Translational Oncology: How Far Have We Come & Where Do We Need to Go Next?

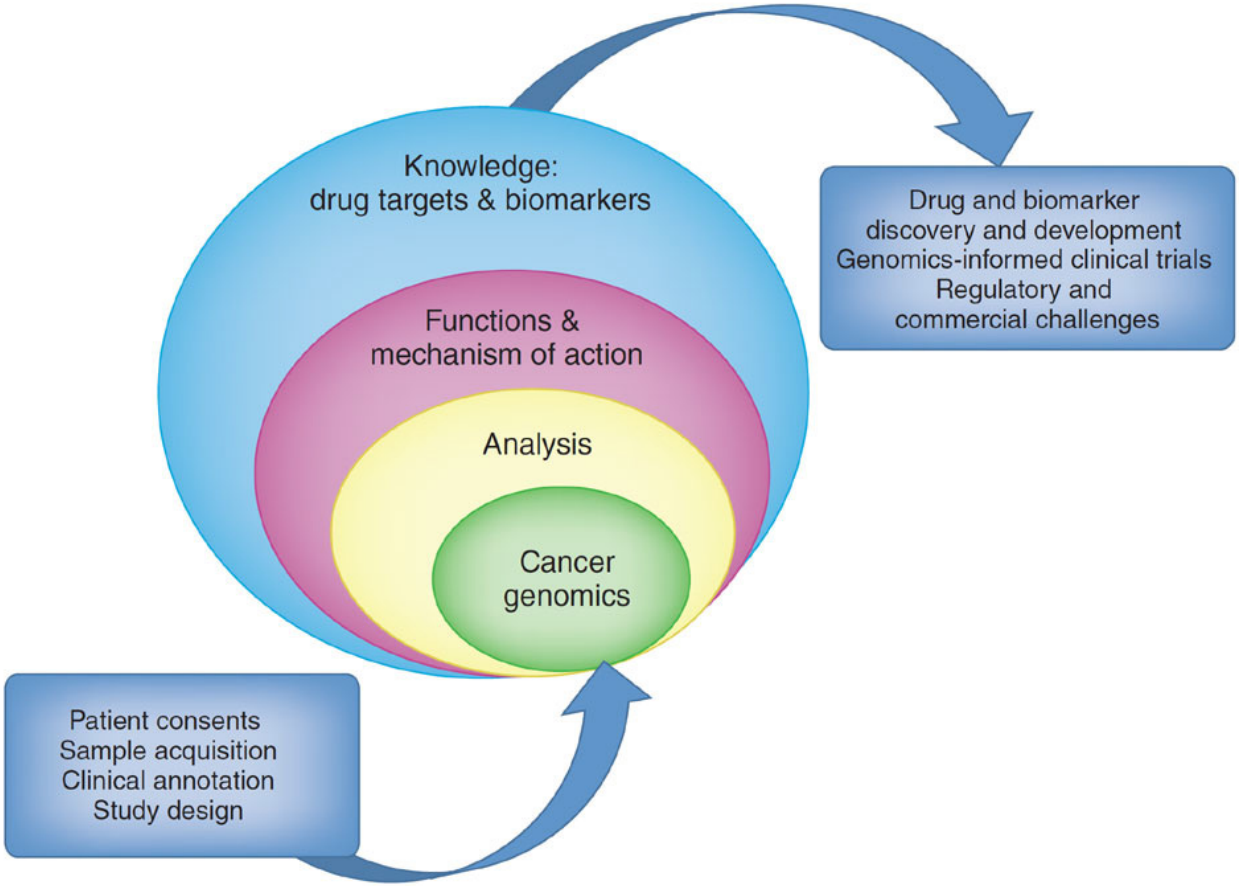
Moderator: Jeff Bockman, PhD, Vice President, Defined Health

Panelists:

- Chris H. Takimoto, MD, PhD, Vice President, Translational Medicine Early Development, Oncology Therapeutic Area, Janssen
- Greg Plowman, MD, PhD VP Oncology Research, Eli Lilly
- Pamela Carroll, PhD, Vice President, Oncology, Innovation Center, Janssen
- Dirk Jan Reitsma, MD, Vice President, Global Product Development Head, Oncology, PPD

