

Follow-up to GWAS Discoveries: Just the beginning.....



Fine Mapping of Notable Regions

Genotyping & Sequencing

Bio-informatics

Analysis of Population Genetics

Functional Determination of Causal Variant(s)

Exploration of Pathways

Etiology

Drug Targets

Design Issues for Clinical Evaluation

Population-based studies

Sequence of Clinical Studies

Validation of Clinical Use

Defining Causality for Moderate to Low Effect Variants

Getting the Right Variant(s)

1. Definition of Variants- Nominating Variants for Parallel Studies
2. Fine Mapping and Sequencing
3. *In Silico* Analysis Tools
4. Published Observations

Large Scale Screening Tools

1. Germline-Expression Data Base
2. Germline-Protein Data Base
3. Animal Models- *but what ones???*

Laboratory Evidence- Detailed and Refined

1. Mechanism for Rapid Transition to Laboratory Expertise
2. Supporting Analysis
3. Standards for Causality

Ultimately- need to provide plausibility....

Sample Procurement & Bio-Repositories: Asynchronous Parallel Activities

•First Stage Discovery

- Establish Basis for Integrative Study
 - “Normal”
 - Disease-driven
- Utilize existing resources

•Second Stage Discovery

- Validation
- Mine Existing Data Sets
- New Studies
 - Cohorts
 - Case Control
 - Family-based

**Bind together existing studies:
Looking where at new places....**

First Stage Discovery

- **“Canonical Discovery Set”**
 - **Germ-line-Somatic-Tissue Reference**
- **Existing Data Sets of Cohorts and Case Control Studies**
 - **Clinical Trials**
 - **NCI Clinical Center Model**
 - **Reach Back Based on Current Observations**
 - **Genomic DNA**
 - **RNA**
 - **Serum**
 - **Tissue**
 - **Urine**
 - **Toe/Finger Nails**
 - **Hair**

Total Collection for Second Stage Discovery and Validation

- **New Studies**
 - Cohorts- sufficient size!
 - Case-Control
 - Family
- **Clinical Samples**
 - Storage
 - “One-way” Availability
- **Prospective Collection**
- **New Tools for Rapid Extraction**
 - Guthrie Card model

Clinical Studies: When Do Epidemiology & Genomics Enter the Arena??

Flashpoint for Gathering Data

Pharmacogenomics

Etiology

Gene-Environment Interactions

Possible Study Requests

Sample procurement

More is Better

Consent for Analysis

Integrative Analysis

FDA Approval & Genomics

Infrastructure

Analytical Capacity

Shift in Paradigm (one gene to multi-gene)