Can High Performance Computing Help Cure Pharma R&D ?

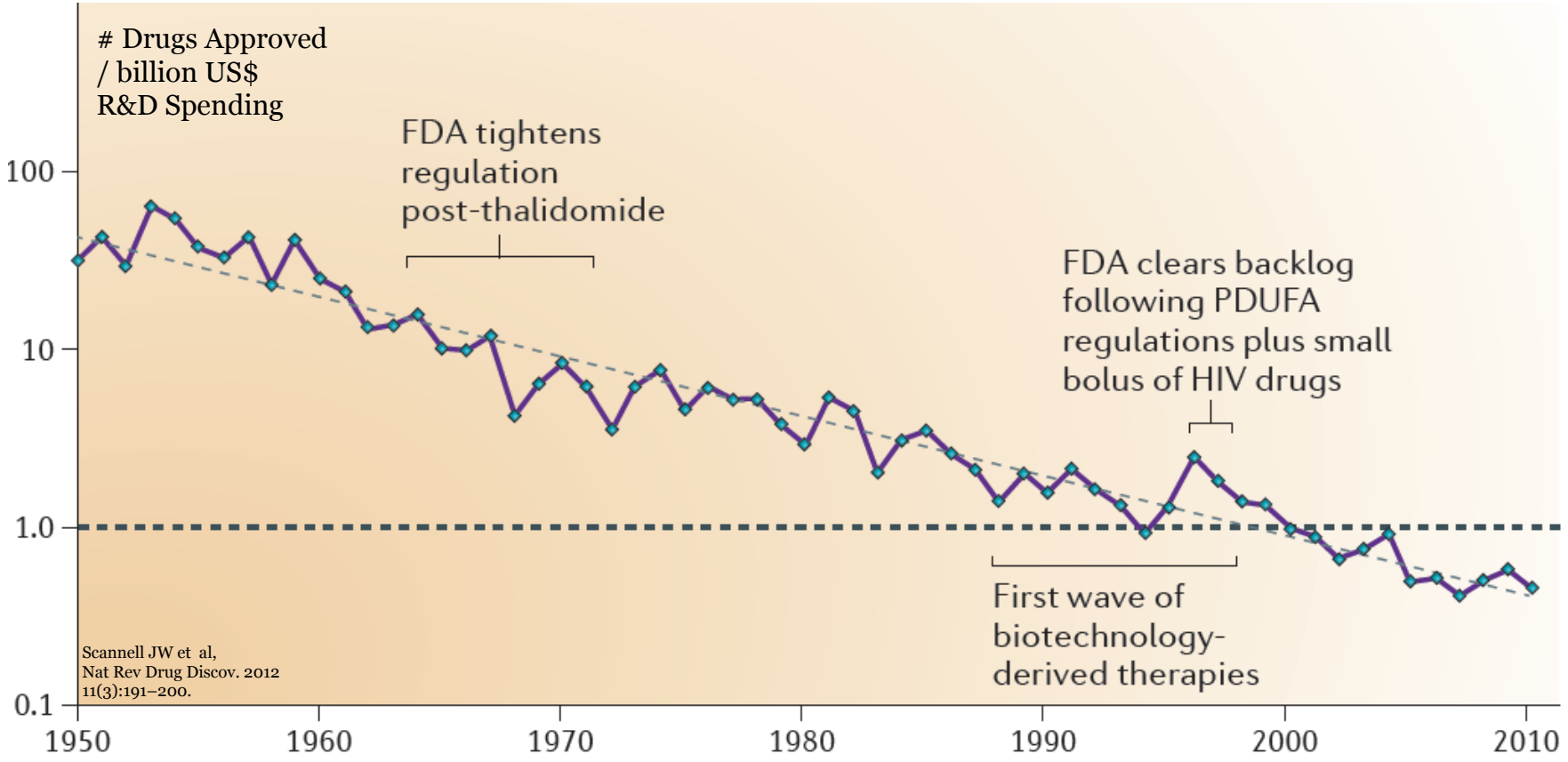
Philippe Guillet, MD

Unité Vieillissement
Sanofi R&D

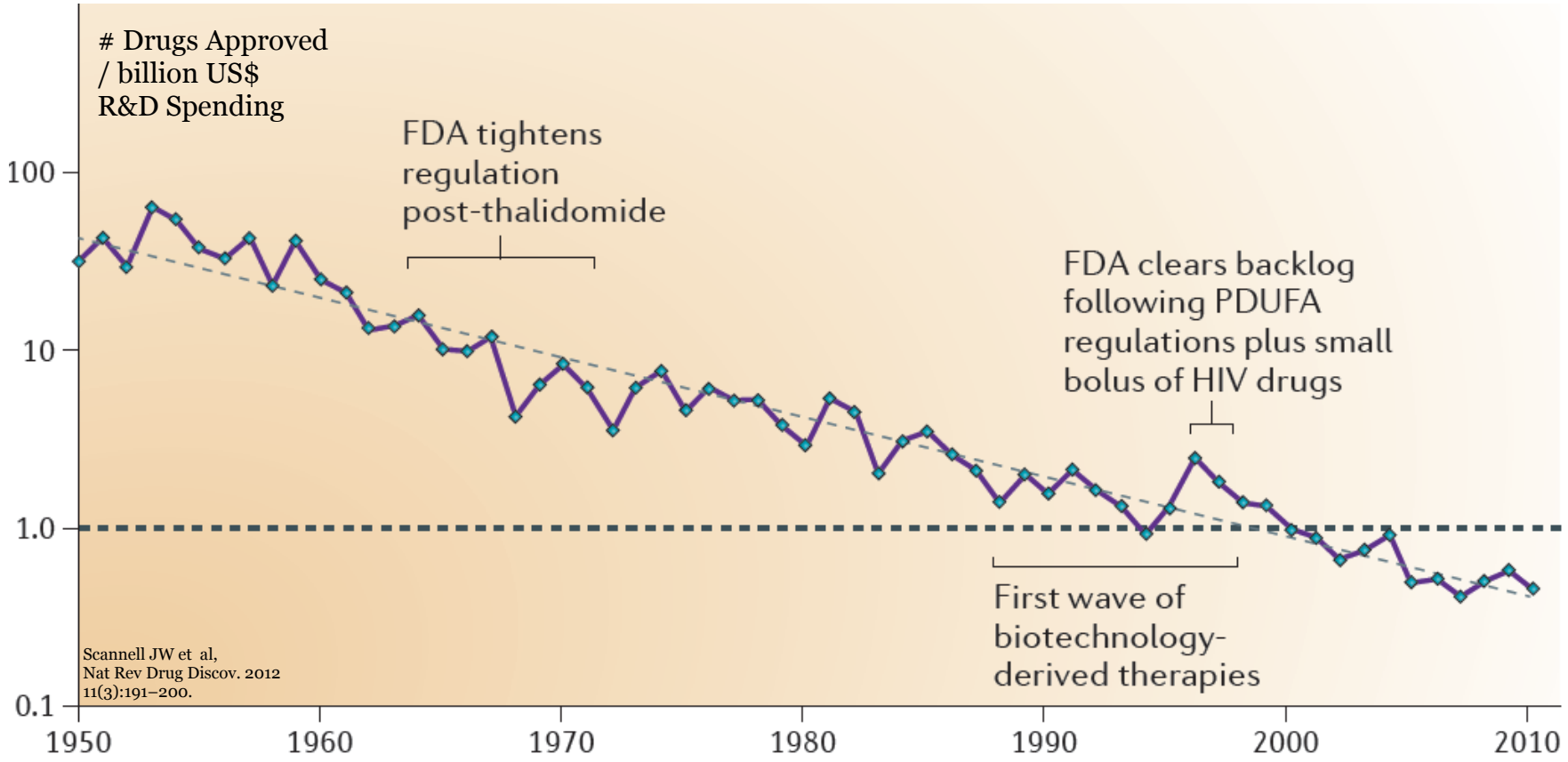
TERATEC Forum 2013
Ecole Polytechnique
Palaiseau
June 25 -26 2013

The views expressed in this talk are those of the author, not those of Sanofi R&D