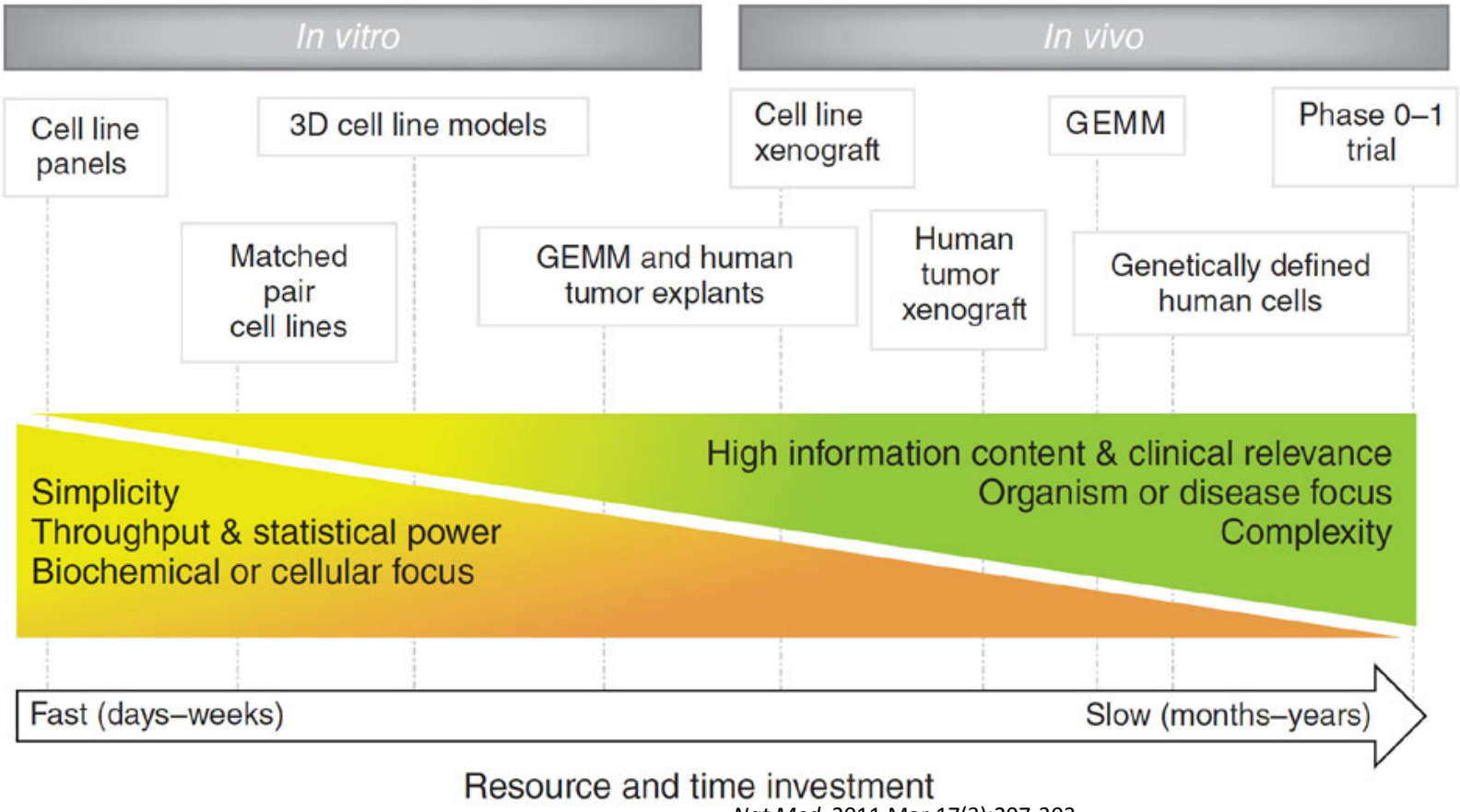
CANCER PROGRESS by Defined Health

Translational Oncology: Overview



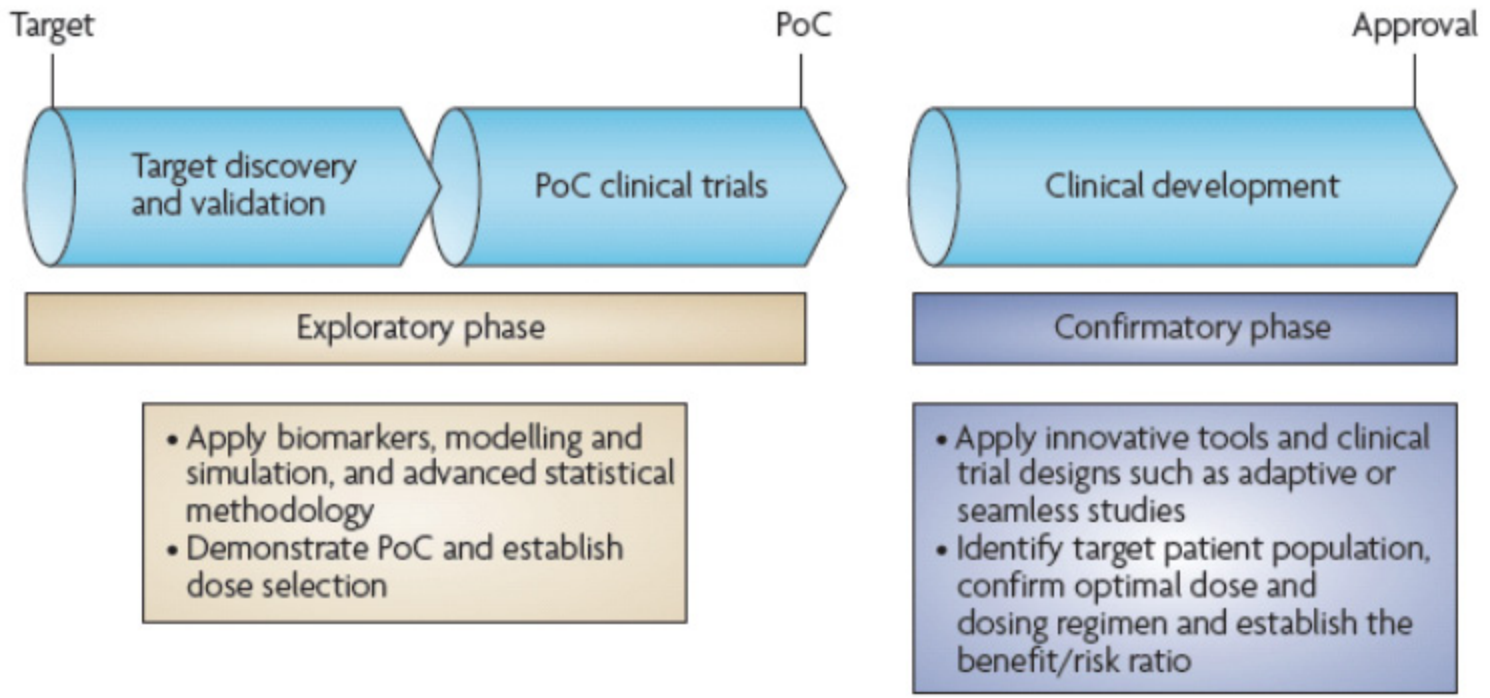
Nat Med. 2011 Mar;17(3):297-303

