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DIABETES AND DIGESTIVE
AND KIDNEY DISEASES

**Personal Genomics: Establishing the Scientific Foundation
for Using Personal Genome Profiles for Risk Assessment,
Health Promotion and Disease Prevention**

NIH GEI Genomics Translation Research

Recent Initiatives

**Paul L Kimmel MD
Kidney Translational
Genetics Program
NIDDK**





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**Personal Genomics: Establishing the Scientific Foundation
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NIH GEI Genomics Translation Research

Recent Initiatives

Rebekah Rasooly, PhD
Genetics and Genomics Program
NIDDK





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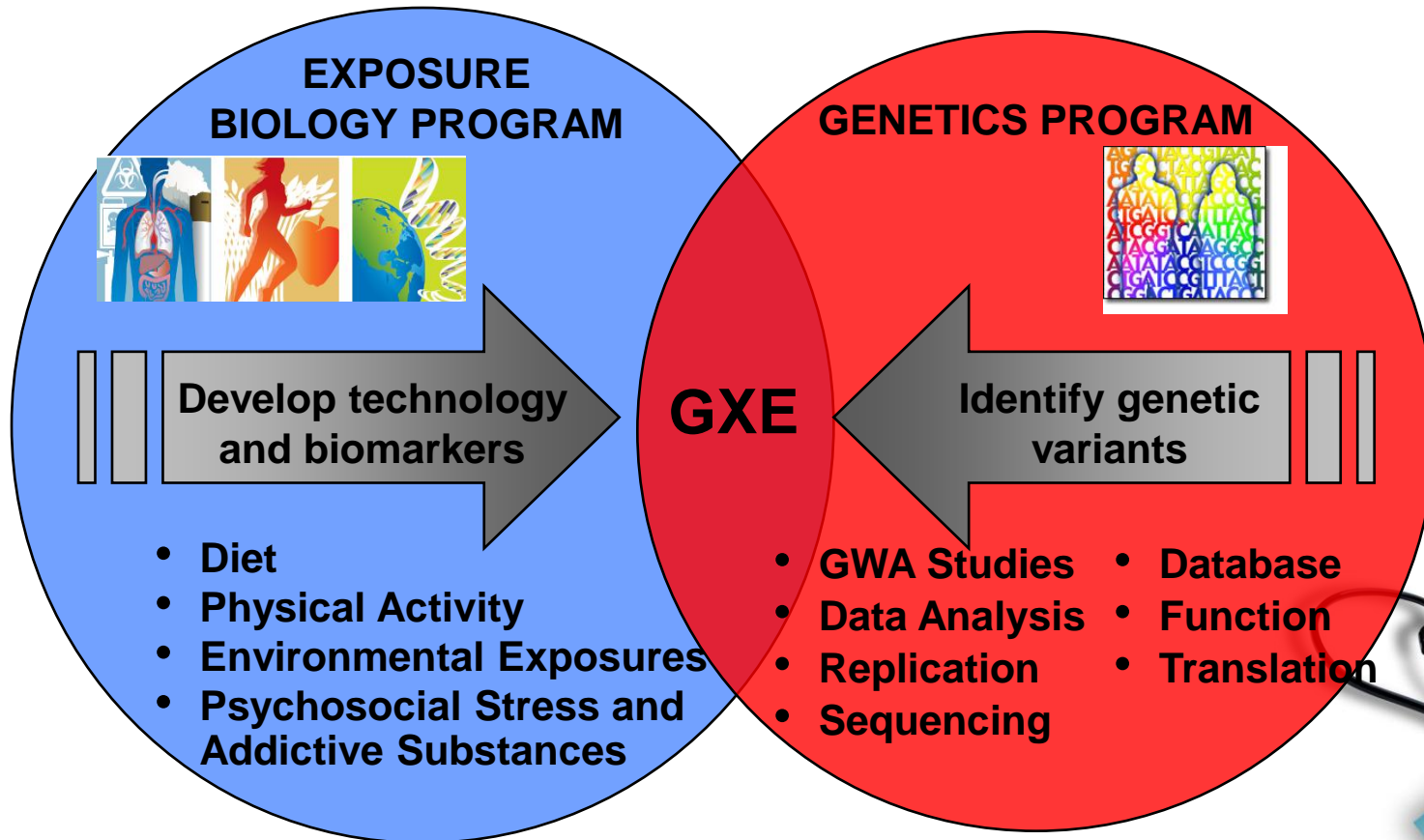
Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice

