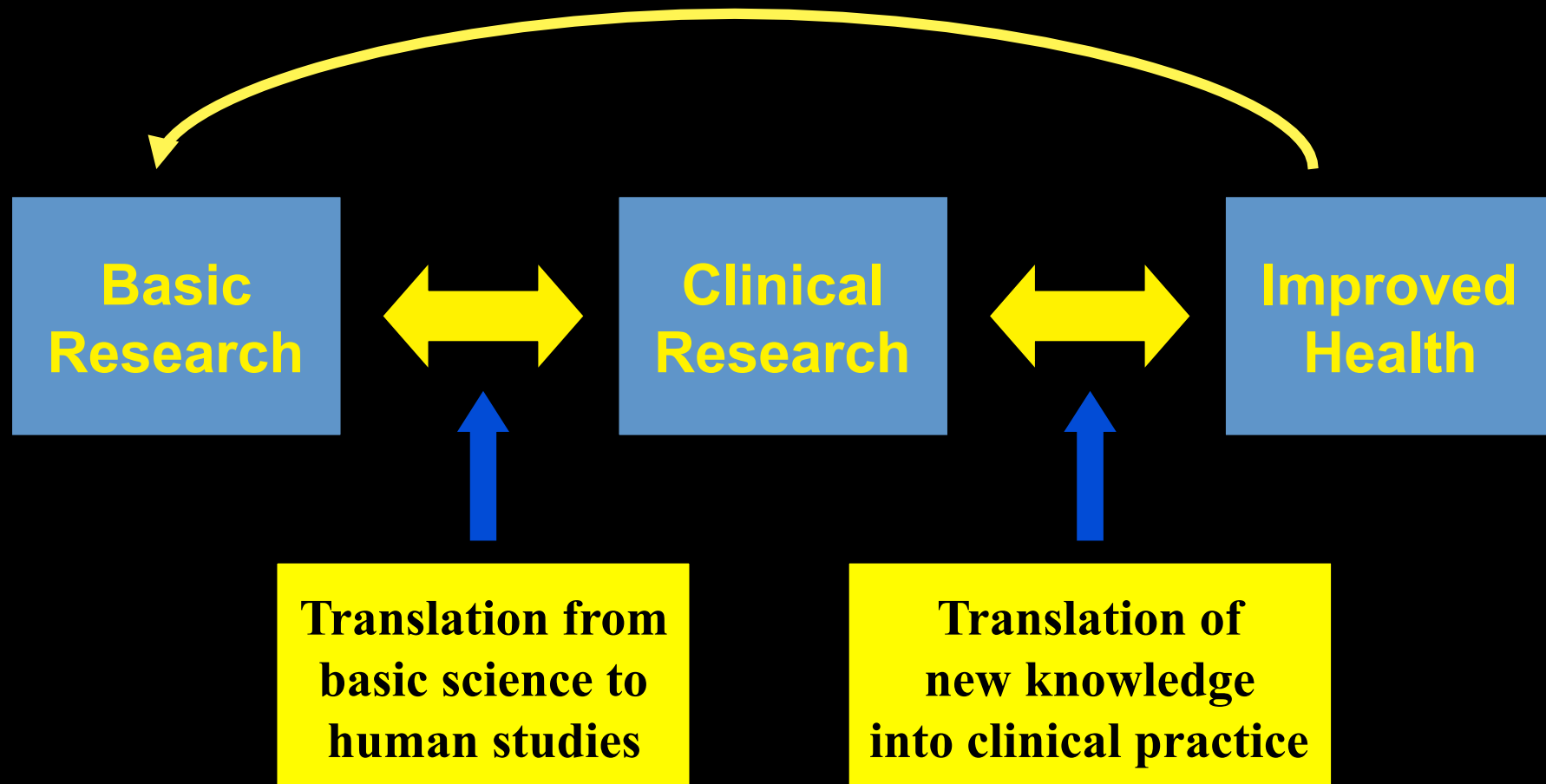


Clinical and Translational Research in the USA

**IPPOSI SYMPOSIUM
DUBLIN 2010**

G.A. FitzGerald
Institute for Translational Medicine and Therapeutics
www.itmat.upenn.edu

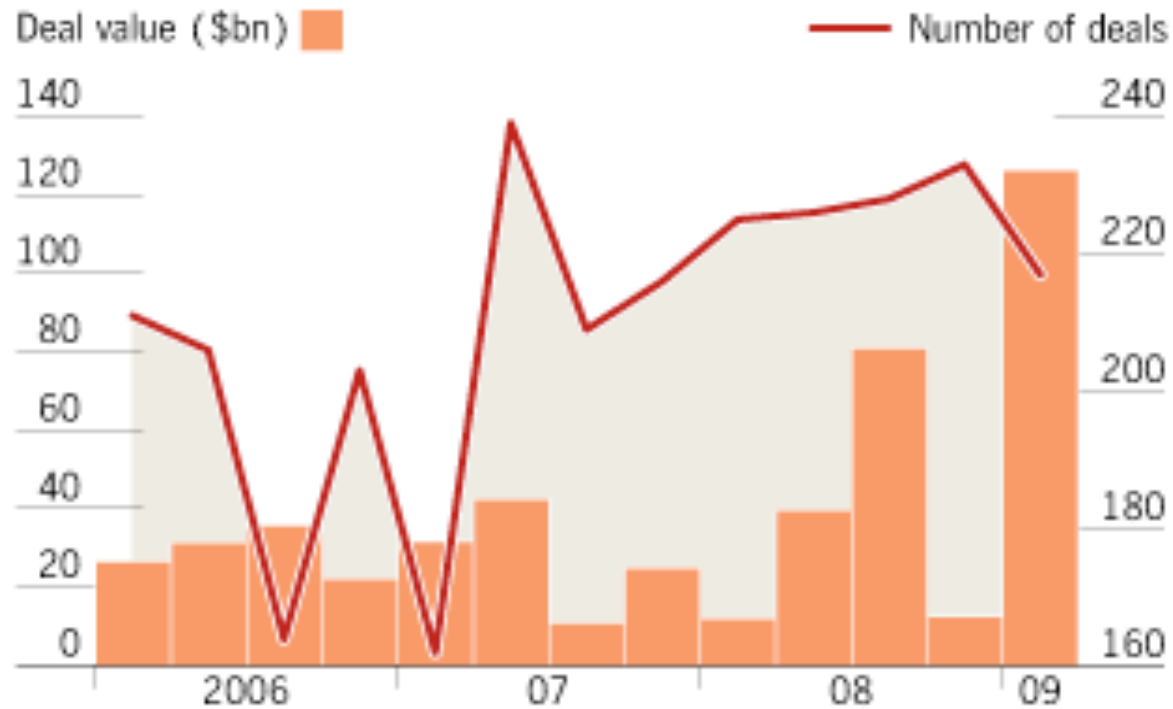
Basic and Clinical Research are Interdependent