Trends in Pharma R&D Productivity



Teratec Forum 2013 26/06/13



Structure of DNA

Restriction Enzymes

DNA Sequencing

Human Insulin

Human Genome v1

High Throughput DNA Sequencing

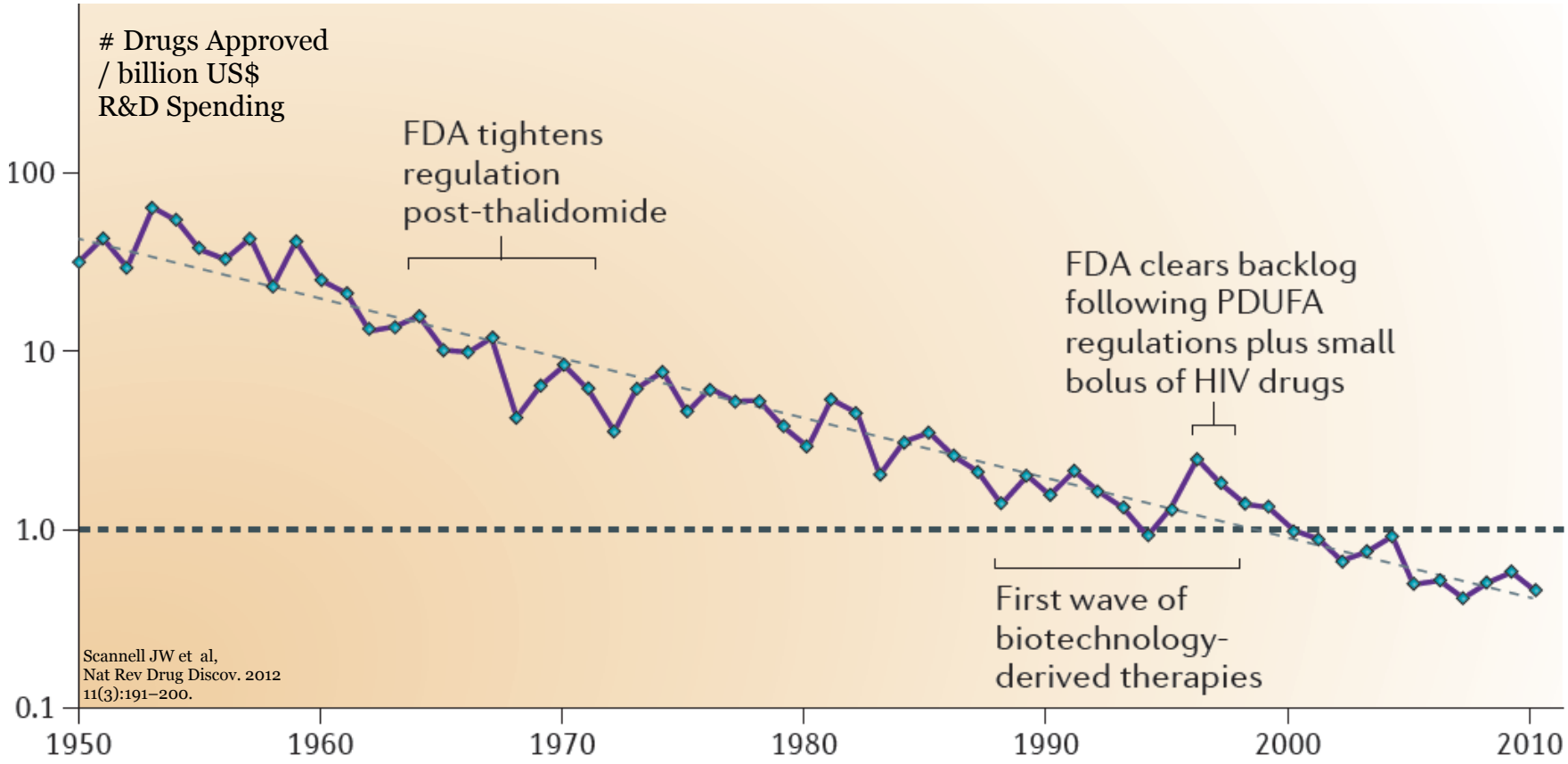
Transgenic Mice

Combinatorial Chemistry

High Throughput Screening