Translational Oncology: Key Steps & Tools



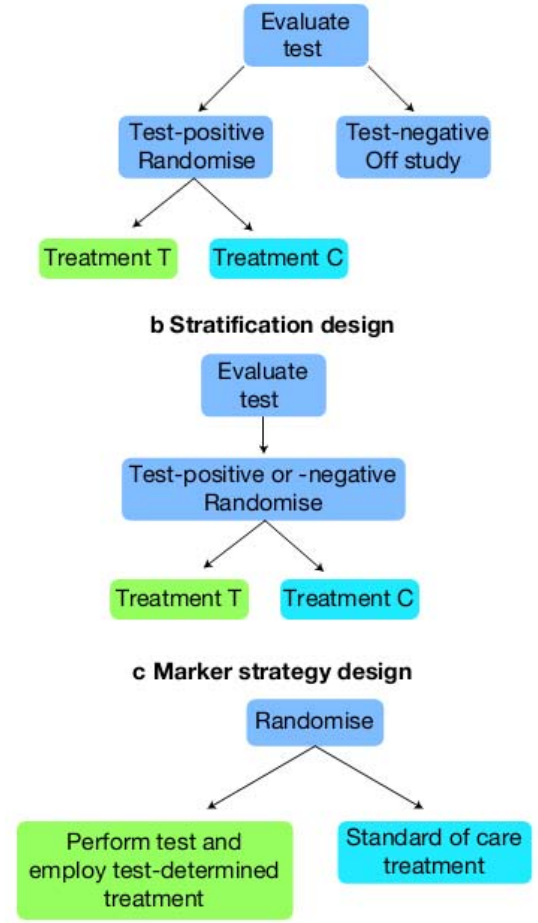
Nat Med. 2011 Mar;17(3):297-303

Translational Oncology: Moving into PoC

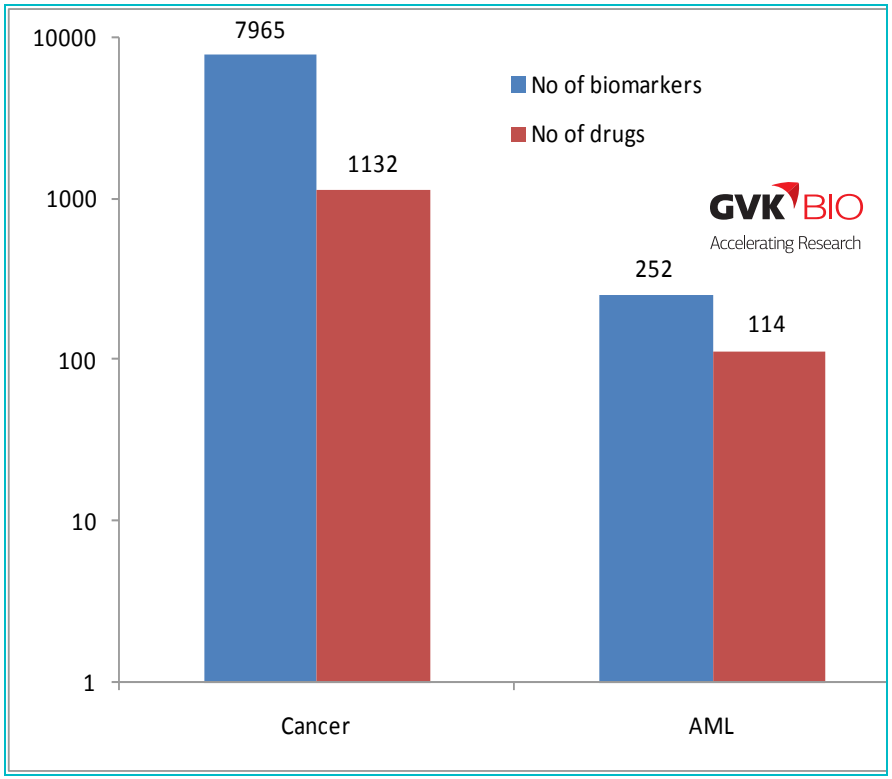


