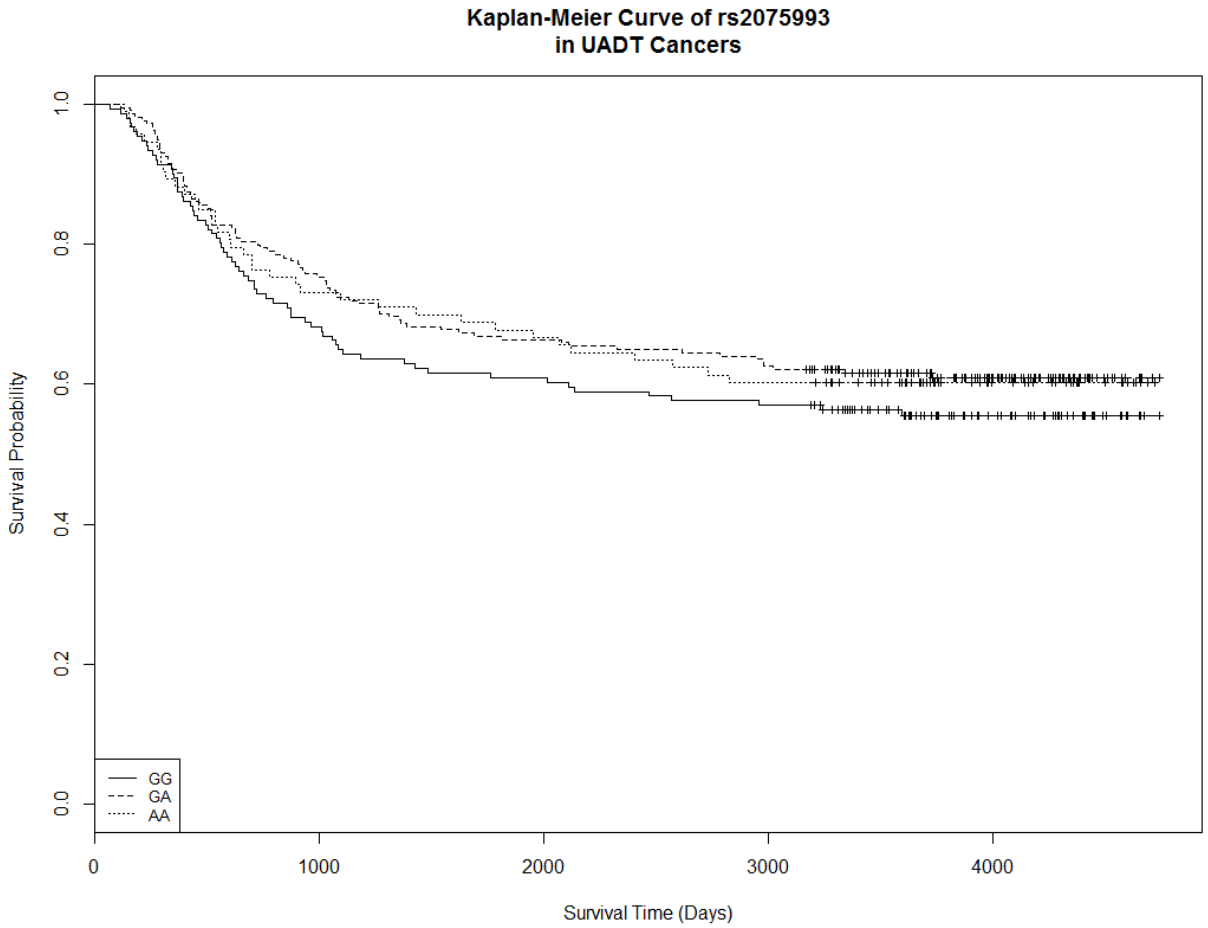

Figure 2.11 Kaplan-Meier curve of *E2F2* rs2075993 in UADT cancers

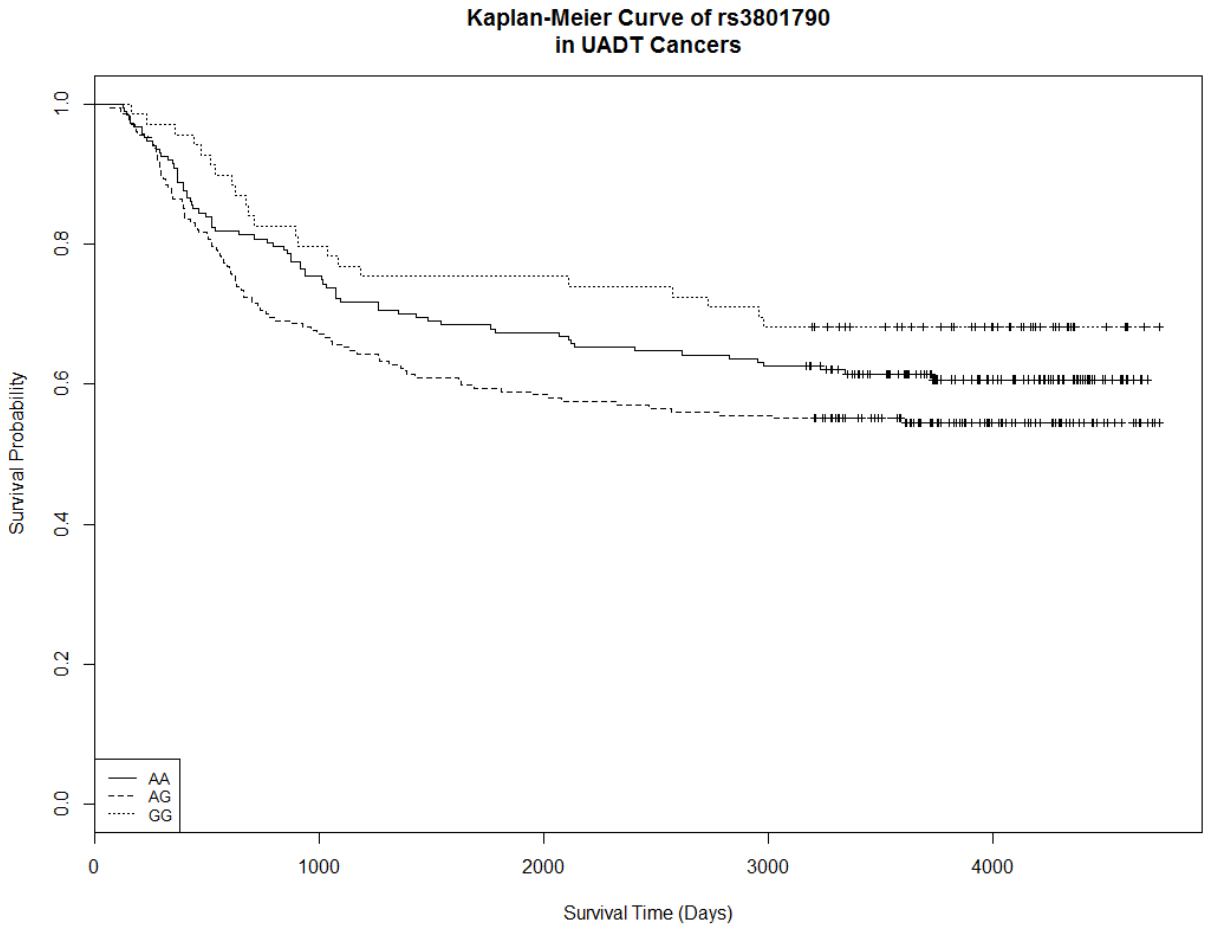

Figure 2.12 Kaplan-Meier curve of *DOCK4* rs3801790 in UADT cancers