Computational Drug Design & Screening

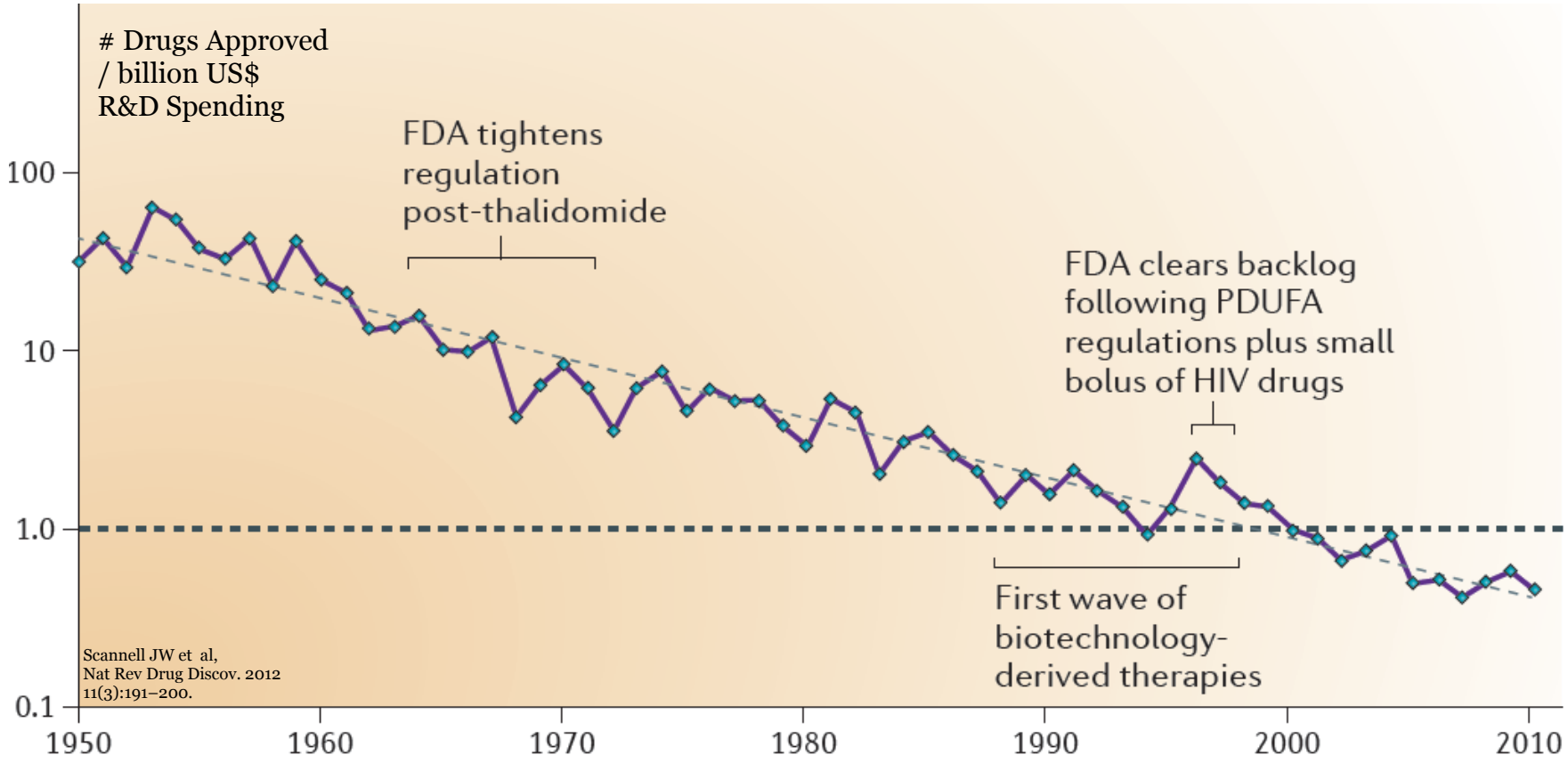
Teratec Forum 2013 26/06/13



Natural → Products → Synthetic

Phenotypic Screening → Assays → Biochemical

Teratec Forum 2013 26/06/13



Aging Population

Single Disorder
« Simpler »

Multimorbidity
« Complex »

