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**Recent Work** 

### **Title**

CRADA Final Report: Genetic Testing for Evaluation of Heart Disease Risk

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### CRADA Final Report CRADA No. BG98-203

1. Parties:

Roche Molecular Systems, Inc. and UC Regents/LBNL

2. Title of the Project: "Genetic Testing for Evaluation of Heart Disease Risk"

# 3. Summary of the specific research and project accomplishments:

The goal of this CRADA was to identify the relationships of common genetic variants with heart disease risk factors in humans. This was carried out by testing associations of a number of candidate genotypes with plasma measurements of lipid and lipoprotein fractions that are known to predict heart disease risk. In a subset of individuals (395), these associations were tested on both high and low fat diets to examine gene-diet interactions affecting heart disease risk. Preliminary analyses of the results indicate that several genotypes are significantly related to lipoprotein profiles, and to responsiveness of these profiles to reduced fat diets. Thus, analysis of these and other genotypes may ultimately have a role in identifying individuals most likely to benefit from such diets.

### 4. Deliverables:

Deliverable Achieved	Party (LBNL, Participant, Both)	Delivered to Other Party?
11,850 genotypes in 395 subjects participating in diet studies	Performed by LBNL with reagents from Roche Molecular Systems	Yes
11,070 genotypes in 369 subjects selected for leanness	Same as above	Yes

5. Identify publications or presentations at conferences directly related to the CRADA?

None

6. List of Subject Inventions and software developed under the CRADA:

None

# 7. A final abstract suitable for public release:

We have examined relationships of common genotypes in candidate genes to variations in plasma lipids, lipoproteins, lipoprotein subfractions, and other parameters related to cardiovascular disease risk in two study cohorts. The first cohort consisted of 395 healthy individuals studied on their usual diets, and again after consumption of high fat (40-46%) and low fat (20-24%) diets. The second cohort consisted of 369 subjects selected for leanness (body mass index < 25 kg/m2). For both cohorts, 30 genotypes in 14 genes were examined by PCR using reagents from Roche Molecular Systems. In the diet study cohort, significant associations with various lipoprotein measurements were observed for variants in 9 genes related to lipoprotein metabolism. Some of these associations were significant for the high fat or low fat diet only, and/or for diet-induced lipoprotein changes. In addition some associations were significant in the cohort of lean subjects only. Collectively these preliminary analyses suggest that analysis of these genotypes, together with others that will be added on the basis of new gene discovery, can be of value in delineating gene-diet interactions of importance for cardiovascular disease risk.

## 8. Benefits to DOE, LBNL, Participant and/or the U.S. economy.

One of the most significant taxes on the U.S. economy is the loss of productivity due to an ailing work force. Cardiovascular disease affects an enormous segment of the U.S. work force. To be able to treat these diseases with effective therapeutics, or develop alternative preventative regimes, would save the nation billions in health care costs and offset the substantial loss in productivity.

Access to new detection reagents and technology which would have PCR's exquisite sensitivity, will enable earlier diagnosis of cardiovascular disease risk and to monitor disease progression and response to therapy. New applications of the technique will allow it to predict disease predisposition and to individualize patient therapy, all resulting in earlier treatment and improved patient care. This CRADA will enhance the DOE research interests in the area of Functional Genomics. If this work is successful, it would provide a powerful methodology for testing of genotypes of various diseases (KP110201).

#### 9. Financial Contributions to the CRADA:

DOE Funding to LBNL	\$ 0
Participant Funding to LBNL	\$ 43,000
Participant In-Kind Contribution Value	\$ 88,575
Total of all Contributions	\$ 131,575

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