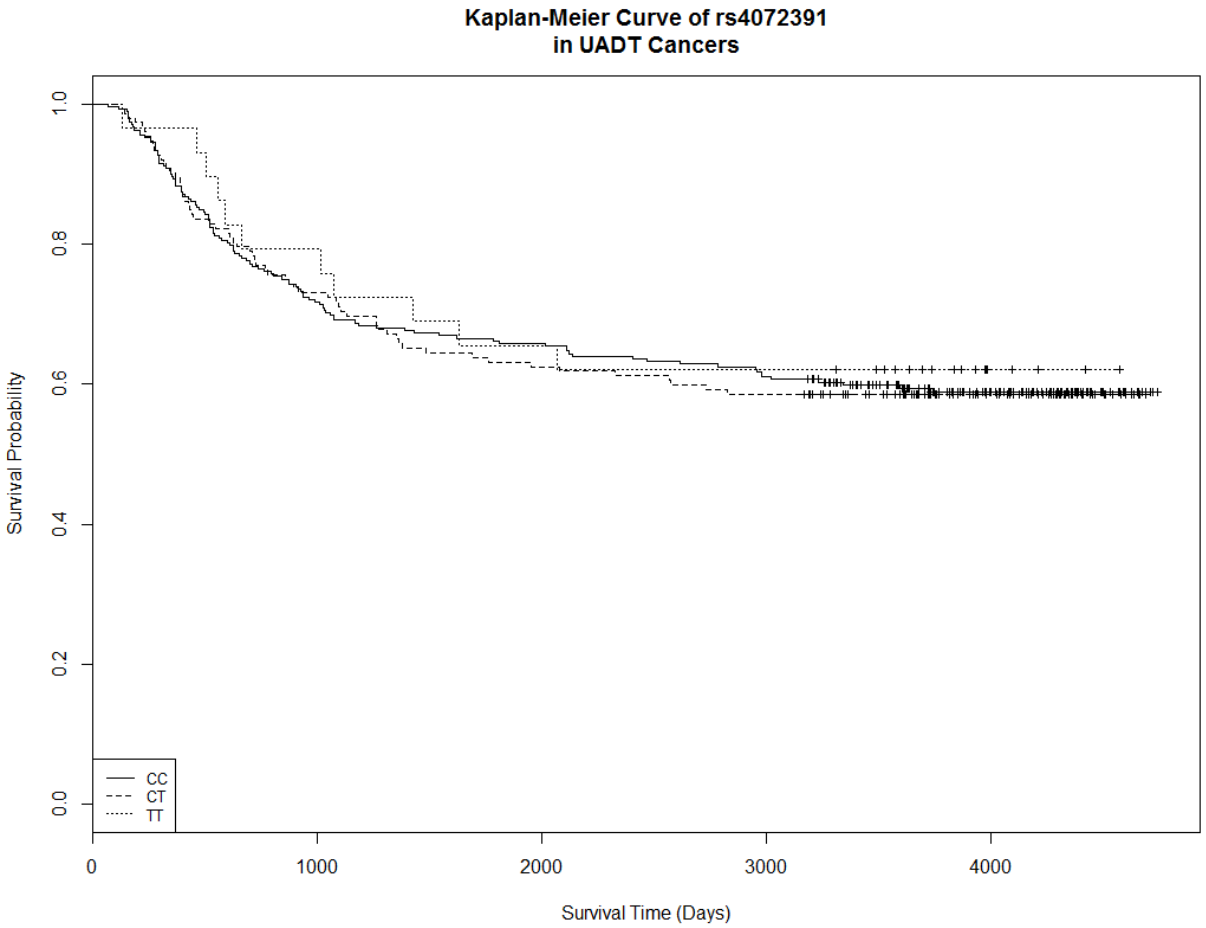

Figure 2.13 Kaplan-Meier curve of *IL6R* rs4072391 in UADT cancers

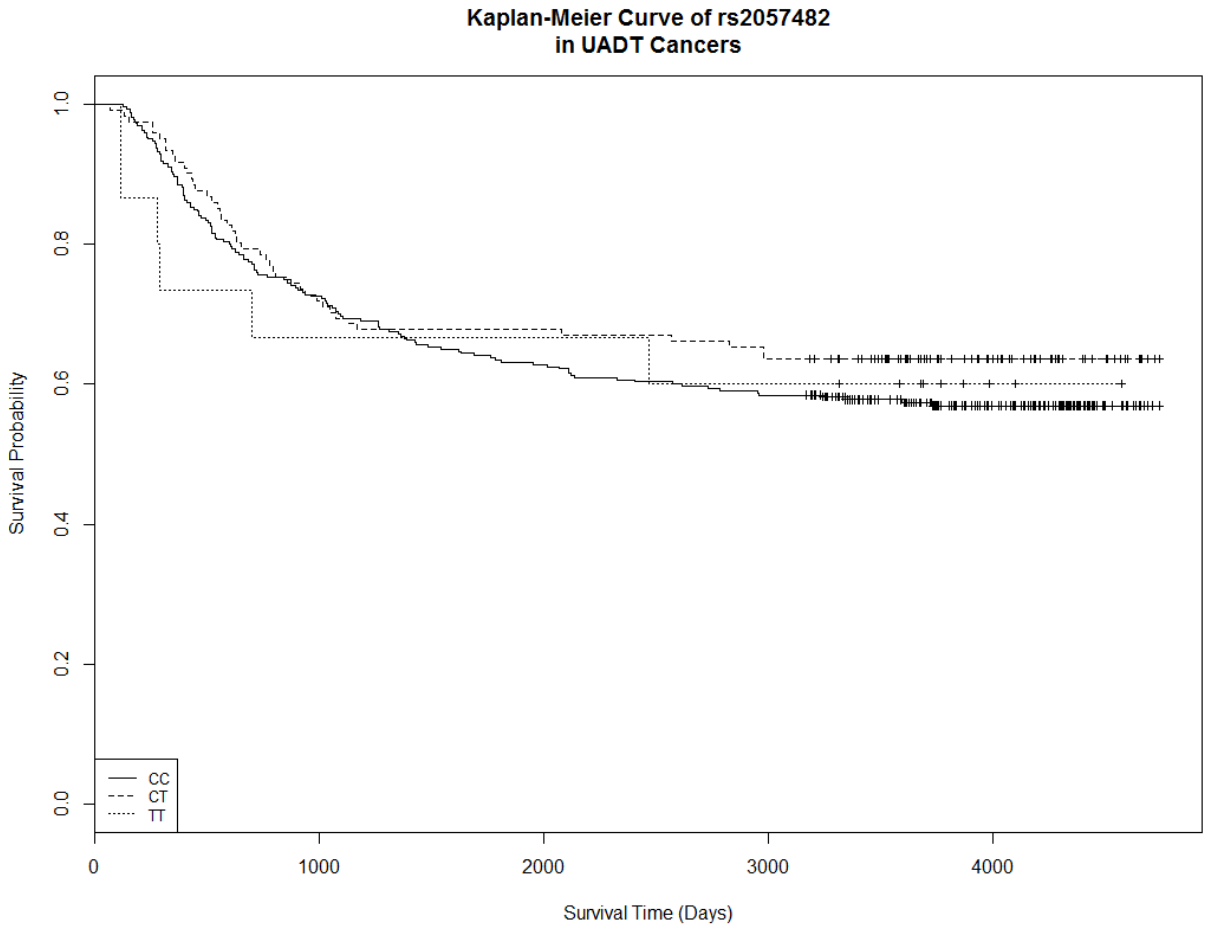

Figure 2.14 Kaplan-Meier curve of *HIF1A* rs2057482 in UADT cancers

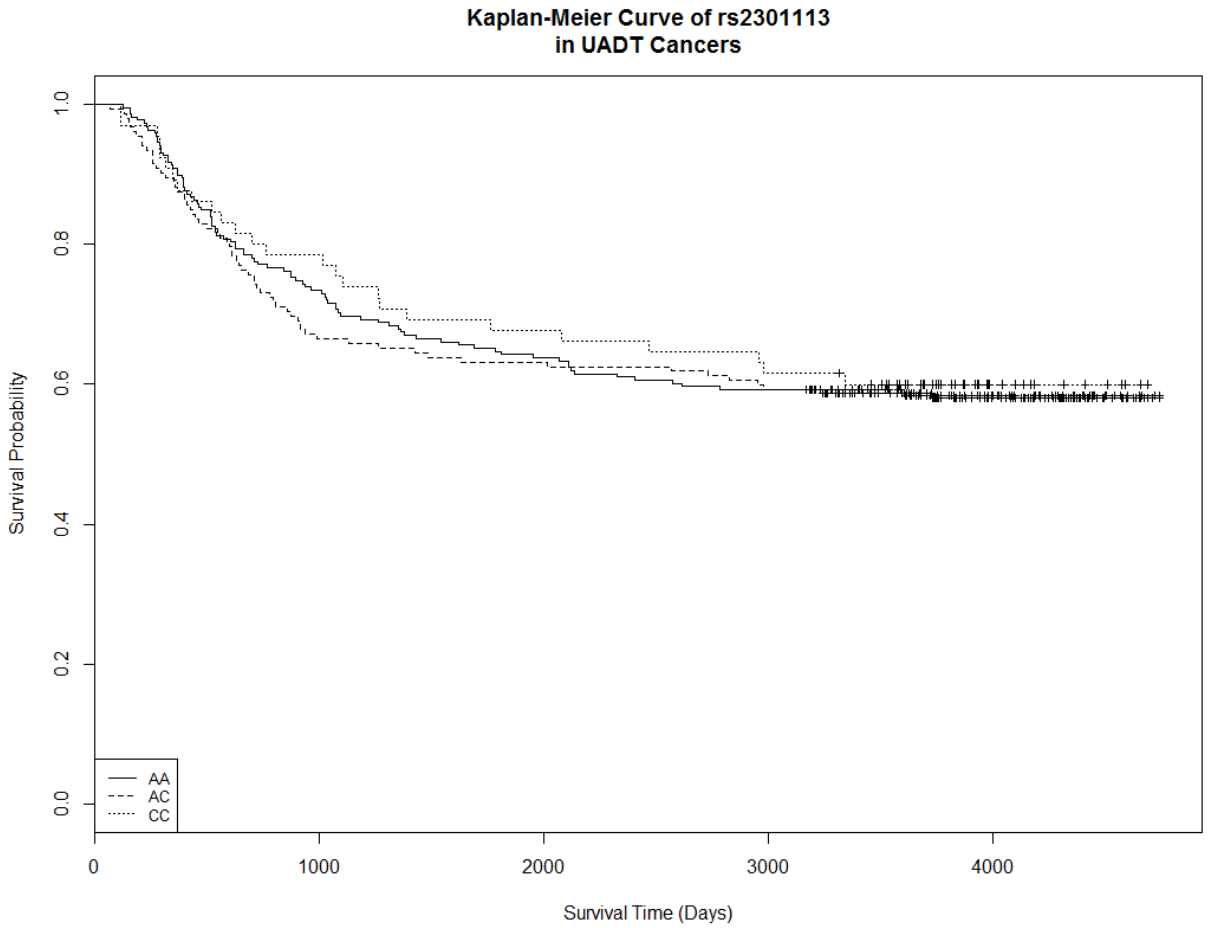