March 10-11, 2008





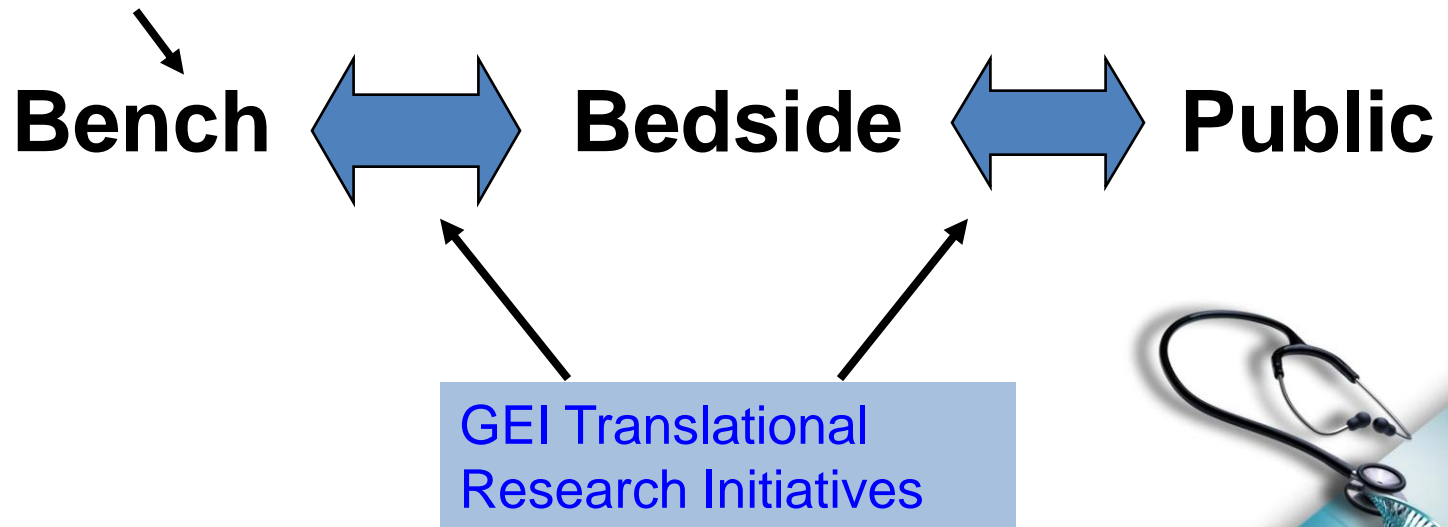
The Genes, Environment and Health Initiative (GEI): Research on Complex Diseases



Translation is a key part of GEI research

GEI initiatives

Discovery through GWAS
Replication/fine mapping
Sequencing
Functional studies



Translation moves discoveries into health practice



Translation of genome findings in complex disease is challenging

- Although genomic discoveries for monogenic diseases had led to tests for diagnosis and screening, there are few evidence-based genetic applications for complex diseases
- It is often hard to assess the validity and utility of genomic tests for specific applications
- Translation requires input from practitioners, patients and other stakeholders, as well as researchers
- The opportunities are unprecedented as exciting discoveries in many complex disease areas are being published at a remarkable rate.
- Concern regarding the use and interpretation of personal genomic data by consumers, patients and practitioners





SIPRESS

"I got my DNA analysis back. Guess what—I'm a Hapsburg."





Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice – March 10-11, 2008

- **Purpose: To explore the challenges in using GEI basic findings to have a positive impact on health.**
- **20 presentations over two days on new genetic findings in common diseases, approaches to using those findings for therapeutic or diagnostic purposes, and the ethical and social issues inherent in such research.**





Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice – March 10-11, 2008

• Consensus

Development of diagnostics and approaches to development of therapies will be useful

Randomized Clinical Trials using information from GWA studies may be premature

Dissemination of accurate information to patients and practitioners is essential, but there are few data suggesting we know

- a) what is the correct way to use such data,**
- b) whether practitioners can use information from GWA studies to improve patient behaviors and health**
- c) what are patient responses to receipt of information regarding risks outlined from GWA studies, and what are the proper modes of information transmission**





Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice – March 10-11, 2008

- **Clinical Utility – Is it Worth Testing?**
- **Will patients change behaviors according to receipt of genetic risk information?**
 - **For common diseases**
 - **If patients won't exercise, modify diet, and take statins in response to receipt of information regarding traditional risk factors, will they respond to dissemination of genetic data?**





Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice – March 10-11, 2008

- **Are there adverse consequences to the receipt of genetic information regarding common diseases?**
- **What are patients'/consumers' abilities to assess risk, and make decisions on receipt of genetic information?**





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Genes, Environment, and Health Initiative: Translating Whole Genome Association Data into Clinical Practice – March 10-11, 2008

Led to Development of 2 Trans-NIH GEI Initiatives





Request for Applications (RFA) Number: RFA-DK-08-004 Translation of Common Disease Genetics into Clinical Applications (R21)

Rationale: Concerns that the field was not ready for definitive translational or therapeutic studies, but that new tools were necessary and desirable to translate genetic information into clinical practice

The NIDDK on behalf of the NIH Genes, Environment and Health Initiative, solicits Exploratory/Developmental Clinical Research Grant (R21) applications from institutions/ organizations that propose

- a) clinical studies using information from genome wide association or other genetic studies in common diseases;**
- b) development and assessment of diagnostic, clinical trial, epidemiologic and risk analytic tools for use in clinical research or practice; and**
- c) cost-effectiveness studies of clinical applications of genetic information.**





**Request for Applications (RFA) Number: RFA-DK-08-004
Translation of Common Disease Genetics into Clinical Applications (R21)**

Areas of interest included:

Development of diagnostic or other risk factor algorithms that incorporate genetic data;

Pilot interventional studies using findings from genetic studies of common diseases or outcomes related to genetic testing for variants identified in common diseases;

**Pilot research on clinical modification of environmental factors known to interact with specific genes variants identified in common diseases;
and**

Cost effectiveness studies.

The proposed research must focus on using findings from genetic studies of common diseases with complex genetic etiology in clinical or public health settings.

This FOA will support efforts to produce data that may be useful or pivotal in eventually designing large scale clinical trials or studies.





Request for Applications (RFA) Number: RFA-DK-08-004
Translation of Common Disease Genetics into Clinical Applications (R21)

Enthusiastic Response

Variety of proposals

Risk assessment

Cost effectiveness

Genetic guided therapy

Feasibility





Request for Applications (RFA) Number: RFA-DK-08-004
Translation of Common Disease Genetics into Clinical Applications (R21)

Diabetes Mellitus (Type 1 and 2)

Asthma

Crohn's Disease/IBD

Nutrition/Hypertension

Vascular Disease

Venous Thrombosis

Autoimmune Disease

Colon, Breast Cancer

Obesity/Metabolic Syndrome

Prevention/Behavior Modification

Provider Education

ESRD/Complications

Atherosclerosis

Hyperlipidemia

Steroid Hormone Metabolism

Smoking Cessation





Request for Applications (RFA) Number: RFA-DK-08-003 Implementation Planning Grants for Educational, Behavioral, or Social Studies for Translation of Genetic Factors in Common Diseases (U34)