Adapted from Sung et al. (2003) JAMA, 289, 1278-89.

Short Term Response - Merger

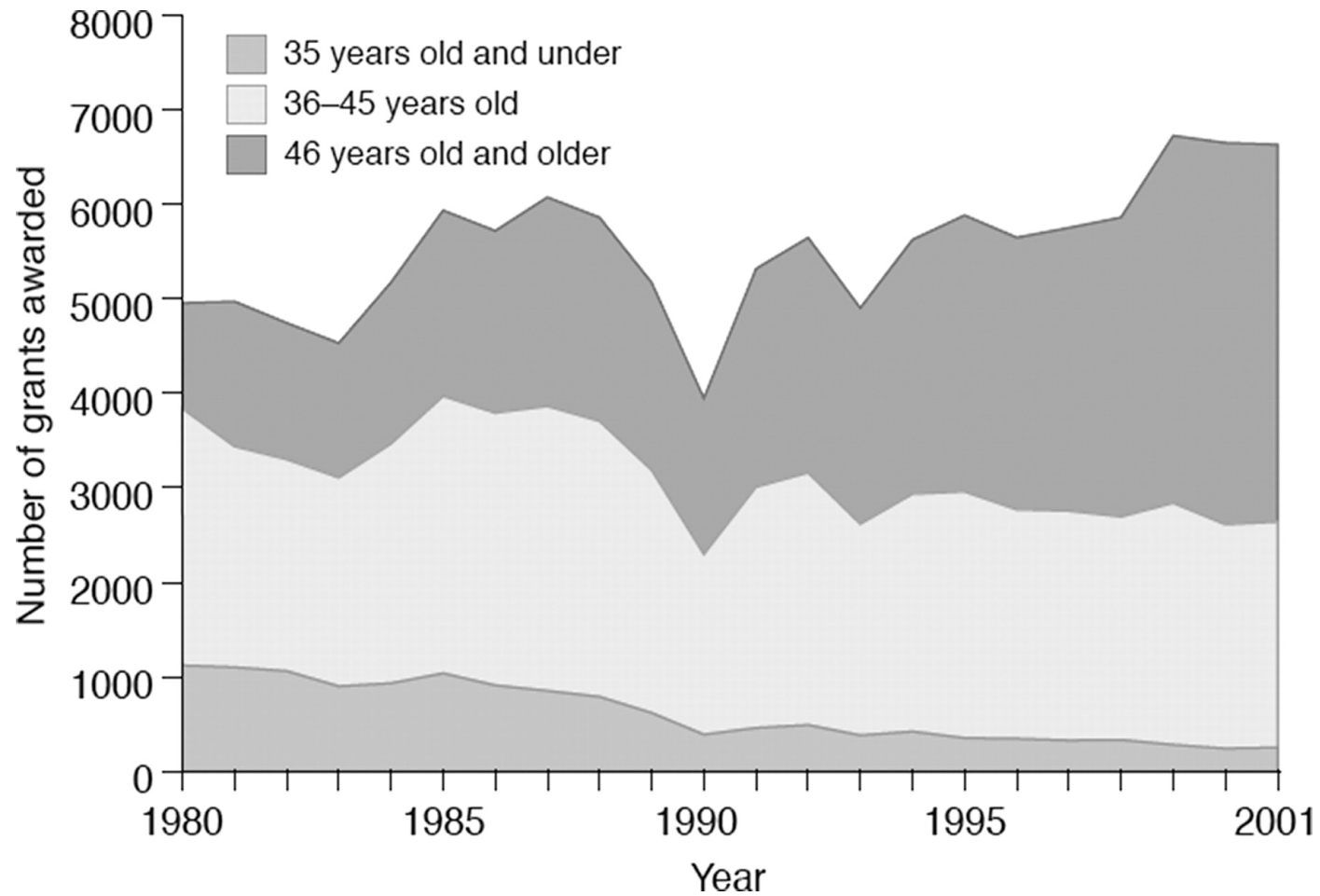
Global pharmaceutical M&A deal volumes



Source: Dealogic

Financial Times Apr. 11th 2009

The Academic Gerontocracy



Fixing the Problem

- Addressing the deficit in human capital with interdisciplinary translational skill sets pertinent to drug action
- Enlarging the precompetitive space by addressing outmoded and unrealistic expectations based on IP
- Creating the informatics substrate for secure, compliant, heterogeneous data sharing across sectors and countries