Figure 2.15 Kaplan-Meier curve of *HIF1A* rs2301113 in UADT cancers

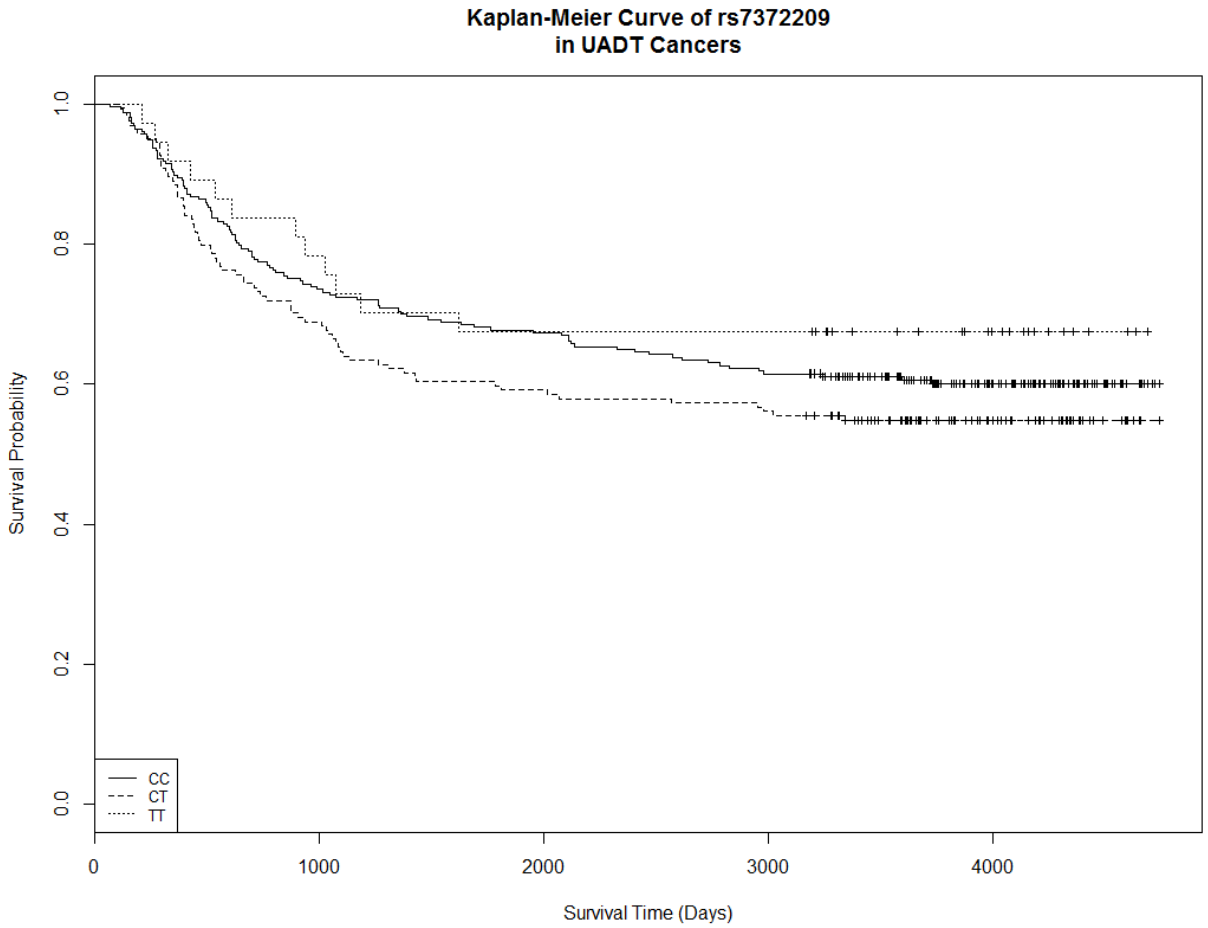

Figure 2.16 Kaplan-Meier curve of *MIR-26A1* rs7372209 in UADT cancers

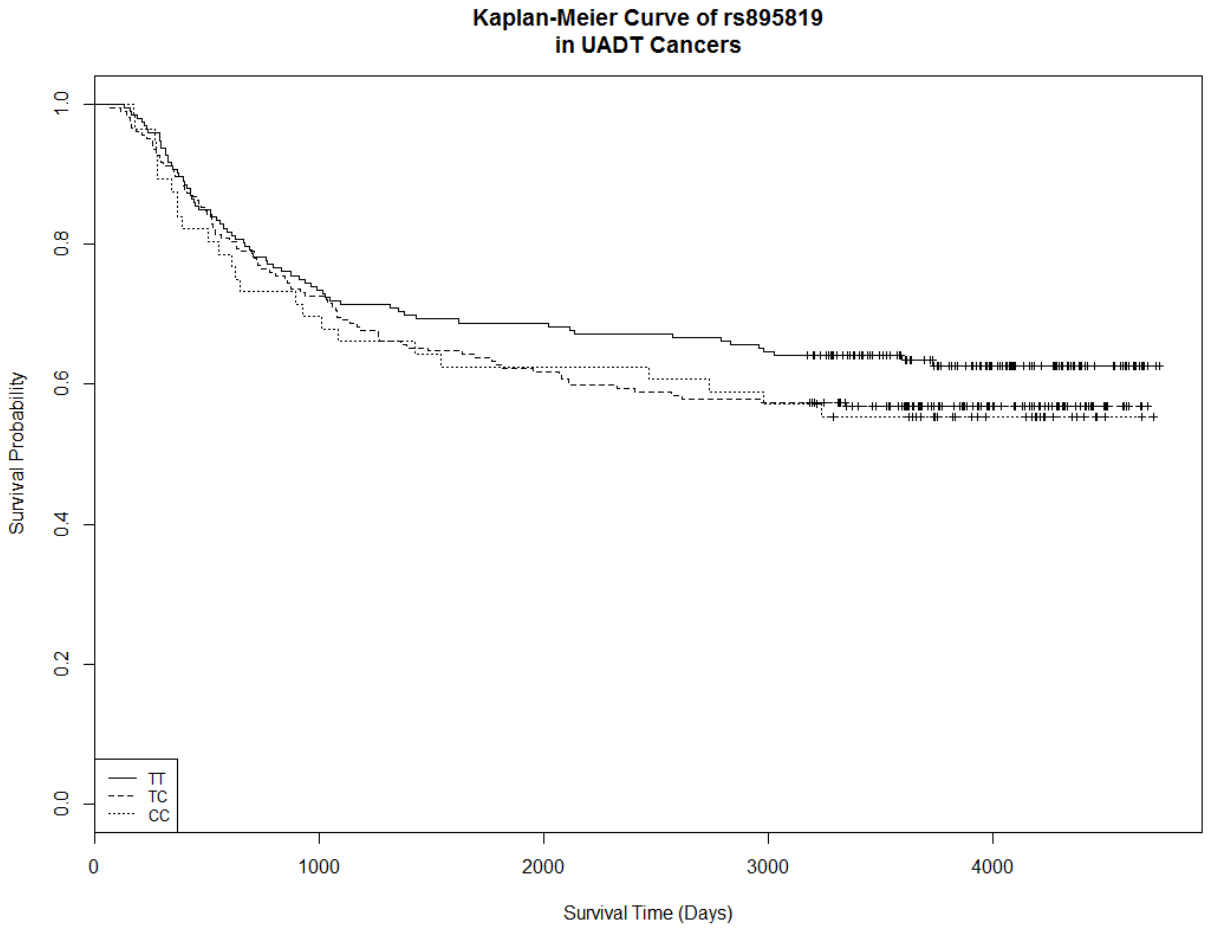

