Genome Database in Clinical Trials to Innovate Personalized Medicine

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ORSI Science Symposium
Regulatory Science Talent Competition
Novel Therapies Follow Linear Discovery/Approval Pathway

- Basic Science/Drug Discovery
- Pre-Clinical
- Phase 1
- Phase 2
- Phase 3
- Manufacturing/Approval
Curated Database of Genome Sequencing from Clinical Trials

• ~1% of Current Clinical Trials are Using Sequencing (Drug Interventions)

Clinicaltrials.gov (Intervention Drug, keyword: genome sequencing)
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• IND Annual Report: Verifies sequences deposited

Clinicaltrials.gov (Intervention Drug, keyword: genome sequencing)
Sequence Variation Provides Innovative Platform for Biomarker Discovery

Patients with (-/0) Drug Response/Side Effects

Patients with (+) Drug Response/No Side Effects

Compare genomes of two patient groups
Strategies to Innovate Personalized Medicine

• Priority Area 2: Stimulate Innovation in Personalized Medicine
• Identify and validate biomarkers
• Increase efficiency in study design
• Sequencing provides innovative genomic approach

http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm268112.htm
Pharmacogenomics Increases Efficiency in Drug Safety

• Screen for Polymorphisms CYP Genes

• 55 FDA approved drugs labels list CYP polymorphism

Warfarin – CYP2C9
Adverse Bleeding Risk

Tramadol & Tamoxifen – CYP2D6 required for drug activity

http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm
Sequencing as an Innovative Approach to Pharmacodynamics

- **Acute Myeloid Leukemia:**
  - *RUNX1* mutations → Refractory to Chemotherapy

- **Cardiovascular Disease:**
  - β1-Adrenergic Receptor polymorphism → β-Blocker insensitive

Mendler et al. JCO (2012)
Efficiency from Sequencing Using Recursive Model

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Genome Sequencing Database