Most Failures occur too late in Drug Development

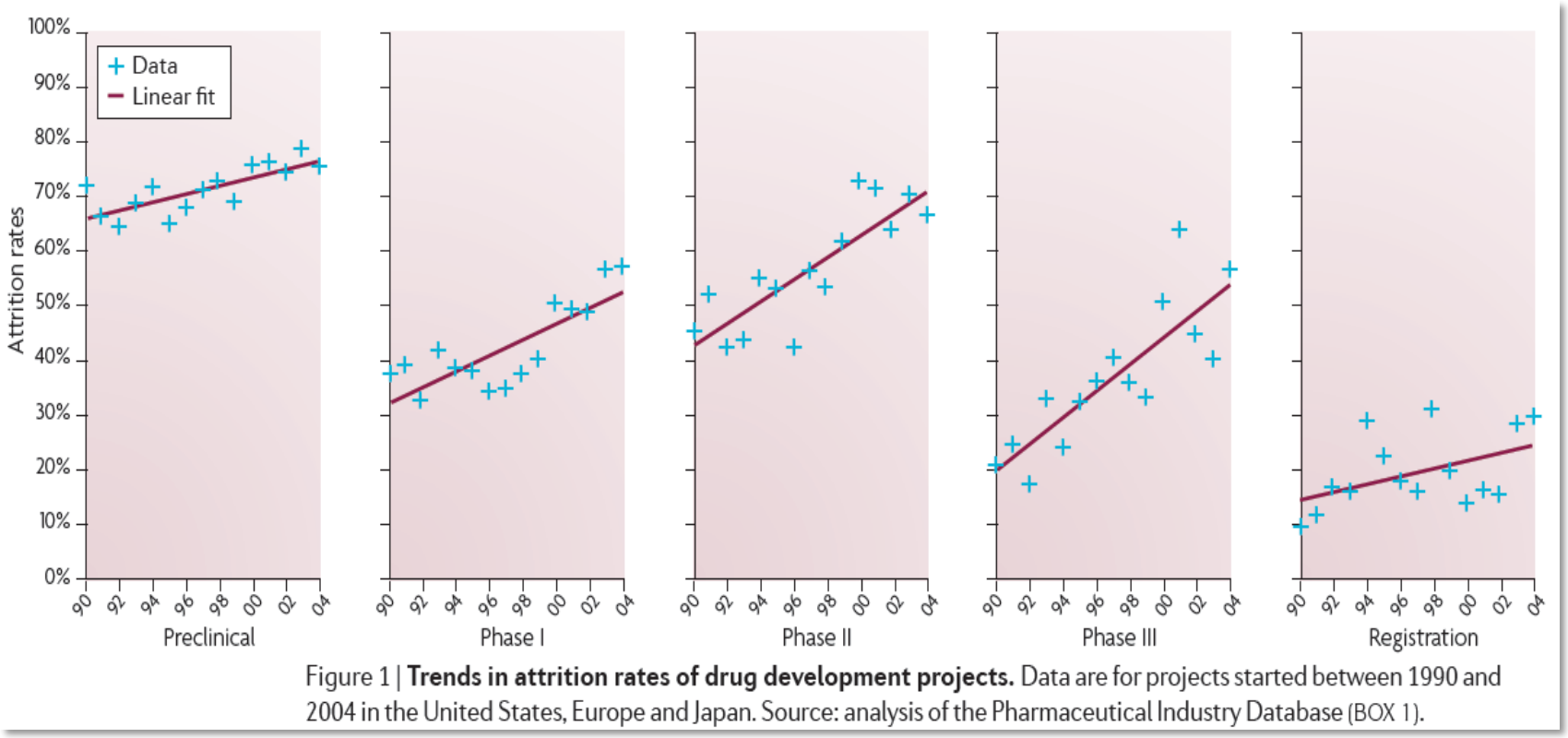
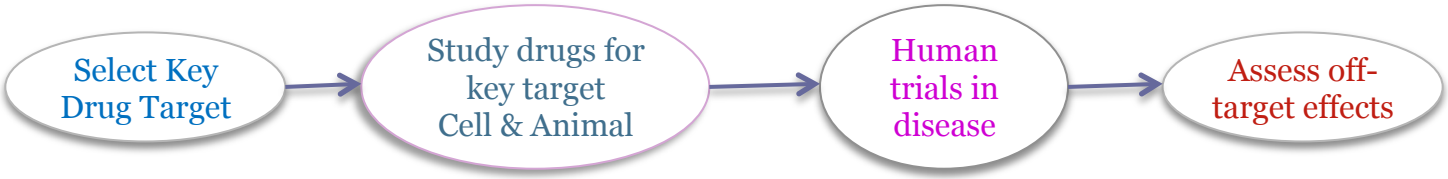


Figure 1 | **Trends in attrition rates of drug development projects.** Data are for projects started between 1990 and 2004 in the United