Figure 2.17 Kaplan-Meier curve of *MIR-27* rs895819 in UADT cancers

Figure Section III

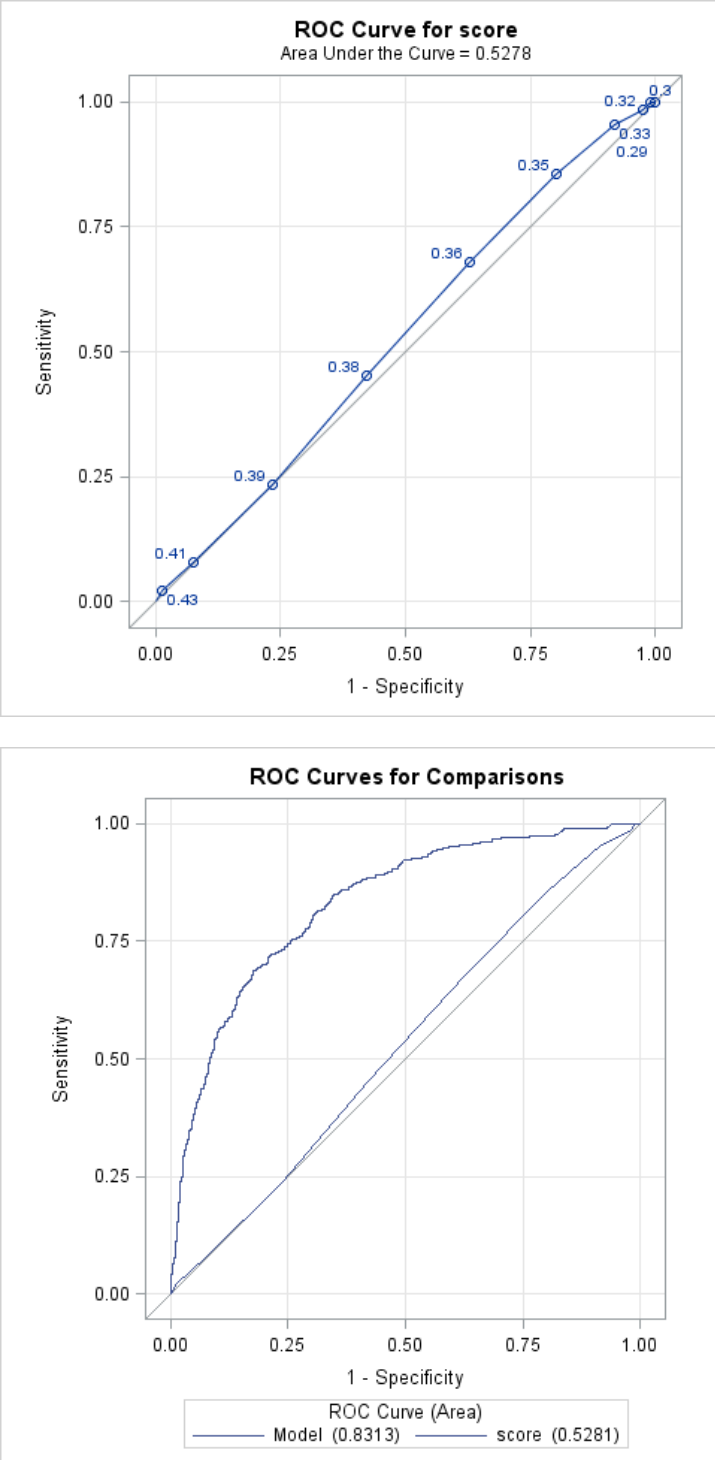

Figure 3.1 ROC curve for miRNA biogenesis gene score and lung cancer development

