From genome exploration to clinical implementation: the challenge of translational pharmacogenomic informatics

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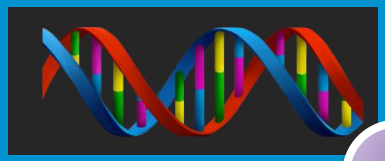
Disclaimer

Remarks are from me, and not my employer.

Silos are morphing into overlapping segments

Discovery



Clinical Development

Biopharma R&D

Approval

Healthcare

Challenges and Opportunities

Validation of New Clinical Endpoints

Personalized Medicine

Post-Market Evidence

Privacy Requirements

Exploratory Clinical Research

- Leverage industry clinical trials to discover & validate biomarkers
- Dual-purpose trials with drug development and exploratory endpoints
- Patient-reported and mobile device data

- Data management strategies that enable exploratory analyses while maintaining compliance and integrity
- Informed consent language, patient engagement

A Tale of Two Toolsets

Bioinformatics - Discovery

- Perl, Python, R, MatLab
- Web-based tools
- Open source software
- Commercial packages
- Pipelines-algorithm chains of various lengths.
- Visualizations galore

Source: wikitravel.org

Biostatistics - Validation

- R for exploratory work
- SAS for official study reports
- Validated R
- Standardized tables, listings and figures

Source: www.londonandpartners.com

VALIDATION

Discovery

- Self / Peer / Customer review
- Tolerance for variability
- Iterative changes/adjustments

Clinical

- “Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.”
  - General Principles of Software Validation: Final Guidance for Industry and FDA Staff

Style and Culture

Discovery

- Exploratory science-driven
- Flexible
- Communal

Clinical

- Clinical endpoint-driven
- Pre-specified, controlled
- Specific stakeholders

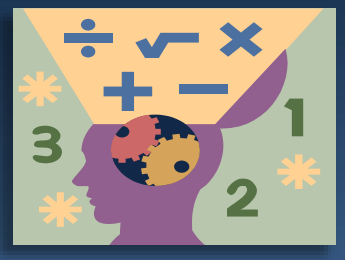
Building Bridges

- Discovery → Clinical
  - Pre-qualify scientific questions prior to study design
  - Re-implement, validate algorithms in SAS
  - Find SAS programmers with communication style flexibility
- Clinical → Discovery
  - Establish process for data de-identification
  - Create separate systems/tool environment for secondary use of clinical data
  - Ensure informed consent permits or at least does not disallow secondary use.

Source: gizmodo.com

Genomic Variability and Drug Response

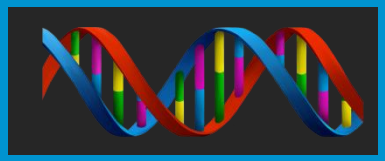




Problem	Objective	Analysis	Findings and Impact
• Unclear whether or how tumor or germline genomic variability might affect response to experimental cancer drug	• Explore whether mutations or copy number changes in genes might serve as markers for response.	• Correlate genetic variants with response in treatment versus control arms **of study supporting NDA.**	• Clinical benefit was apparent in subjects both with and without the genetic markers examined. **Broad label indicated.**

Third and Fourth Legs of the Stool

Discovery



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Pre-Competitive Collaborations – Bridging the Divides

Thank you for your Attention