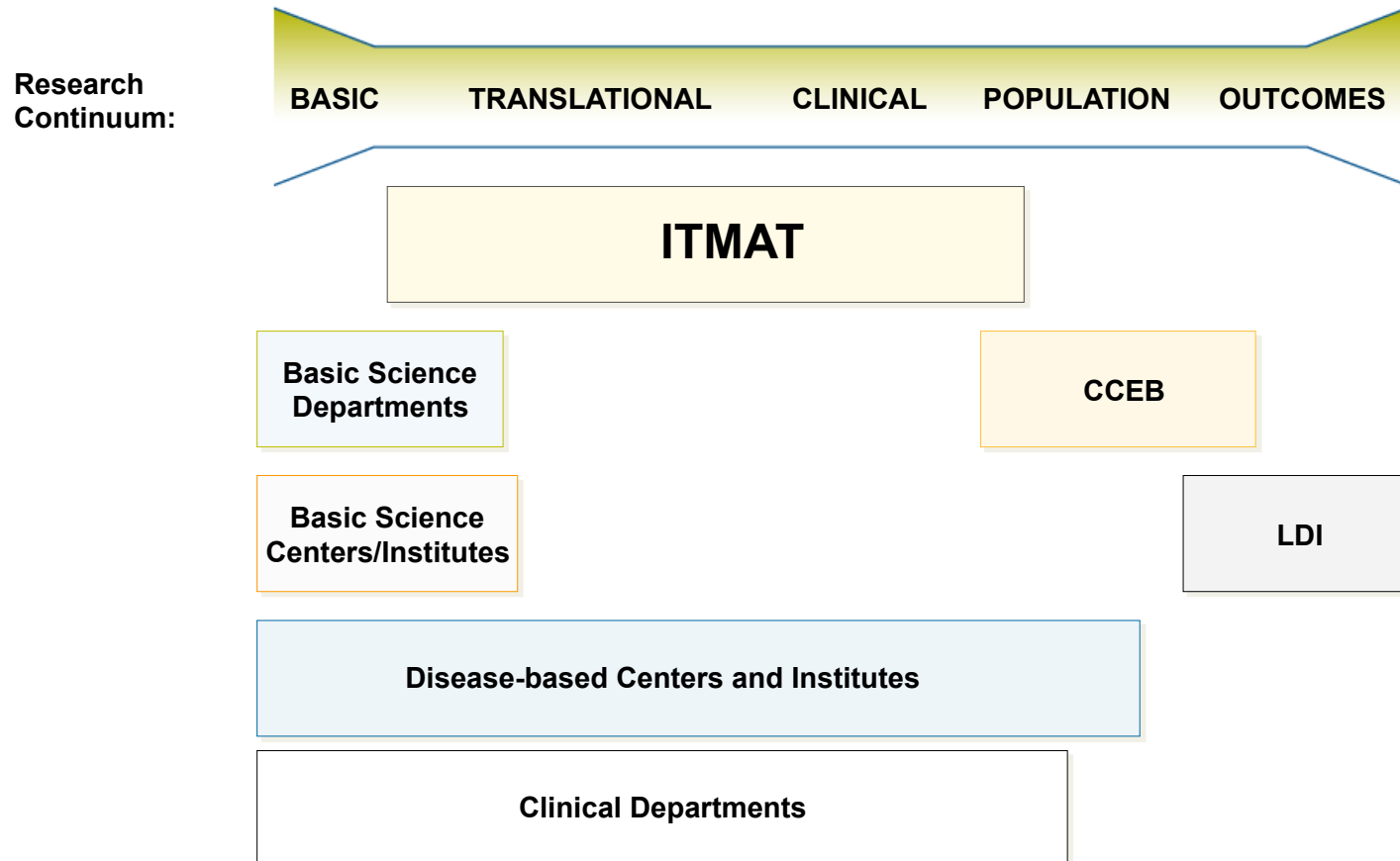
An Appeal to Reason



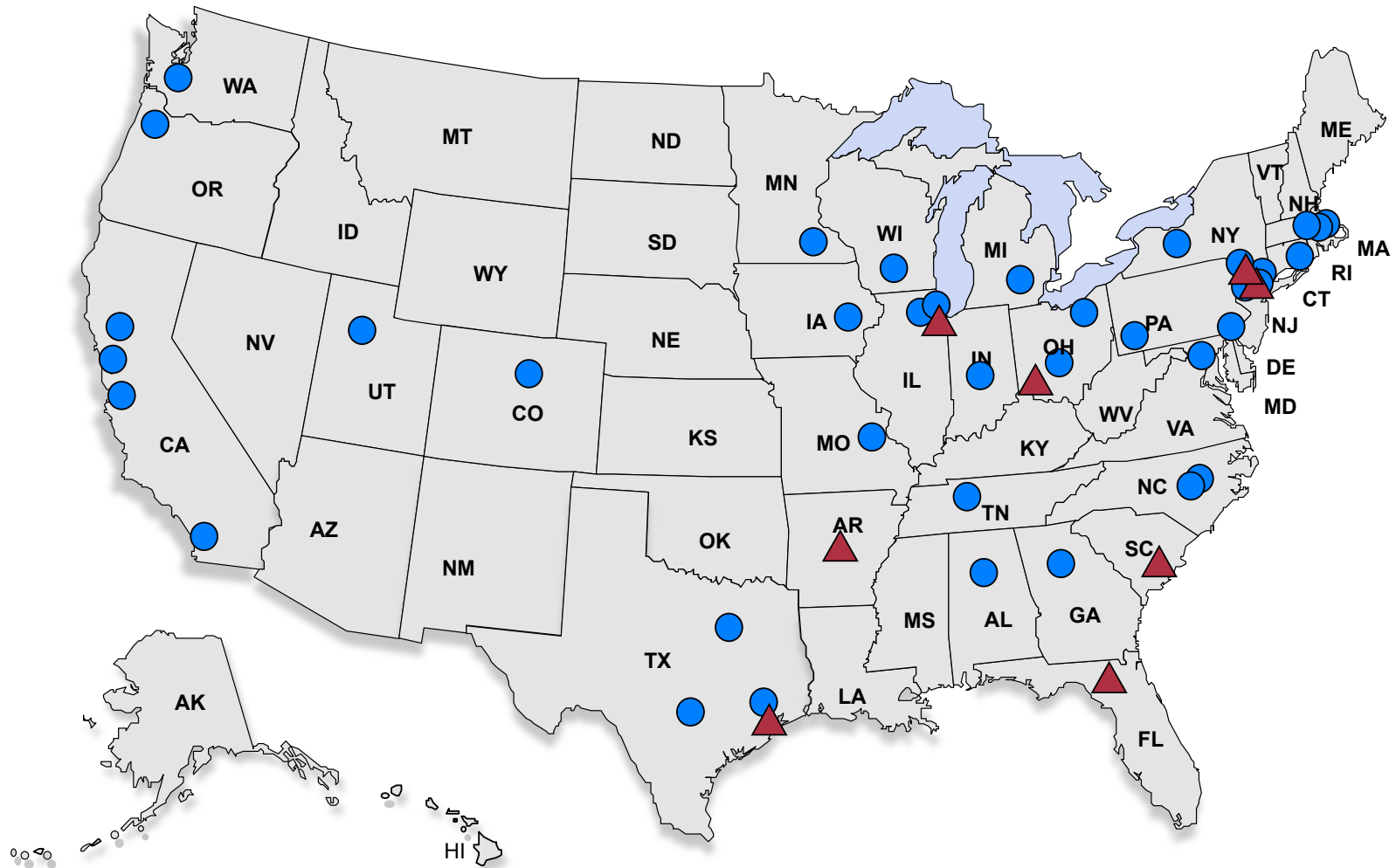
**“If we don’t change the business models,
we’re not going to survive as an industry”.**