Rationale: Preliminary studies suggest field is ripe for design of well-controlled studies of

- a) patient education regarding and responses to receipt of genetic information,**
- b) provider education regarding and responses to receipt and dissemination of genetic information, and**
- c) outcome studies of receipt and dissemination of genetic information, and**

Programmatic input to guide research development will be essential

The NIDDK on behalf of the NIH Genes, Environment and Health Initiative solicits Implementation Planning Grant (U34) applications planning for multicenter research on

- a) educational and communication initiatives for health care providers and consumers regarding interpretation of and findings from genetic studies of common diseases and the results of their dissemination, and**
- b) behavioral or psychosocial aspects of clinical application of genetic findings.**





Request for Applications (RFA) Number: RFA-DK-08-003 Implementation Planning Grants for Educational, Behavioral, or Social Studies for Translation of Genetic Factors in Common Diseases (U34)

Areas of interest included:

- a) research on patient or provider education regarding genetic findings or clinical outcomes of genetic testing;**
- b) research on patient or provider perceptions of environmental or other risk factors that may have specific interactions with gene variants; and**
- c) assessments of responses to use of personal genetic information in clinical care and disease prevention.**

The proposed research must focus on using findings from genetic studies of common diseases with complex genetic etiology in clinical settings.

This FOA supports planning and preliminary or feasibility studies for investigator-initiated, multi-center clinical studies through implementation planning (U34) grants.





**Request for Applications (RFA) Number: RFA-DK-08-003
Implementation Planning Grants for Educational, Behavioral, or Social
Studies for Translation of Genetic Factors in Common Diseases (U34)**

**The U34 planning grant is designed to allow Institutes and
multi-center groups of investigators to plan for major
clinical studies conjointly**

**The product of a U34 grant is the proposal of a multi-
center clinical study cooperative agreement (U01)**





Request for Applications (RFA) Number: RFA-DK-08-003
Implementation Planning grants for Educational, Behavioral or Social
Studies for Translation of Genetic Factors in Common Diseases (U34)

Moderate Response

Patient Education

Physician Education

Behavioral Change

**Diabetes Mellitus Type 1, Metabolic
Syndrome and common diseases**





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Request for Applications (RFA) Number: RFA-DK-08-004
Translation of Common Disease Genetics into Clinical Applications (R21)

**\$4.8 M for RFA-DK-08-004 (and
RFA DK-08-003)**

\$250 K DC/yr for 2 yrs





**Request for Applications (RFA) Number: RFA-DK-08-003
Implementation Planning grants for Educational, Behavioral or Social Studies
for Translation of Genetic Factors in Common Diseases (U34)**

**Request for Applications (RFA) Number: RFA-DK-08-004
Translation of Common Disease Genetics into Clinical Applications (R21)**

Step forward for NIH Clinical Translational Studies in Common Diseases based on GWAS findings

Generate data for use in clinical trials

**Clinically meaningful use of new
genetic data**

**Move from bench to bedside and
public health domains**





Thank you for your attention!

Any questions?





Request for Applications (RFA) Number: RFA-DK-08-003 Implementation Planning Grants for Educational, Behavioral, or Social Studies for Translation of Genetic Factors in Common Diseases (U34)

The U34 planning grant is designed to:

- (1) permit early peer review of the rationale for the proposed clinical study;
- (2) permit assessment of the design/protocol of the proposed study;
- (3) provide support for the development of a complete study protocol and associated documents including a manual of operations,
- (4) support the development of other essential elements required for the conduct of a clinical study, and
- (5) carry out key preliminary or feasibility studies.

Required product of a U34 grant is a prerequisite for submission of a multi-center clinical study cooperative agreement (U01) application, which will support the actual conduct of the study.