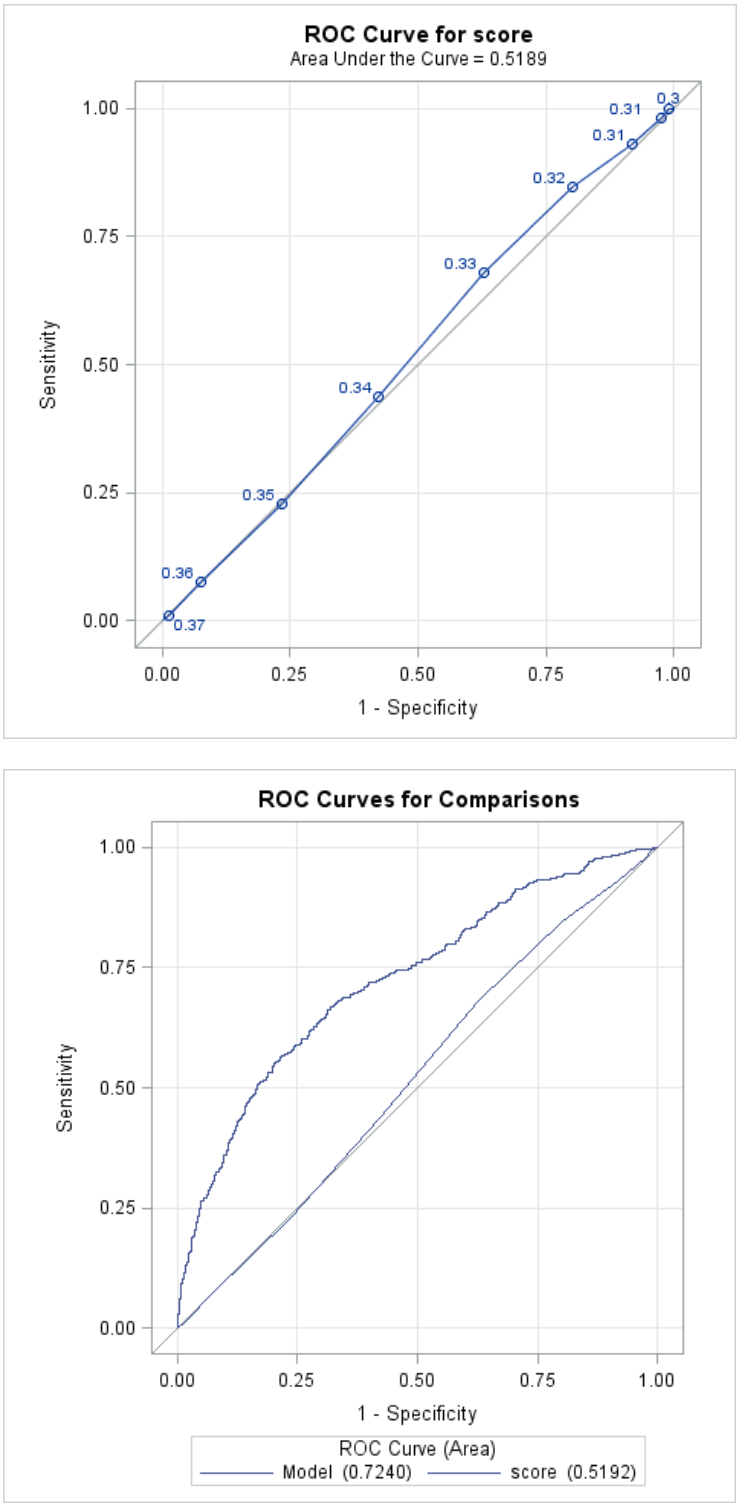

Figure 3.2 ROC curve for miRNA biogenesis gene score and UADT cancer development

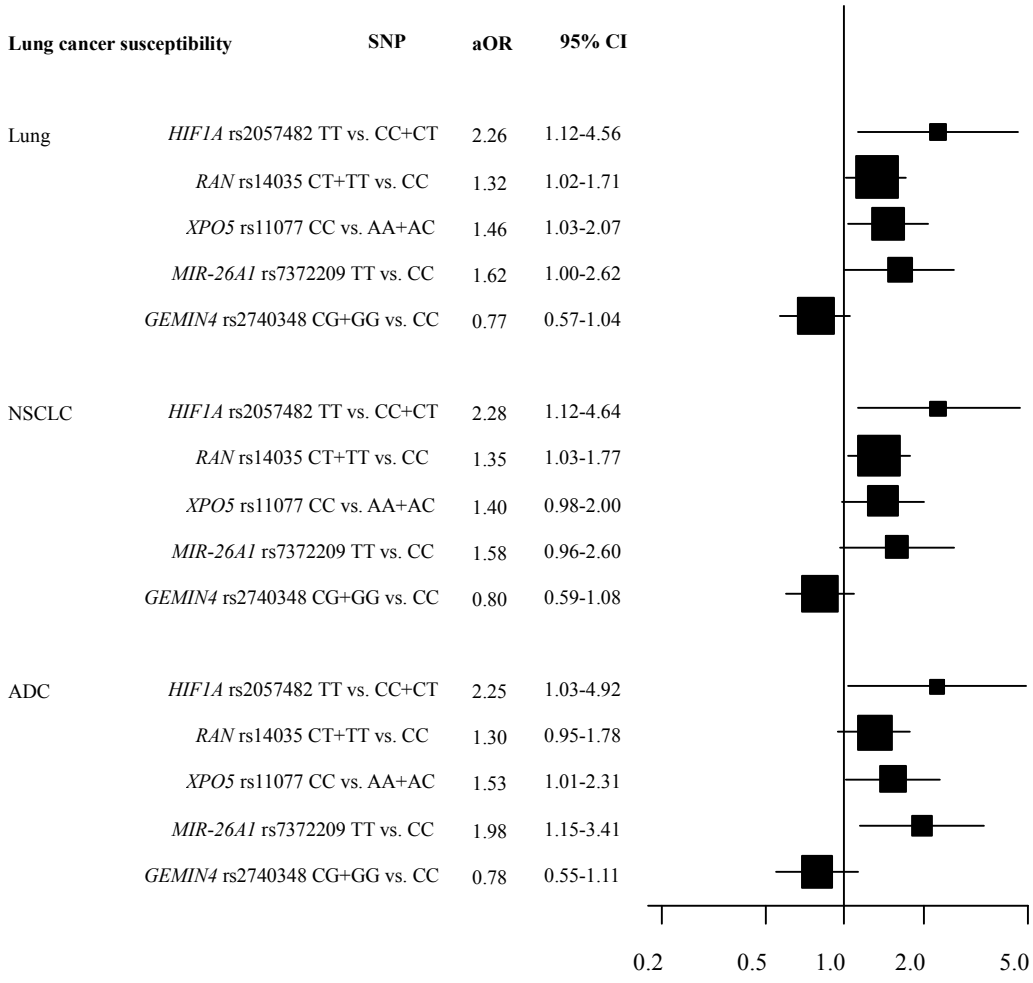

Figure 4.1.1 Forest plot of lung cancer susceptibility, stratified by histology types