Richard Clarke, Merck CEO
Financial Times, Oct 22nd 2008

Creation of the Penn Institute for Translational Medicine and Therapeutics (ITMAT)



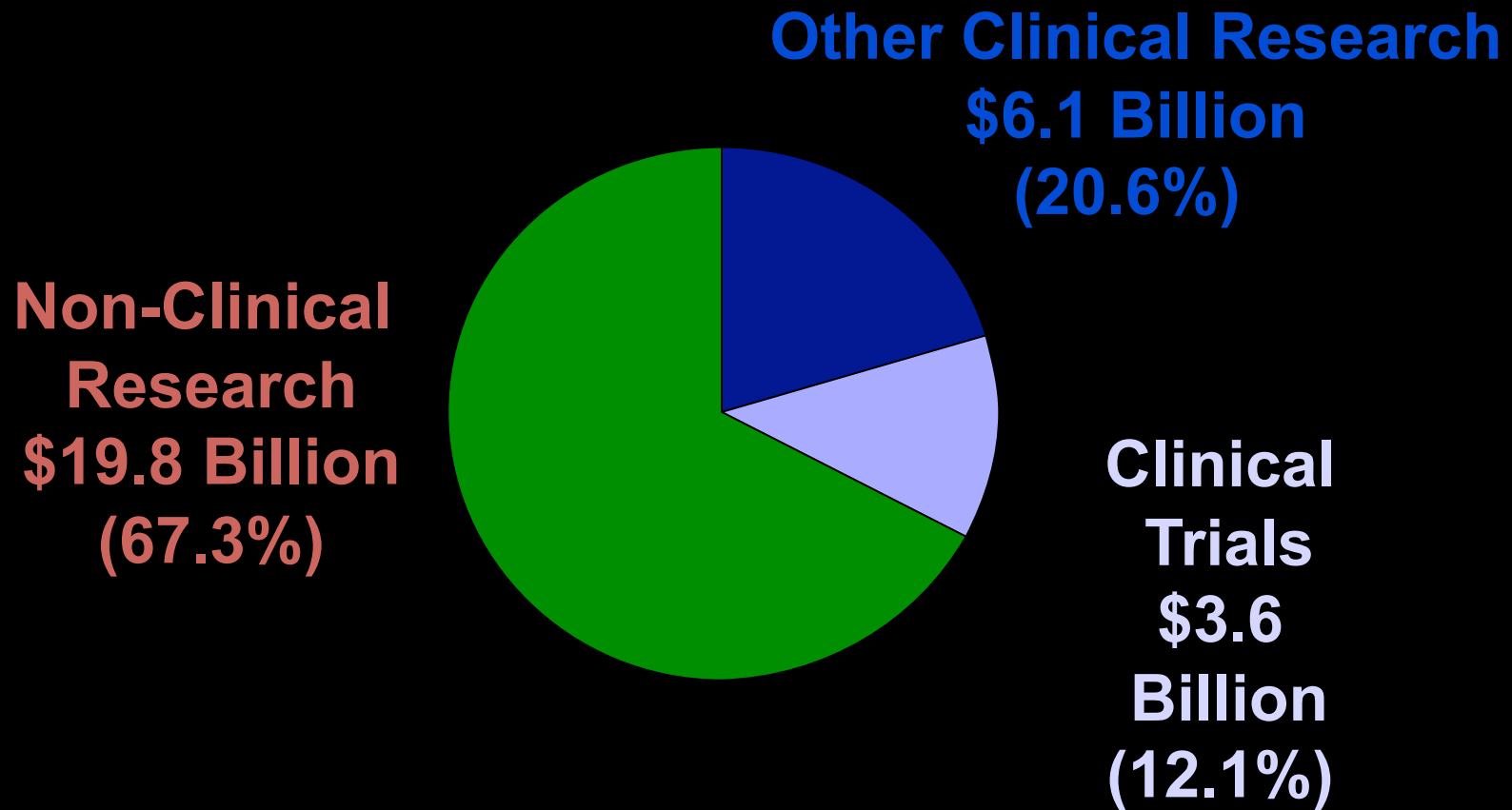
National CTSA Consortium



Participating Institutions

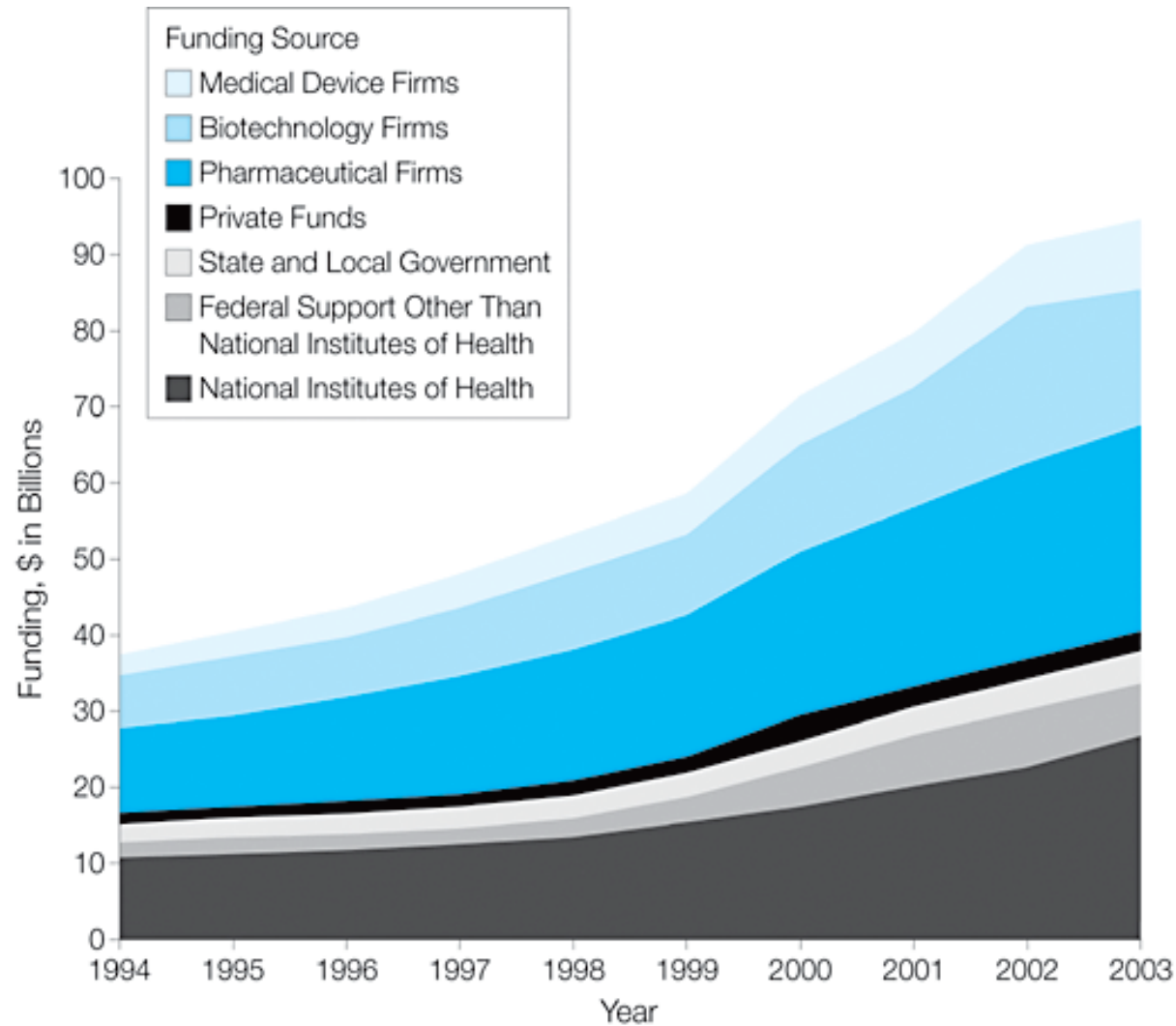
- ▲ New members 2009
- Members

NIH Spending on Clinical Research



<http://officeofbudget.od.nih.gov/ui/2008/tabular%20data.pdf>
<http://www.nih.gov/news/fundingresearchareas.htm#content>