Nat Rev Drug Disc 2009.

Translational Oncology: Incorporating Biomarkers



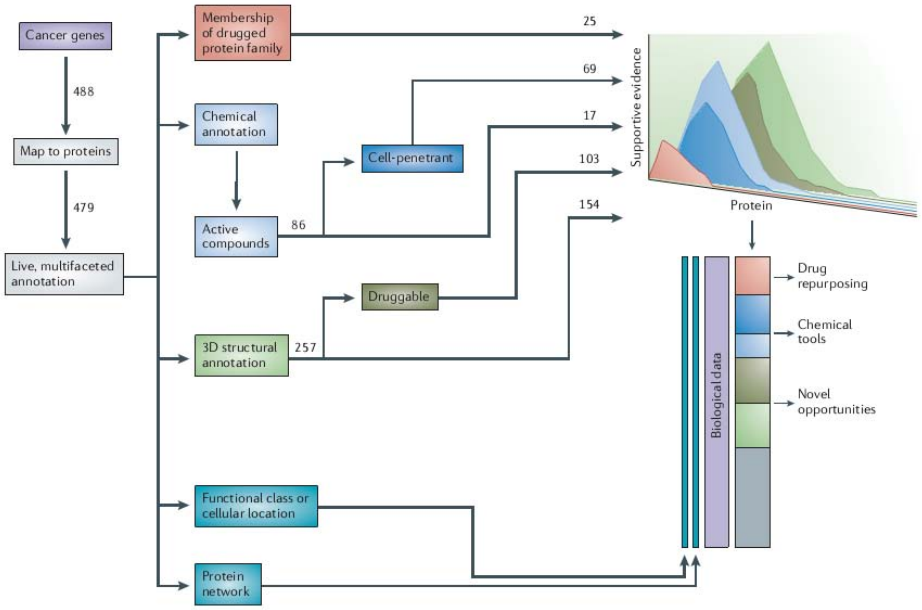
Three designs for prospective clinical trials of predictive biomarker classifiers