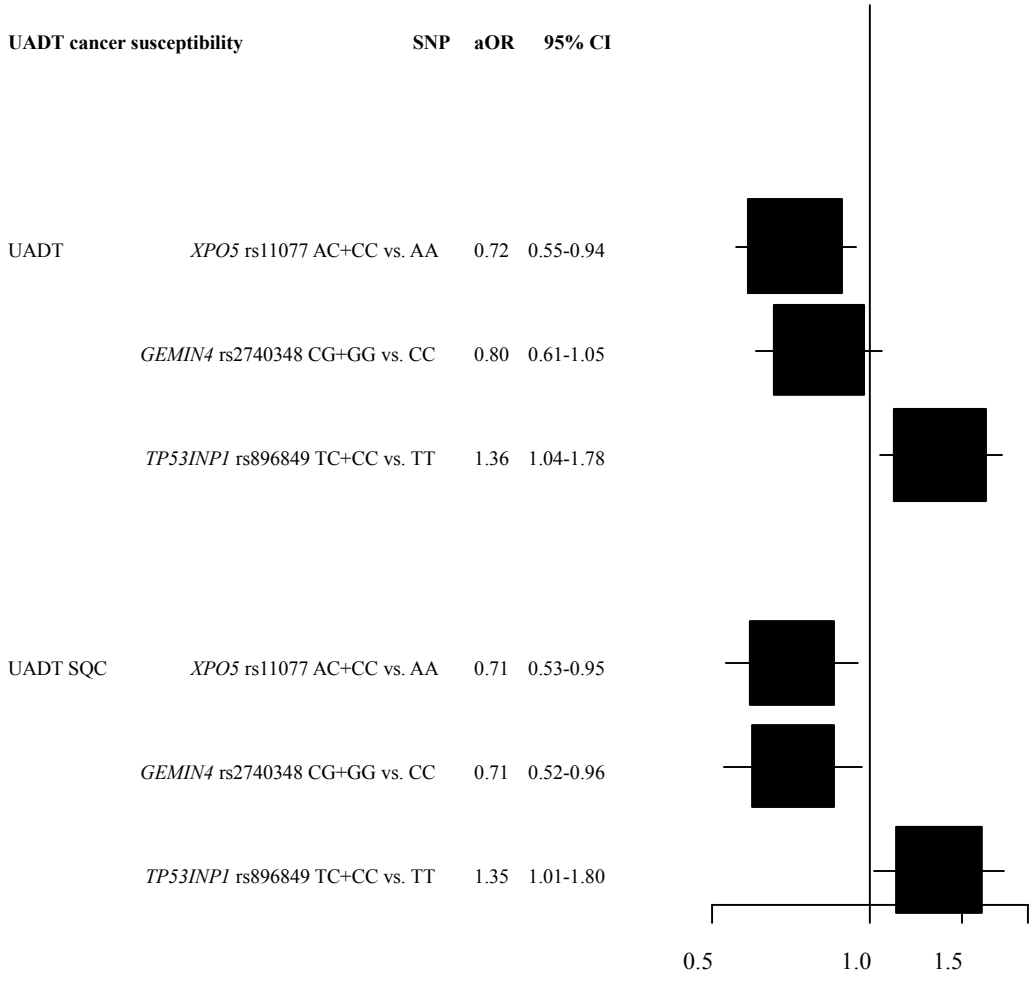

Figure 4.1.2 Forest plot of UADT cancer susceptibility, stratified by histology types