Sponsors of Biomedical Research (Basic and Clinical)



Moses et al. (2005) JAMA, 294, 1333-42

Challenges to Academia

1. HUMAN CAPITAL

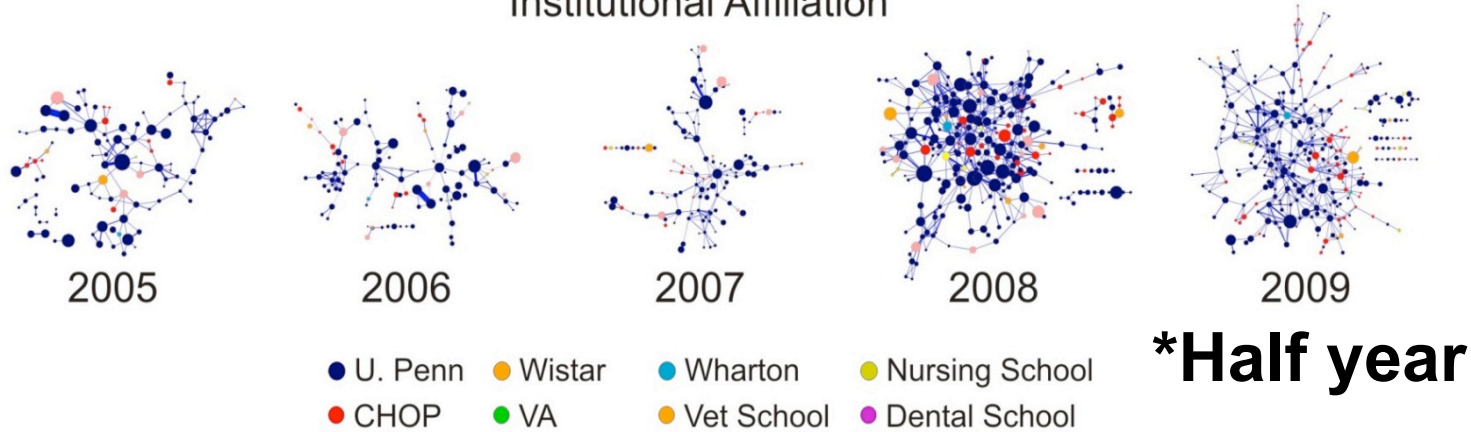
- Disintegration of Translational Therapeutics
- Incentives poorly aligned for team science
- Few incentives to interdisciplinary research
- Time lines of promotion and funding
- Specific deficits in medicinal chemistry
- Trainee/Expertise mismatch

