

# UC Irvine

## UC Irvine Previously Published Works

### Title

Abstract 1179: Unique metabolic profile of Vemurafenib-resistant melanoma cells: a quantitative proteomics approach

### Permalink

<https://escholarship.org/uc/item/5vd376n7>

### Journal

CANCER RESEARCH, 75(15\_Supplement)

### ISSN

0008-5472

### Authors

Syed, Deeba N  
Lall, Rahul K  
Majeed, Iram  
[et al.](#)

### Publication Date

2015-08-01

### DOI

10.1158/1538-7445.am2015-1179

### Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

## Abstract 1179: Unique metabolic profile of Vemurafenib-resistant melanoma cells: a quantitative proteomics approach

Deeba N. Syed, Rahul K. Lall, Iram Majeed, Feng Liu, Frank L. Meyskens, and Hasan Mukhtar

DOI: 10.1158/1538-7445.AM2015-1179 Published 1 August 2015

Article

Info & Metrics

Proceedings: AACR 106th Annual Meeting 2015; April 18-22, 2015; Philadelphia, PA

### Abstract

Malignant melanoma is noted for its aggressive clinical behavior and propensity for lethal metastasis. Despite the remarkable success of BRAF inhibitor Vemurafenib in clinics, emergence of resistance remains a limiting factor in increasing overall survival. Thus, comprehensive studies are needed to increase the biological understanding of BRAF-resistant tumors in order to develop effective therapeutic regimens. To study the molecular mechanism(s) involved in acquired resistance, we generated a Vemurafenib-resistant cell line in the BRAFV600E mutated SK-Mel28 melanoma cell background. Incubation of SK-Mel28 cells with Vemurafenib (0.1  $\mu\text{M}$ ) resulted in an initial loss of cell viability after which majority of cells resumed proliferation. Thereafter, cells were exposed to gradually increasing Vemurafenib concentrations and allowed to proliferate in the presence of 5  $\mu\text{M}$  Vemurafenib, to generate the A2-1b resistant cell line. Viability assays established the IC<sub>50</sub> of parental SK-Mel28 cells as 0.2  $\mu\text{M}$ , while IC<sub>50</sub> > than 12  $\mu\text{M}$  was noted for the Vemurafenib-resistant A2-1b population. We utilized a quantitative proteomics strategy, employing label-free nano-LC-MS/MS technology on a Q-exactive, to compare the proteome of A2-1b with SK-Mel28 cells. The data searched against the human proteome using the Sequest search engine and further analyzed with SIEVE software resulted in the positive identification of 1720 proteins ( $\leq 1\%$  FDR). This data set containing proteins with only uniquely identified peptides with a high level of confidence ( $p < 0.05$ ) was uploaded into Ingenuity Pathway Analysis and Panther softwares, with number of peptides and corresponding ratio between the two groups, set as observational parameters. Notably, the largest fraction (49%) of identified proteins belonged to cellular metabolic processes. Glycolysis, gluconeogenesis and NADH repair were the major pathways modulated in Vemurafenib-resistant A2-1b cells. In addition, TCA cycle and unfolded protein response was significantly affected. A subset of 13 proteins, linked to these pathways and not previously associated with acquired resistance was identified. The upregulated proteins included CALD1, OR4A15, PTPRK, CALU, IDH3A, RNH1, CLIC4, SPAG17, SND1 and VCP while ENO2, TPI1 and GAPDH were significantly downregulated. In summary, the proteomic approach applied for the first time to study acquired resistance to BRAF inhibition identified novel targets which upon further validation in appropriate models has the potential to provide valuable therapeutic strategies against Vemurafenib-resistant melanomas.

**Citation Format:** Deeba N. Syed, Rahul K. Lall, Iram Majeed, Feng Liu, Frank L. Meyskens, Hasan Mukhtar. Unique metabolic profile of Vemurafenib-resistant melanoma cells: a quantitative proteomics approach. [abstract]. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; Cancer Res 2015;75(15 Suppl):Abstract nr 1179. doi:10.1158/1538-7445.AM2015-1179

©2015 American Association for Cancer Research.