States, Europe and Japan. Source: analysis of the Pharmaceutical Industry Database (BOX 1).

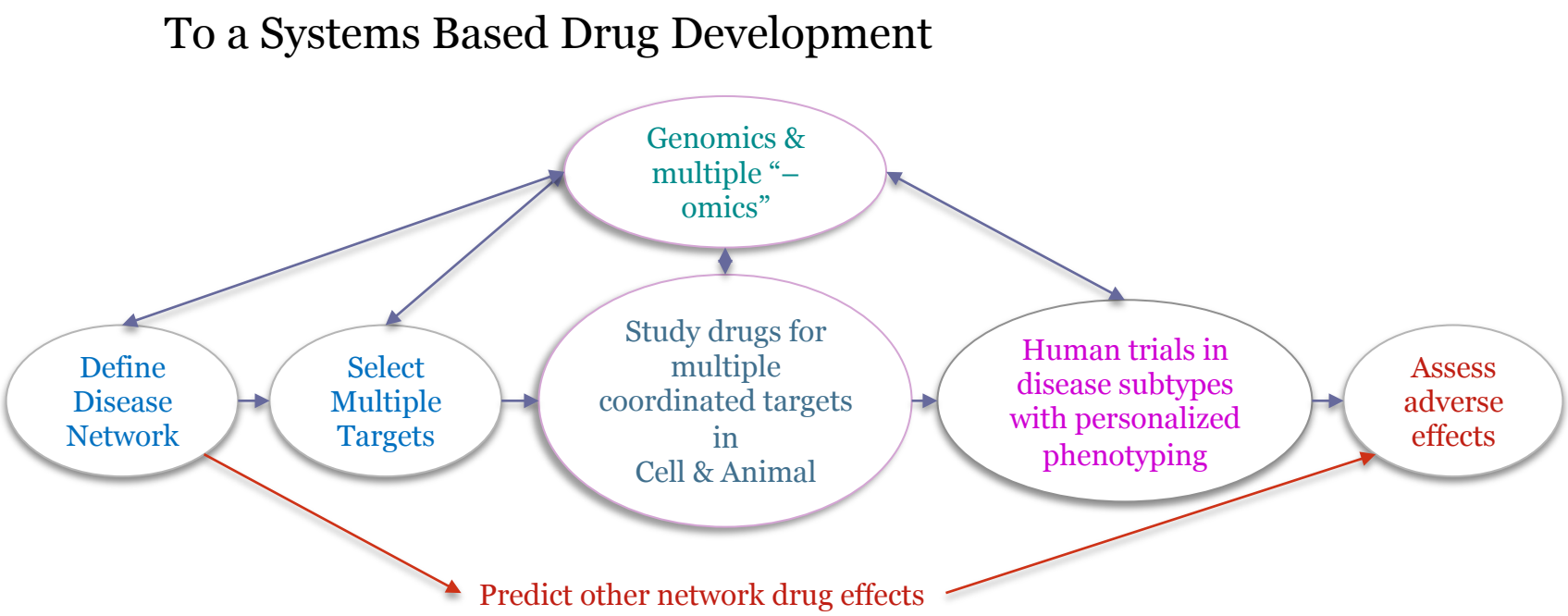
Pammolli F, Magazzini L, Riccaboni M. The productivity crisis in pharmaceutical R&D. Nat Rev Drug Discov. Nature Publishing Group; 2011;10(6):428–38.