ITMAT Response

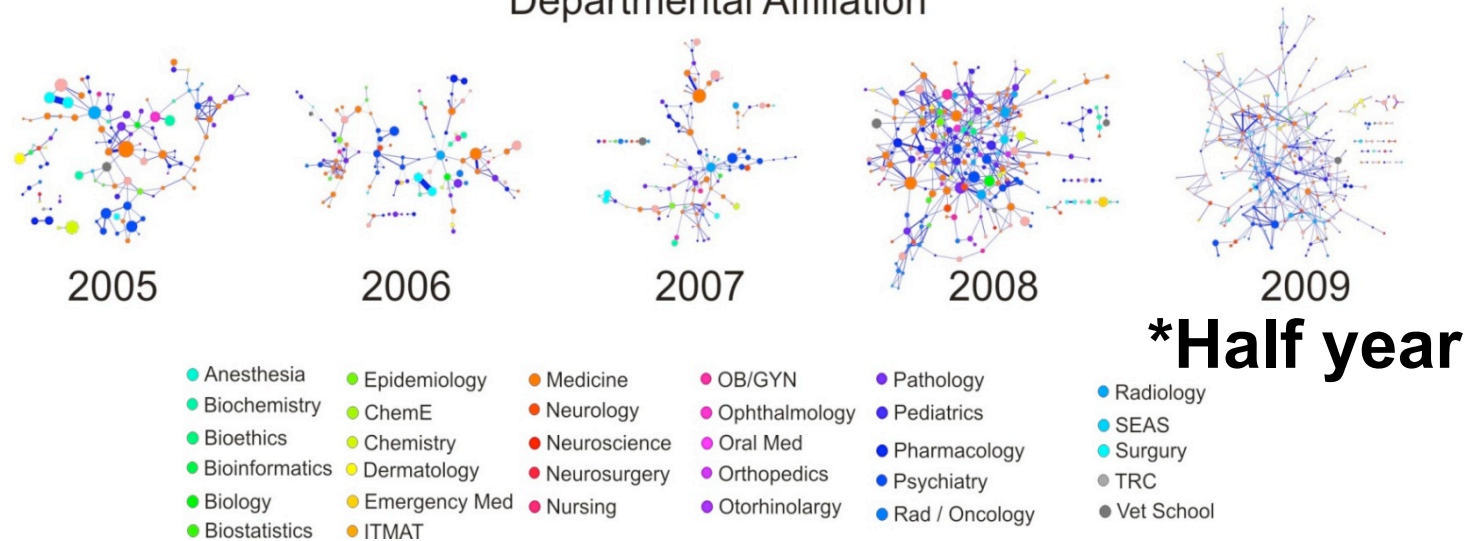
- Diversified educational offerings in clinical and translational research; masters and certificate programs, farm teams, workshops
- Multiple funding initiatives to foster truly interdisciplinary translational research
- Fostering commercialization and addressing IP barriers

