Medical Education and Research Grant Outcome Report

Name: Integrating Variation at Single Nucleotides and Short Tandem Repeats to Identify Genetic Associations with Complex Diseases

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Department: Genetics

Program: New Investigator Program

Grant Duration: 03-01-2007 to 03-31-2009 (25 months)

Expenditures: $100,000 (100%)

Use of Funds (Taxonomy): Basic research

Research Keywords: complex disease, mutation, population genetics, association mapping, short tandem repeat

Description: A powerful approach to identifying the genes that cause human disease is to associate disease with DNA markers in large populations. This project compared two different types of DNA markers commonly used by researchers, in part to help clinical scientists decide which type is best for their particular study. Additionally, this project aimed to develop new methods for associating markers with disease.

Contributions/Results: The investigators provided the first description of associations between the two most widely used classes of DNA variants across the human genome, short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs). The investigators found increased statistical significance for STR-SNP associations over SNP-SNP associations, suggesting that the two variants differ in ways that affect their use as markers in studies of complex diseases.

With these findings, the investigators were able to develop computer simulations allowing for consideration of the complex models and histories that characterize human populations. They found that STRs can identify rare genetic mutations often missed by SNPs. Combinations of SNPs display similarities to STRs and are better predictors of complex diseases than individual SNPs. Finally, the relative abilities of different variants to identify disease-causing mutations depend on mutational mechanisms and population histories. These findings are expected to help researchers choose markers for genome-wide association studies.

Met Objectives: Project completed.

Timeline for Application of Results: Unknown

New Partnerships or Collaborations: This project resulted in a new and productive collaboration with a major contributor in the field of DNA testing and banking, Dr. James Weber, President and Founder of PreventionGenetics in Marshfield, WI.

Matched Dollars (cash or in-kind): None

Dissemination:

- Publications: *Molecular Biology and Evolution; American Journal of Human Genetics.*

  A paper in the *American Journal of Human Genetics* earned a "must read" rating from the website Facultyof1000.com. This site evaluates and features important papers in biology.

- Presentations: Canadian Genetic Epidemiology and Statistical Genetics Meetings; Gordon Conference on Molecular Evolution.

Additional Funding: Received R01 funding of $558,250 over five years from the National Institute of Health Human Genome Research Institute, expanding the MERC-supported research.