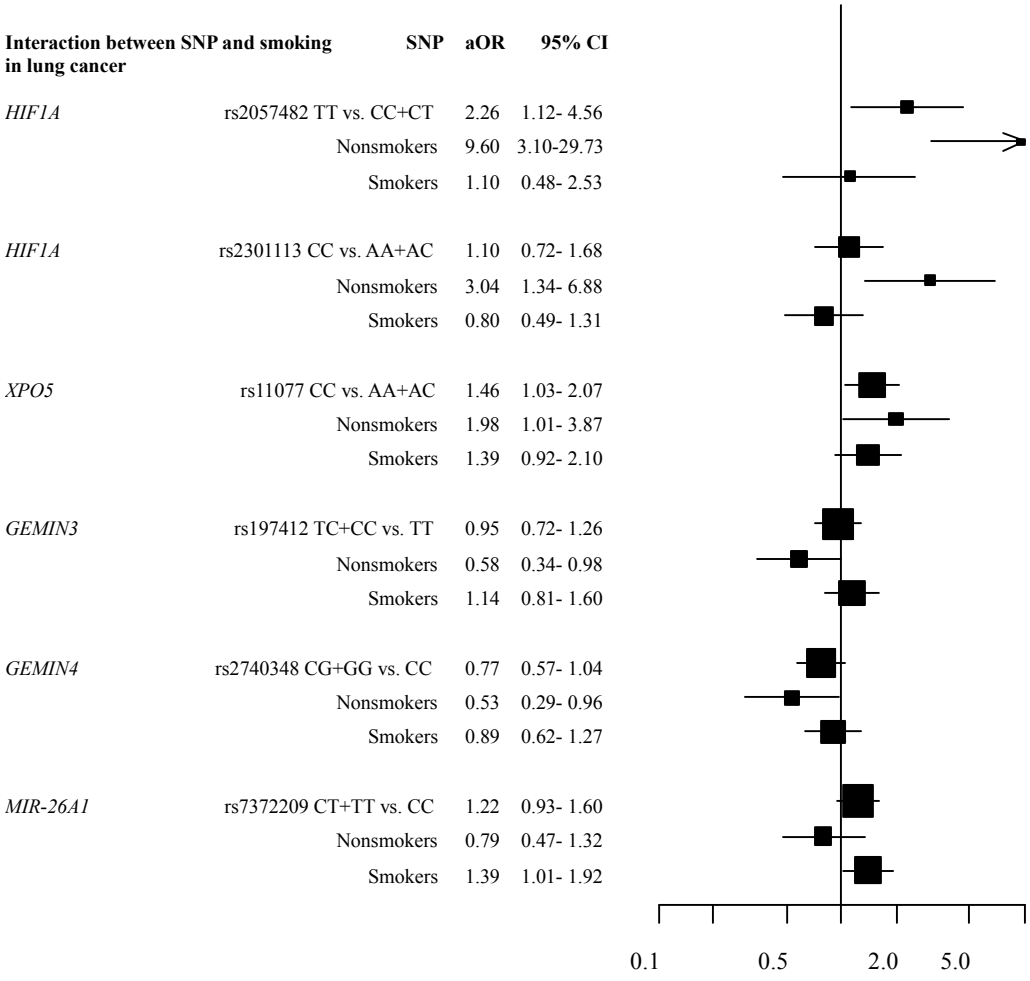

Figure 4.1.3 Forest plot of stratified analysis by smoking in lung cancer

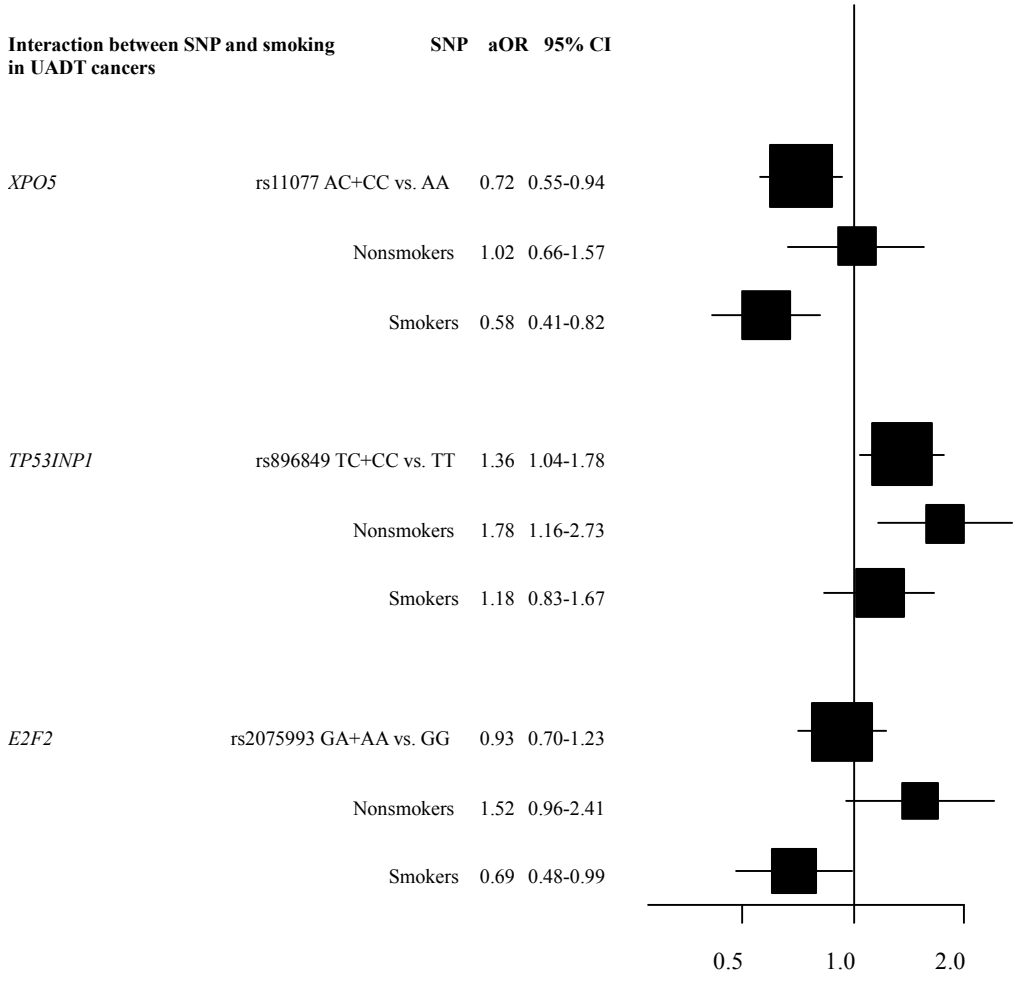

Figure 4.1.4 Forest plot of stratified analysis by smoking in UADT cancers

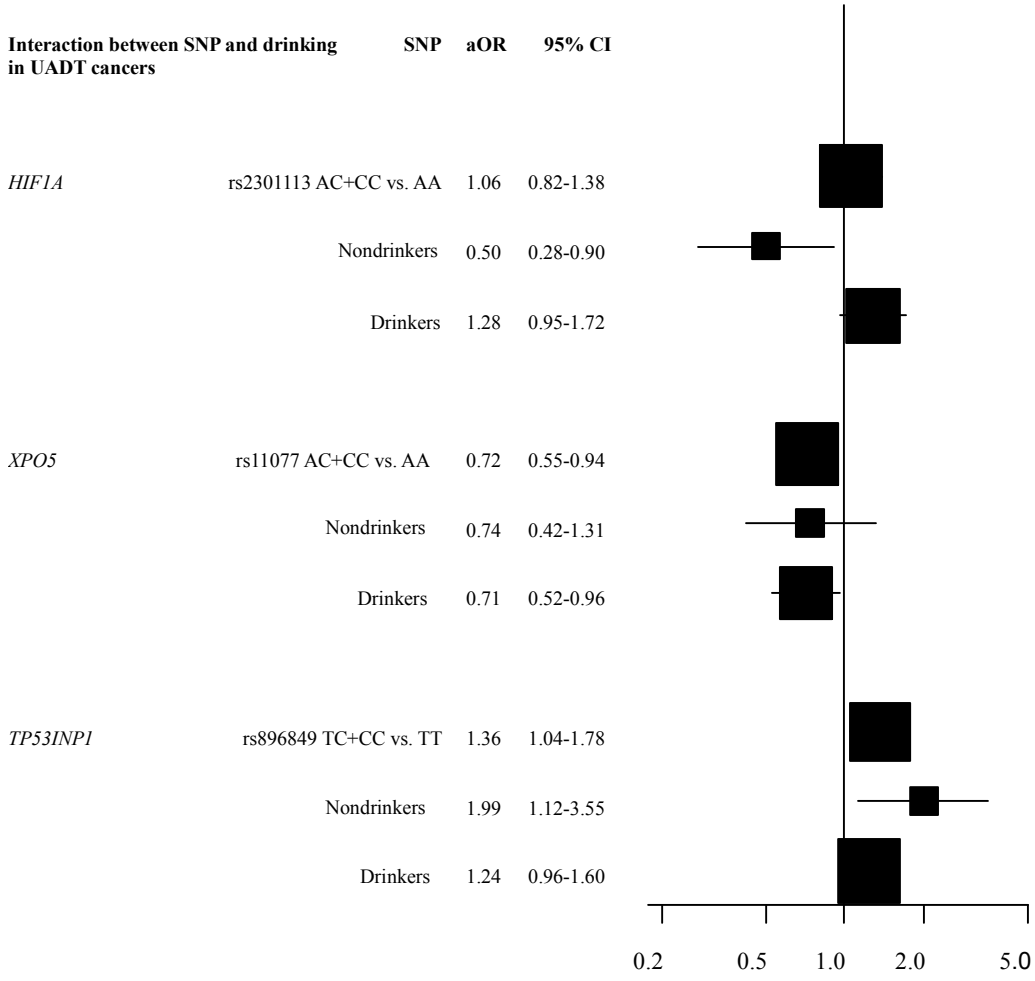

Figure 4.1.5 Forest plot of stratified analysis by drinking in UADT cancers

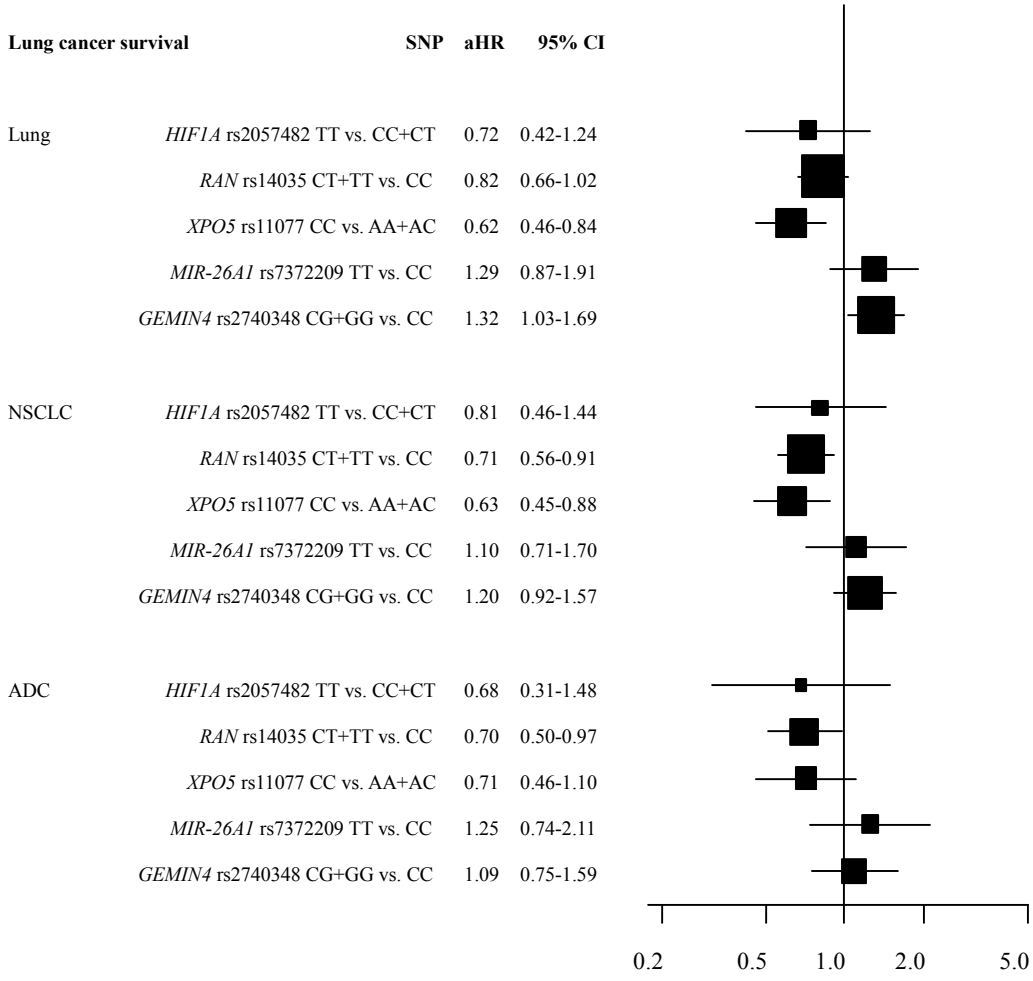

Figure 4.2.1 Forest plot of UADT cancer susceptibility, stratified by histology types