Temporal dynamics of ITMAT

Institutional Affiliation



Departmental Affiliation



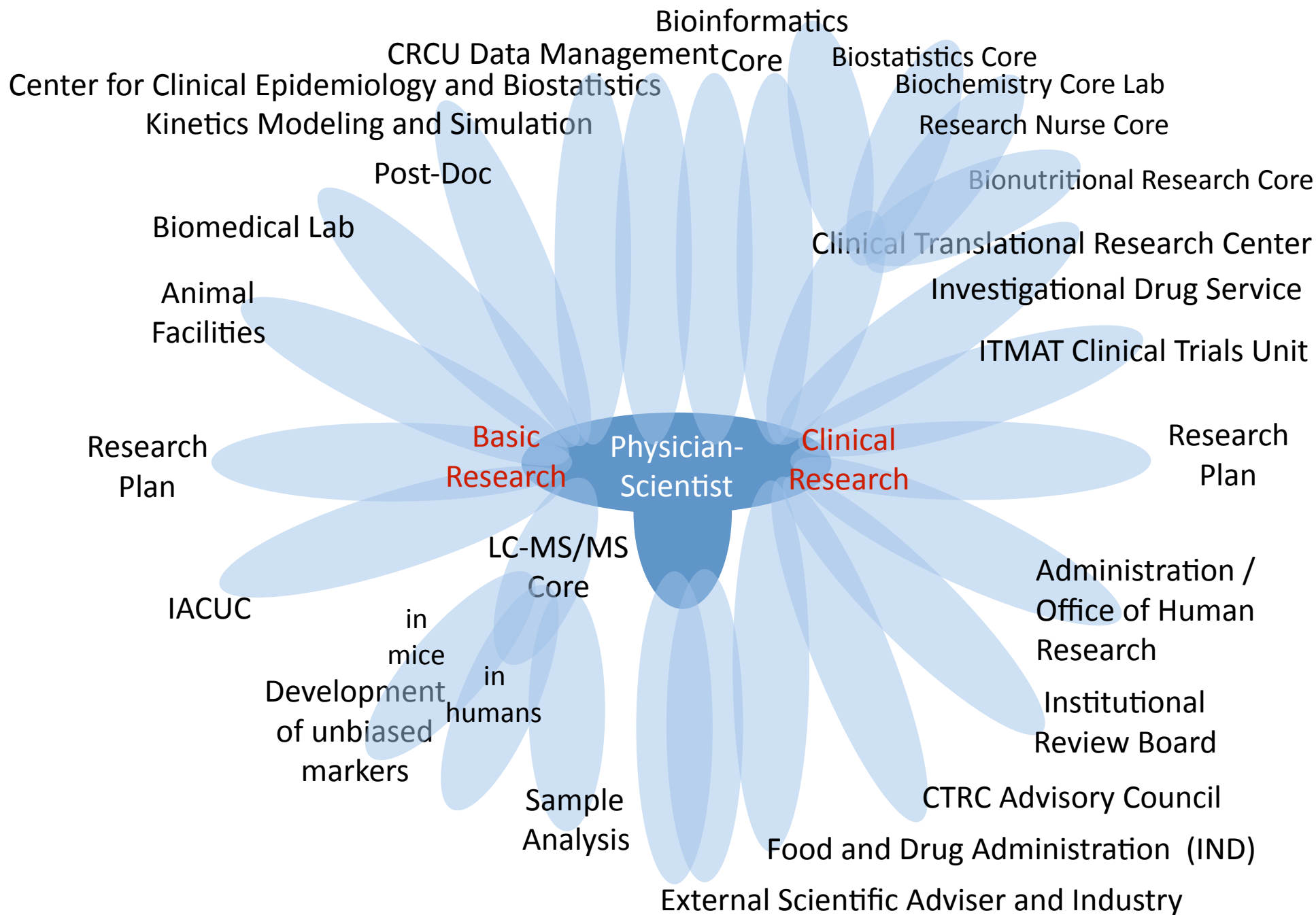
Challenges to Academia

INFRASTRUCTURE

- Access to HTS and medicinal chemistry
- Access to seed funding for commercial POC
- Informatics infrastructure – data sharing and mining, sample tracking, scanning for collaboration
- Analytical biochemistry, kinetics and modeling
- POC in humans

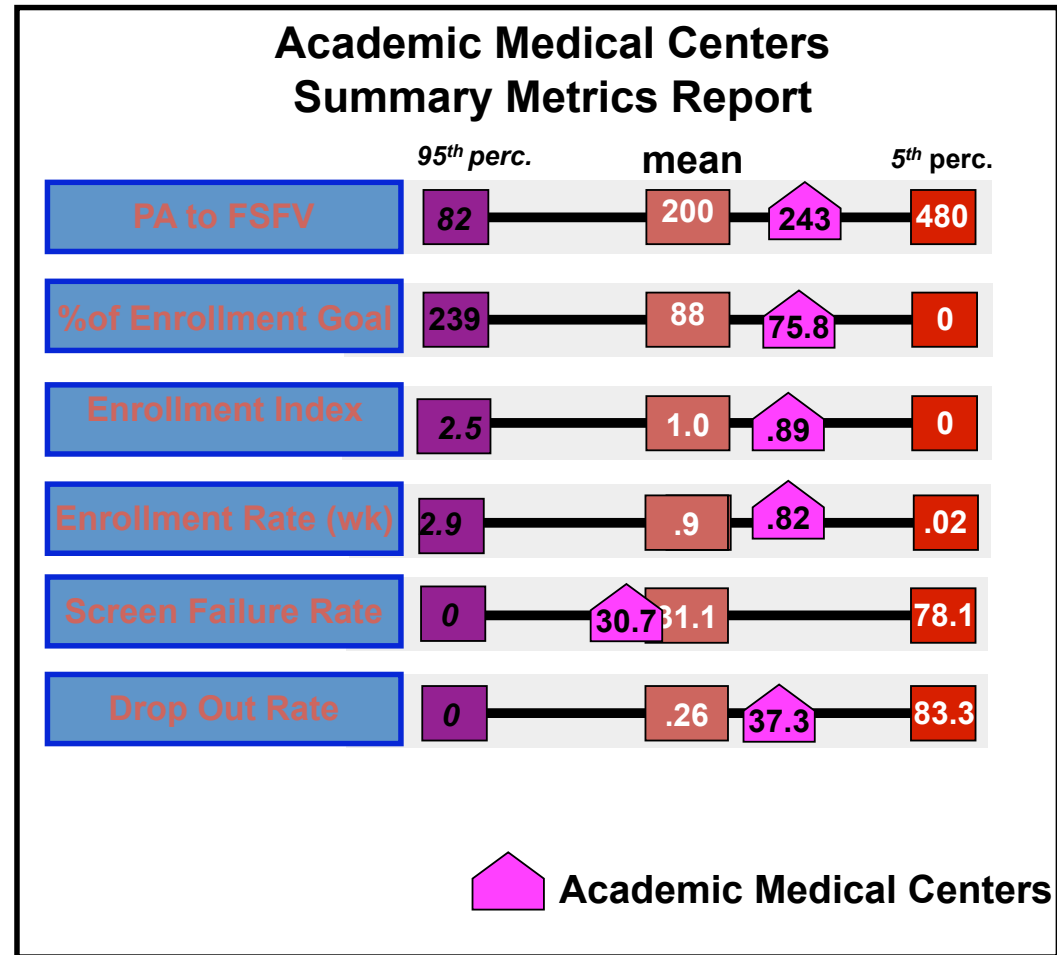
ITMAT Response

- Clinical and Translational Research Center and Laboratory
- Investigational Drug Service and Kinetics and Modeling Core
- Co-investment in informatics, proteomics, genomics, imaging and biotherapeutics infrastructure
- Discounted access to expertise – stats, trial design, databases
- Accelerated CTRC/IRB approval