Towards a Systems based Strategy for Drug Development

From a reductionist approach

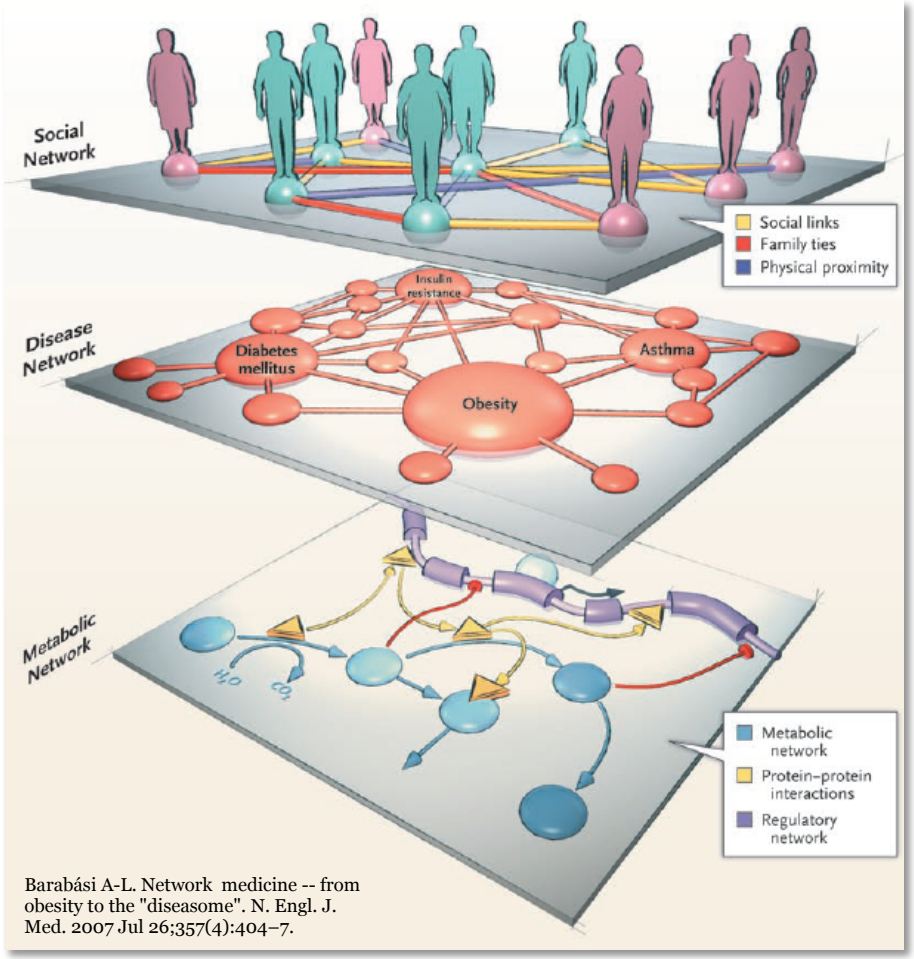


Towards a Systems based Strategy for Drug Development



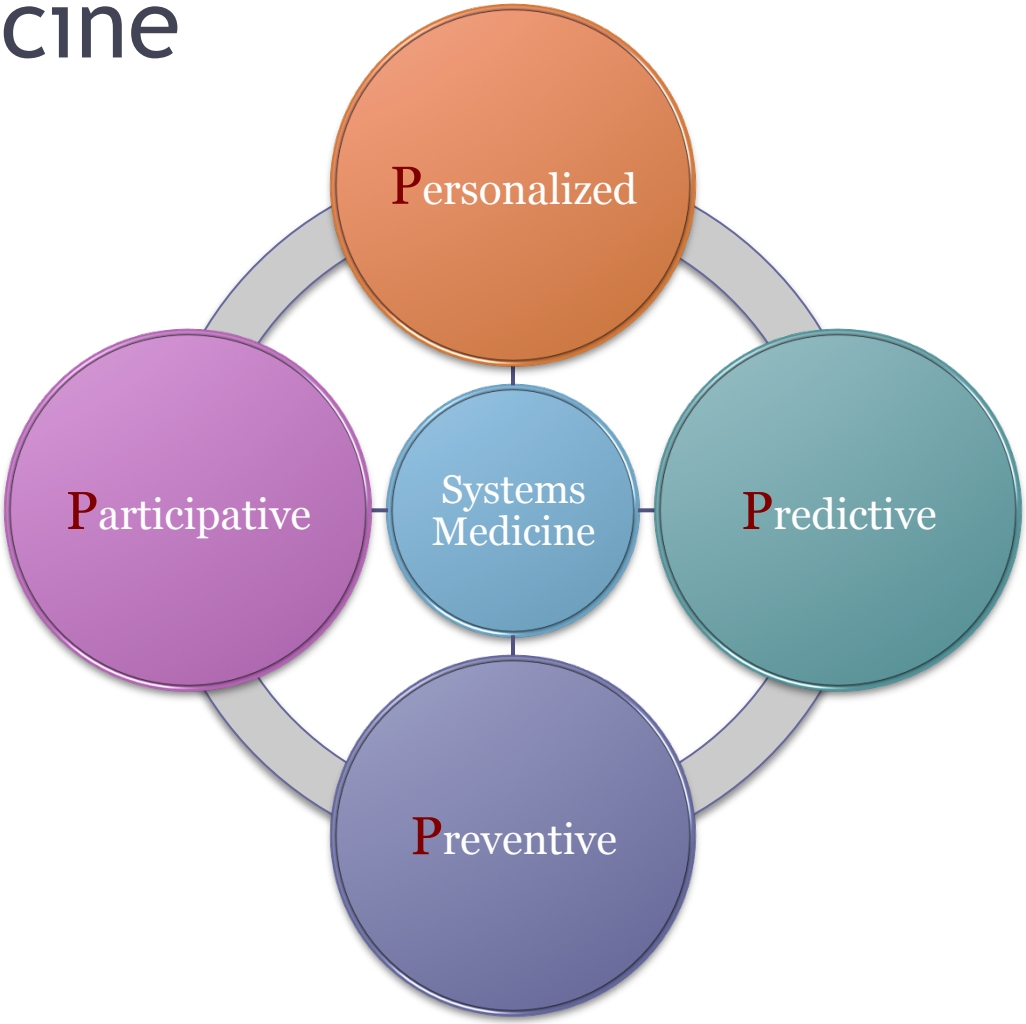
Systems Medicine

- Application of systems biology to medical
  - Research
  - Practice
- Objective
  - Integrate biological / medical data
    - At all levels of organization
  - Understand
    - Pathophysiology
    - Diagnosis / Prognosis
    - Treatment of disease
- Data Intensive approach
  - Data Collection
  - Computational & mathematical modeling
  - High Performance Computing



Barabási A-L. Network medicine -- from obesity to the "diseasome". N. Engl. J. Med. 2007 Jul 26;357(4):404–7.

From Reactive to Pro-Active 4P Medicine



Personalized

- Customization of healthcare
  - Accommodate individual differences
    - Prevention
    - Diagnosis
    - Treatment
    - Treatment follow-up

- Large amount of heterogeneous data
  - "- Omics"
    - Genome
    - Epigenome
    - …
    - Physiome
  - Environmental Exposures
  - Life-Style
    - Nutrition
    - Physical Activity
    - …
  - Functional Imaging
  - Physiological Sensors in daily life
  - Minimally Invasive Tissue Samples
  - Social Media
  - Geolocalised information
- From as many individuals as possible
- Representative samples of Populations
- Over Time

