



Tufts Medical Center



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Jean Mayer USDA Human  
Nutrition Research Center on  
Aging at Tufts University



**BONRC Epidemiology and Genetics Core  
Mini Symposium  
Gene-Environment Interactions in Obesity**

**Tuesday April 28, 2009  
2:00 – 5:00 p.m.**

**Harvard School of Public Health  
665 Huntington Avenue, Kresge G2**

**“Molecular epidemiology of gene x environment interactions”**

Paul W. Franks PhD MPhil MS BS (Hons)  
Associate Professor of Experimental Medicine  
Umeå University Hospital, Sweden

**“Genes, diet, and risk of obesity & type 2 diabetes”**

Lu Qi, MD PhD  
Research Scientist  
Harvard School of Public Health

**“Nature and nurture: statistical methods for assessing the joint  
contribution of genes and environment to human traits”**

Peter Kraft, PhD  
Associate Professor of Epidemiology and Biostatistics  
Harvard School of Public Health

Moderated by Frank B. Hu, MD PhD and Rob M. van Dam, PhD  
Director and co-Director of the BONRC Epidemiology and Genetics Core

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Please note that you must register in order to attend this workshop. Please visit <http://www.bonrc.org/programregistration/registergene.cfm> to register for this program.

## **ABSTRACTS:**

### **Molecular epidemiology of gene x environment interactions**

Paul W Franks PhD MPhil MS BS (Hons)

Associate Professor of Experimental Medicine, Umeå University Hospital, Sweden

Observations of gene x environment interactions made within the epidemiological setting provide numeric representations of the underlying biological processes. However, inferring casual relationships from observational data is often difficult and studies of interaction may be more prone to false discovery than conventional genetic or non-genetic association studies. In my talk I will discuss how epidemiological observations of gene x environment interactions might aid our comprehension of human disease biology. I will also describe some of the potential pitfalls that sometimes hinder the interpretation of epidemiological data on gene x environment interactions and propose ways in which these hindrances might be overcome in future studies.

### **Genes, diet, and risk of obesity & type 2 diabetes**

Lu Qi, MD PhD

Research Scientist, Harvard School of Public Health

Obesity and Type 2 diabetes has become a major public health challenge worldwide. It is now widely accepted that both environment (e.g. lifestyle) and genetic components affect the development of these conditions. Recently, the genome-wide association studies (GWAS) have identified novel susceptibility genes for obesity and diabetes. In our analyses in the Nurses' Health Study and Health Professionals' Follow-up Study, we found that obesity variants such as MC4R and SH2B1 might affect dietary intakes of total energy and energy-dense macronutrients, and interact with energy balance in relation to obesity. In addition, we found that the genetic background defined by confirmed loci of type 2 diabetes might modify the effects of Western Dietary Pattern in predicting diabetes risk. The interactions are likely driven by foods/nutrients high in western diet such as red meat, processed meat, and heme iron.

### **Nature and nurture: statistical methods for assessing the joint contribution of genes and environment to human traits**

Peter Kraft, PhD

Associate Professor of Epidemiology and Biostatistics, Harvard School of Public Health

Recent advances in genomic annotation and technology have enabled the discovery of over 120 genetic variants associated with over 50 human traits and diseases via genome-wide association studies—discoveries that promise greater understanding of basic human biology and might have immediate application in identifying individuals who would benefit from preventive interventions. However, despite universal agreement that human traits are produced by the joint action of genes and “the environment”—broadly conceived as exposure to environmental toxins, differences in diet, behavior, and social context, and differences in personal physical characteristics—the vast majority of these studies have only considered the effect of the genetic variation averaged over the environment.

This raises the possibility that variants with context-dependent effects have yet to be discovered, as the observed average effect may be smaller than the effect in the subset of exposed individuals. Moreover, algorithms for disease risk prediction should incorporate both known environmental and clinical risk factors as well as newly discovered risk markers.

I will briefly review design, analysis and interpretation of epidemiologic studies of the joint effect of genes and environment on human disease. In particular, I will discuss scenarios where taking heterogeneity in the genetic effect across environmental exposures into account can increase power to detect loci associated with disease. I will also touch on the importance of incorporating both genes and environment into risk prediction models. While current genetic risk scores may not provide clinically actionable information for most people, they might provide useful information in an “exposed” subgroup.