US Academic Centers and Industry Sponsored Randomized Clinical Trials

- Study initiation at academic centers is 49 days longer than at professional and community sites
- Once up and running, academic sites are roughly 10% slower in enrollment than dedicated and professional sites
- Many centers fail to enroll a single patient



Source: Harvard Business School/
RapidTrials Consortium

Challenges to CTSA CONSORTIUM

1. Festina Lente – Shifting Emphasis from Speed to Quality

- Detailed phenotyping in small numbers in single Centers closely integrated with preclinical research
- Much more emphasis mechanism and variability in drug response as a basis for personalized dose selection
- Projected to scale amongst similar centers
- Traditional Phase 3 – some CTSA, but mostly non CTSA environments

2. LAUNCHING A NEW DISCIPLINE

- Develop and project mechanism based quantitative biomarkers from model systems into humans.
- Evoking phenotypic responses in humans to guide individualization of rational dose selection
- Harness the unbiased technologies to select amongst molecules directed against a single target
- An unintended consequence of nomenclature

3. Expand the Precompetitive Space

- Example of the Not for Profit Sector
- FDA: create a safe haven for Systems Pharmacology and Physiology

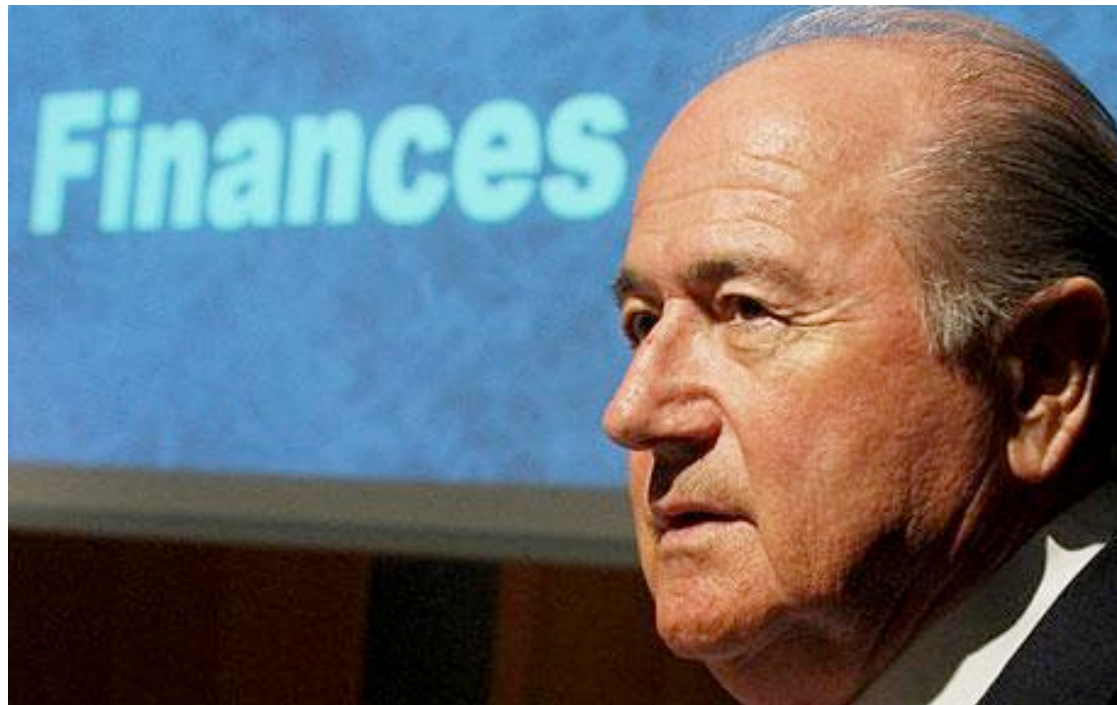
Name	Website
The Biomarkers Consortium	http://www.biomarkersconsortium.org
Critical Path Institute consortia	http://www.c-path.org/consortia.cfm
The Division of Signal Transduction Therapy (also known as the Dundee kinase consortium)	http://www.ppu.mrc.ac.uk/technologies/dstt.php
The EBI Industry Programme	http://www.ebi.ac.uk/industry/ind-prog-index.html
Health Commons	http://sciencecommons.org/projects/healthcommons
The Innovative Medicines Initiative	http://imi.europa.eu/index_en.html
The Serious Adverse Events Consortium	http://www.saeconsortium.org

4. Enhance interaction with the FDA

A JPL for the FDA

- Resource FDA to incent academic centers to afford expertise in emerging science and a site to pursue questions relevant to drug action before and after approval
- Foster collaborative and educational interactions between of FDA and Academic scientists
- Reward innovation
- Staggered approval and drug withdrawal

It's all about the Money



5. Show me the Money

- CTSA cuts compounded by institutional retrenchment
- Shift to consortial activities at expense of individual center resource
- Complement with investment in basic and investigator initiated science
- Sustain and expand public funding for the Translational enterprise; the 17 year rule

Summary

The Health and Wealth of a Nation

- The quality of clinical research depends on basic and translational research.
- This is particularly so as we move towards a more personalized approach to medicine.
- **Sustained** funding is crucial for **all** these interdependent elements; it's not a zero sum game.
- Patients will and should play an increasing role as partners in this process.

Progress in Translational Medicine and Therapeutics