Supplementary table 1. Allele frequencies in controls, stratified by ethnicity

SNP	Caucasian N (%)	Hispanic N (%)	Black N (%)	Asian N (%)	Other N (%)
Micro RNA processing and maturation					
XPO5 rs11077					
AA	192 (30.28)	51 (25.00)	10 (9.80)	41 (66.13)	11 (29.73)
AC	308 (48.58)	101 (49.51)	42 (41.18)	11 (17.74)	17 (45.95)
CC	78 (12.30)	37 (18.14)	27 (26.47)	0 (0)	3 (8.11)
Missing	56 (8.83)	15 (7.35)	23 (22.55)	10 (16.13)	6 (16.22)
RAN rs14035					
CC	271 (42.74)	103 (50.49)	38 (37.25)	33 (53.23)	18 (48.65)
CT	251 (39.59)	67 (32.84)	25 (24.51)	14 (22.58)	8 (21.62)
TT	51 (8.04)	18 (8.82)	14 (13.73)	4 (6.45)	5 (13.51)
Missing	61 (9.62)	16 (7.84)	25 (24.51)	11 (17.74)	6 (16.22)
DICER1 rs3742330					
AA	466 (73.50)	129 (63.24)	73 (71.57)	24 (38.71)	24 (64.86)
AG	106 (16.72)	59 (28.92)	6 (5.88)	24 (38.41)	5 (13.51)
GG	5 (0.79)	1 (0.49)	0 (0)	5 (8.06)	1 (2.70)
Missing	57 (8.99)	15 (7.35)	23 (22.55)	9 (14.52)	7 (18.92)
AGO2 rs4961280					
CC	379 (59.78)	99 (48.53)	67 (65.69)	31 (50.00)	18 (48.65)
CA	169 (26.66)	68 (33.33)	10 (9.80)	18 (29.03)	13 (35.14)
AA	24 (3.79)	21 (10.29)	0 (0)	2 (3.23)	0 (0)
Missing	62 (9.78)	16 (7.84)	25 (24.51)	11 (17.74)	6 (16.22)
GEMIN3 rs197412					
TT	220 (34.70)	38 (18.63)	12 (11.76)	21 (33.87)	15 (40.54)
TC	263 (41.48)	110 (53.92)	26 (25.49)	25 (40.32)	10 (27.03)
CC	89 (14.04)	41 (20.10)	39 (38.24)	6 (9.68)	5 (13.51)

SNP	Caucasian N (%)	Hispanic N (%)	Black N (%)	Asian N (%)	Other N (%)
Missing	62 (9.78)	15 (7.35)	25 (24.51)	10 (16.13)	7 (18.92)
GEMIN4 rs7813					
CC	202 (31.86)	78 (38.24)	53 (51.96)	32 (51.61)	12 (32.43)
CT	270 (42.59)	81 (39.71)	21 (20.59)	14 (22.58)	14 (37.84)
TT	97 (15.30)	25 (12.25)	4 (3.92)	5 (8.06)	3 (8.11)
Missing	65 (10.25)	20 (9.80)	24 (23.53)	11 (17.74)	8 (21.62)
GEMIN4 rs2740348					
CC	390 (61.15)	117 (57.35)	71 (69.61)	39 (62.90)	22 (59.46)
CG	166 (26.18)	61 (29.90)	6 (5.88)	11 (17.74)	6 (16.22)
GG	15 (2.37)	10 (4.90)	1 (0.98)	1 (1.61)	1 (2.70)
Missing	63 (9.94)	16 (7.84)	24 (23.53)	11 (17.74)	8 (21.62)
miRNA downstream					
CDK6 rs42031					
AA	371 (58.52)	149 (73.04)	65 (63.73)	45 (72.58)	25 (67.57)
AT	180 (28.39)	35 (17.16)	13 (12.75)	7 (11.29)	6 (16.22)
TT	23 (3.63)	3 (1.47)	1 (0.98)	0 (0)	0 (0)
Missing	60 (9.46)	17 (8.33)	23 (22.55)	10 (16.13)	6 (16.22)
TP53INP1 rs896849					
TT	418 (65.93)	150 (73.53)	35 (34.31)	39 (62.90)	23 (62.16)
TC	139 (21.92)	37 (18.14)	36 (35.29)	13 (20.97)	7 (18.92)
CC	20 (3.15)	1 (0.49)	8 (7.84)	1 (1.61)	1 (2.70)
Missing	57 (8.99)	16 (7.84)	23 (22.55)	9 (14.52)	6 (16.22)
CXCL12 rs1804429					
TT	548 (86.44)	167 (81.86)	68 (66.67)	47 (75.81)	27 (72.97)
TG	32 (5.05)	22 (10.78)	9 (8.82)	6 (9.68)	4 (10.81)
GG	0 (0)	0 (0)	1 (0.98)	0 (0)	0 (0)
Missing	54 (8.52)	15 (7.35)	24 (23.53)	9 (14.52)	6 (16.22)
E2F2 rs2075993					

SNP	Caucasian N (%)	Hispanic N (%)	Black N (%)	Asian N (%)	Other N (%)
GG	142 (22.40)	68 (33.33)	58 (56.86)	13 (20.97)	9 (24.32)
GA	311 (49.05)	92 (45.10)	18 (17.65)	21 (33.87)	13 (35.14)
AA	123 (19.40)	26 (12.75)	2 (1.96)	19 (30.65)	9 (24.32)
Missing	58 (9.15)	18 (8.82)	24 (23.53)	9 (14.52)	6 (16.22)
DOCK4 rs3801790					
AA	253 (39.91)	51 (25.00)	36 (35.29)	23 (37.10)	13 (35.14)
AG	266 (41.96)	92 (45.10)	34 (33.33)	22 (35.48)	12 (32.43)
GG	58 (9.15)	46 (22.55)	8 (7.84)	8 (12.90)	6 (16.22)
Missing	57 (8.99)	15 (7.35)	24 (23.53)	9 (14.52)	6 (16.22)
IL6R rs4072391					
CC	377 (59.46)	120 (58.82)	41 (40.20)	36 (58.06)	18 (48.65)
CT	177 (27.92)	48 (23.53)	30 (29.41)	14 (22.58)	10 (27.03)
TT	19 (3.00)	17 (8.33)	8 (7.84)	2 (3.23)	3 (8.11)
Missing	61 (9.62)	19 (9.31)	23 (22.55)	10 (16.13)	6 (16.22)
HIF1A					
HIF1A rs2057482					
CC	428 (67.51)	155 (75.98)	38 (37.25)	34 (54.84)	17 (45.95)
CT	135 (21.29)	34 (16.67)	36 (35.29)	17 (27.42)	11 (29.73)
TT	15 (2.37)	0 (0)	5 (4.90)	1 (1.61)	2 (5.41)
Missing	56 (8.83)	15 (7.35)	23 (22.55)	10 (16.13)	7 (18.92)
HIF1A rs2301113					
AA	325 (51.26)	103 (50.49)	6 (5.88)	22 (35.48)	11 (29.73)
AC	186 (29.34)	67 (32.84)	25 (24.51)	16 (25.81)	16 (43.24)
CC	34 (5.36)	8 (3.92)	46 (45.10)	9 (14.52)	2 (5.41)
Missing	89 (14.04)	26 (12.75)	25 (24.51)	15 (24.19)	8 (21.62)
miRNAs					
MIR-26A1 rs7372209					
CC	322 (50.79)	66 (32.35)	65 (63.73)	23 (37.10)	18 (48.65)

SNP	Caucasian N (%)	Hispanic N (%)	Black N (%)	Asian N (%)	Other N (%)
CT	219 (34.54)	98 (48.04)	12 (11.76)	25 (40.32)	11 (29.73)
TT	35 (5.52)	22 (10.78)	2 (1.96)	5 (8.06)	2 (5.41)
Missing	58 (9.15)	18 (8.82)	23 (22.55)	9 (14.52)	6 (16.22)
MIR-27 rs895819					
TT	256 (40.38)	93 (45.59)	25 (24.51)	22 (35.48)	16 (43.24)
TC	267 (42.11)	77 (37.75)	35 (34.31)	22 (35.48)	10 (27.03)
CC	45 (7.10)	13 (6.37)	18 (17.65)	5 (8.06)	5 (13.51)
Missing	66 (10.41)	21 (10.29)	24 (23.53)	13 (20.97)	6 (16.22)

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