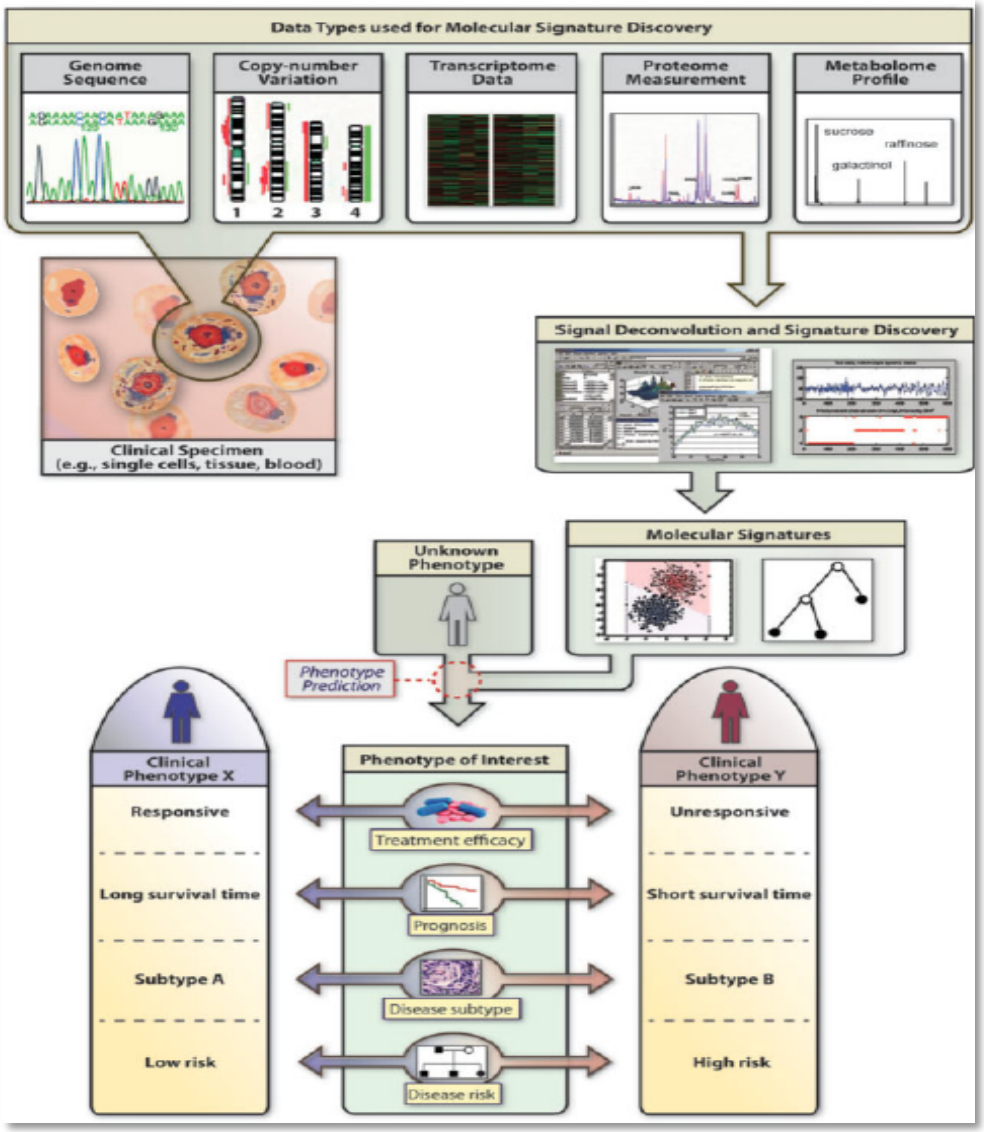
Predictive

Development of Molecular Signatures & Biomarkers

Already implemented in several fields, e.g. Oncology

Need to be extended to other

- Data types
- Fields



Sung J, et al.. Molecular signatures from omics data: from chaos to consensus. Biotechnol J. Wiley Online Library; 2012;7(8):946–57.

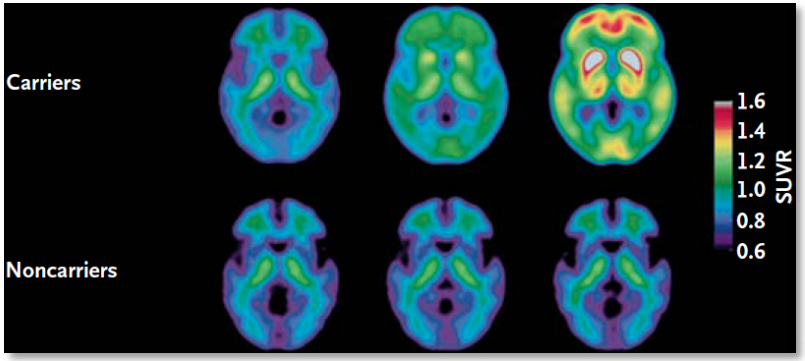
Preventive

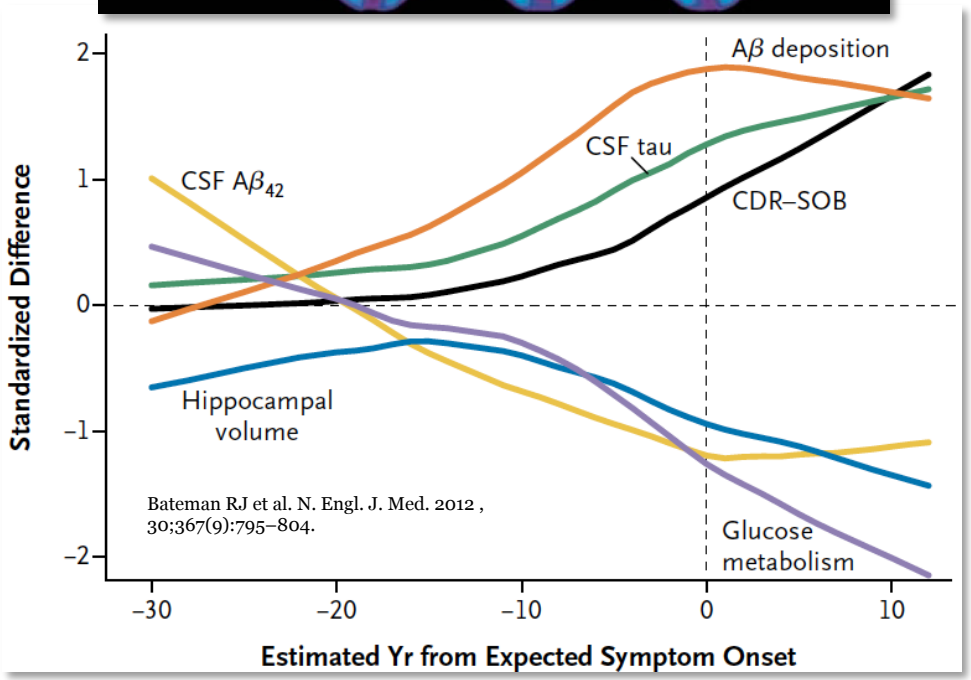
Biomarker to Identify risk of slowly developing diseases

Issue : False Positive findings

Dominantly Inherited Alzheimer's Disease

Mutation PSEN1 – APP - PSEN2





Bateman RJ et al. N. Engl. J. Med. 2012 , 30;367(9):795–804.

Participatory

- Acknowledges the position of patients /citizens as
  - Active contributors of Personal data
    - Apps
    - Mobile sensors
    - Social networks
  - Participants in
    - Decision making
    - Pharmacovigilance

