

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

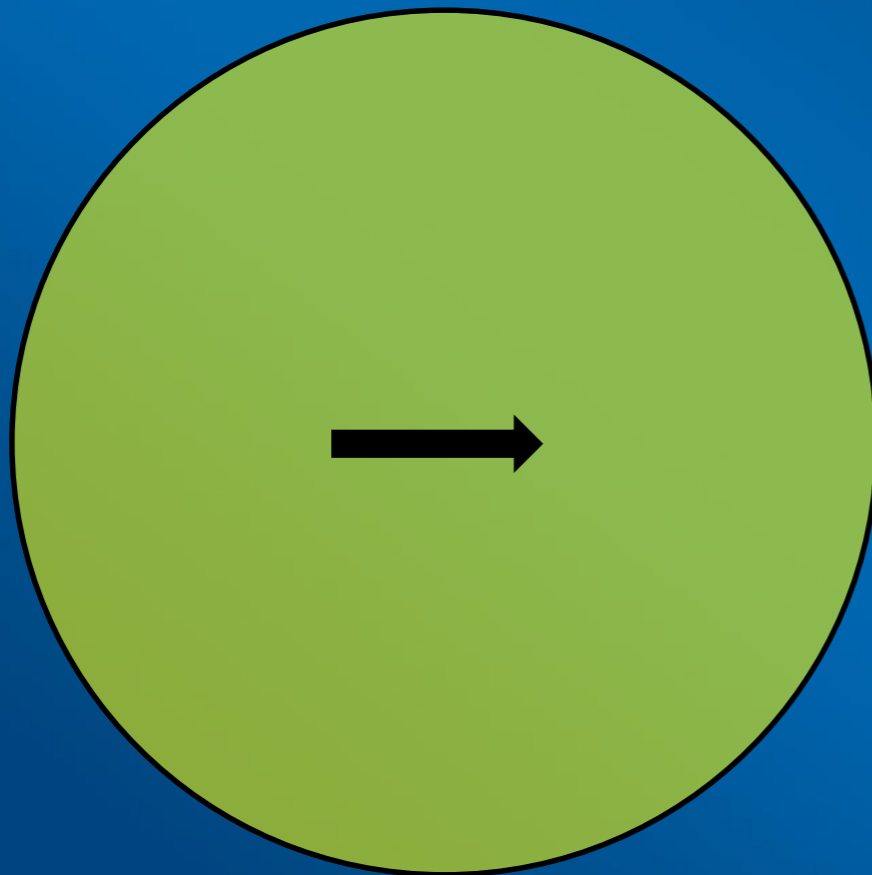
Clinicaltrials.gov (Intervention Drug, keyword: genome sequencing)

MEDICINE *of* THE HIGHEST ORDER

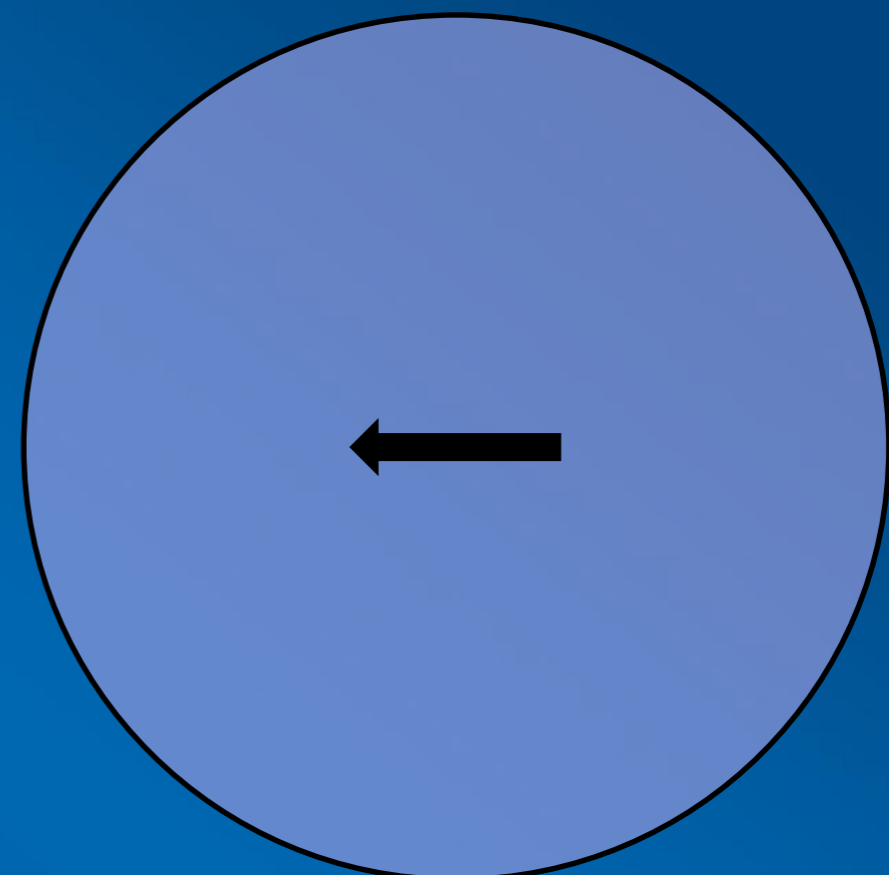


UNIVERSITY *of*
ROCHESTER
MEDICAL CENTER

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:
 - β 1-Adrenergic Receptor polymorphism → β -Blocker insensitive

Mendler et al. JCO (2012)

Johnson and Liggett. Clin Pharmacol Ther. (2011)

Efficiency from Sequencing Using Recursive Model