Expert Rev Mol Med. 2010 Oct 7;12:e32; GVK BIO

Translational Oncology: Computational Methodology for Prioritizing Therapeutic Cancer Targets

- "Although systematic approaches to discover cancer genes are now commonplace, assessing and prioritizing them for biological validation and therapeutic exploitation remains a largely ad hoc exercise that does not necessarily make use of the full breadth and depth of data available from the abundant large-scale initiatives."



Workflow with annotation scheme and assessment criteria. The list of biologically relevant genes is annotated using homology to targets of approved pharmaceuticals; the molecular and cellular properties of any existing published active small molecules; three-dimensional (3D) structure, druggability or ligandability; and functional class and subcellular localization. Through the incorporation of additional disease information — for example, from The Cancer Gene Atlas (TCGA) or International Cancer Genome Consortium (ICGC) — therapeutic hypotheses can be derived. The data are then combined to rank potential targets based on available supporting evidence for their chemical tractability. The ranking and importance of different features will depend on the ultimate requirement of the analysis: for example, whether the aim is to propose a drug repurposing hypothesis or to identify a novel target. Similarly, certain strands of information — such as the existence of cell-penetrant chemical tools — will only be important for certain targets, in this case intracellular proteins. Mapping the information above onto pathways or cellular interaction networks provides an additional informative view of therapeutic intervention points on the pathway: for example, for combination studies.

Nat Rev Drug Discov. 2013 Jan;12(1):35-50

- **While more and more targeted agents are being brought forward with primary biomarker(s), there remain challenges for target discovery and early development around**
  - **feedback loops,**
  - **how to rationally combine agents**
  - **tumor heterogeneity**
  - **resistance.**
- **Strategies to develop more robust translational studies preclinically to reduce clinical failure rates**
  - **Predictive models**
- **Challenges of screening and stratifying patients**
  - **How to use preclinically**
  - **How to best validate**
  - **How to coordinate multiple tests-gene signatures, single biomarkers, etc.**
  - **How to pay for these (differences for large centers vs. smaller ones)**
- **How to move beyond comfort zone to new ways of doing clinical trials**
- **New ways to collaborate with other industry and academic partners (the pre-competitive collaborations)**
- **Novel trial designs – adaptive and beyond**
  - **What can be learned from other trials in other TAs?**

- Is it feasible to validate response in a xenograft model (or a panel of xenografts) as a general predictive biomarker of outcome by tumor type or by class of compound?
  - Role of primary cells in vitro and in xenografts
- What is the best way to identify patients with an uncommon tumor signature amongst patients with a common tumor type?
- Are there good early biomarkers for compounds that target tumor stem cells?

- How do we develop a therapeutic agent hand in hand with a companion diagnostic on the same timeline for IND and diagnostic registration at the same time?
- How is translational scientific planning for early clinical development optimized? Or in other words, how do we integrate clinical teams with the discovery and biomarker teams to allow for seamless transitions into the clinic?

- What are some of the most exciting cancer breakthroughs of the past few years? Where do big challenges still remain?
- In an era of Obama's Affordable Care Act, sequestration, and patent cliffs in the pharmaceutical industry why is now the right time to invest in innovation?
- What specific reasons would you provide to the uncertain scientist or investor that Oncology initiatives are the best investment for their next dollar?