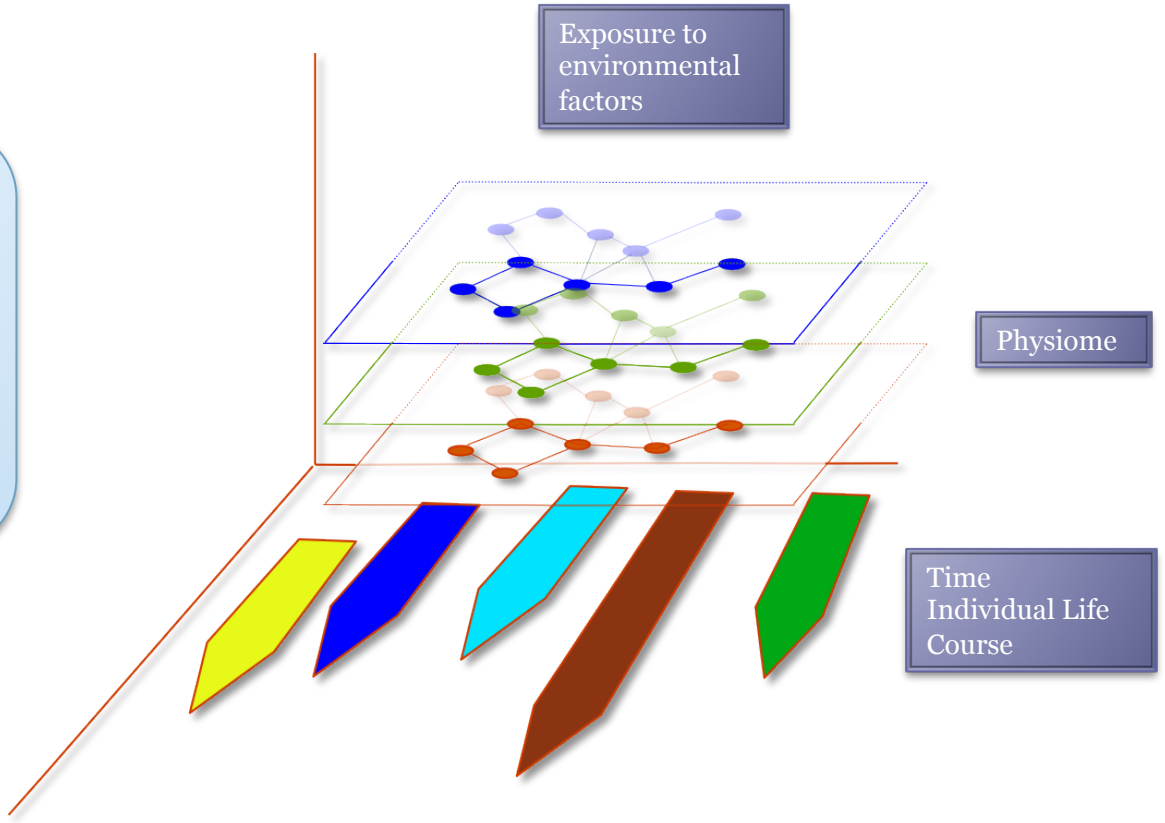
Education & Information

Ethical & Legal

4P Medicine - Modeling & Simulation

High Computing Requirements

Multilevel modeling across
- Space
- Organization
  - Cell
  - Tissue
  - Organ
- Life Span

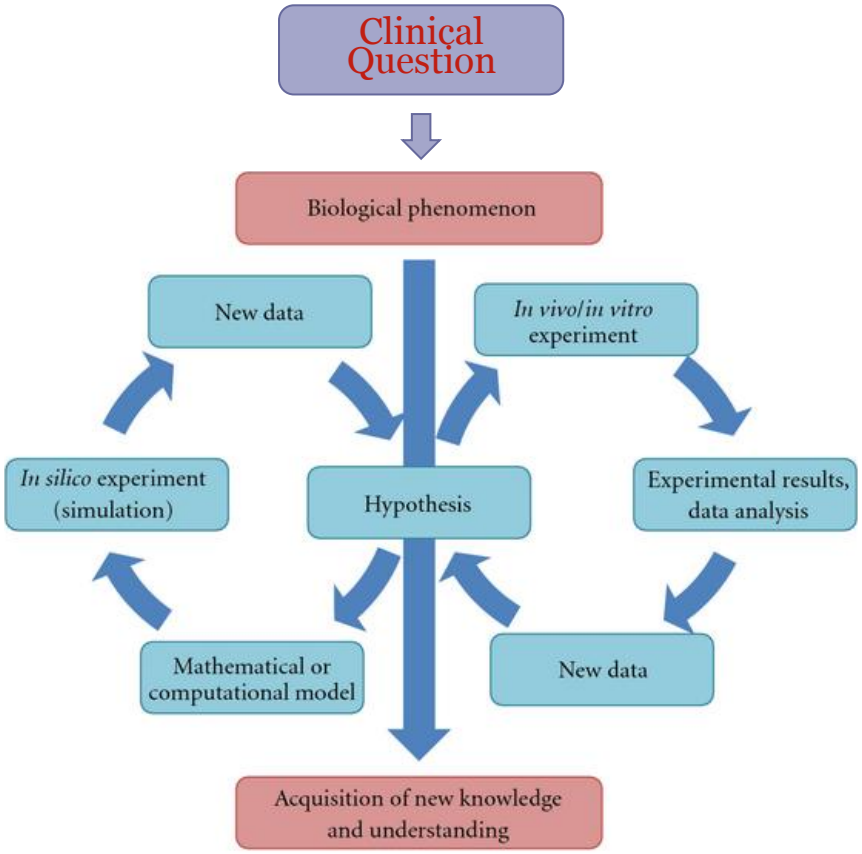


Redrawn from Kauffmann F, Demenais F. ‚J. Allergy Clin. Immunol. 2012 Dec;130(6):1229–40.

Clinically Directed Modeling

Hypotheses generated via computational & mathematical methods

Need testing and validation in clinical context



Woelke AL, Murgueitio MS, Preissner R. Theoretical modeling techniques and their impact on tumor immunology. Clin. Dev. Immunol. 2010;2010:271794.

Infrastructures & Technologies

- Secure Data Platforms
  - Storage
  - Controlled sharing of clinical data
    - Medical records, molecular profiling data,…
  - Integration/analysis of multi-parameter data
- Technology platforms for "–omics"
- Standardized methodologies
- Translational structure
  - Basic sciences & clinical facilities
  - Sharing material, space & human resources
- Biosensors & portable monitoring devices
  - Multiple functions
    - Biological
    - Physiological
    - Environment
  - Miniaturized automated & fast molecular profiling devices
- Imaging
  - whole-body dynamic measurements
- Non-invasive in vivo measurements
  - Cellular
  - Tissue
  - Organ levels
- Modeling & Simulations Platforms
  - Relevant level

Infrastructures & Technologies

- Secure Data Platforms
  - Storage
  - Controlled sharing of clinical data
- Stan
- Translational structure
  - Basic sciences & clinical facilities
  - Sharing material, space & human resources

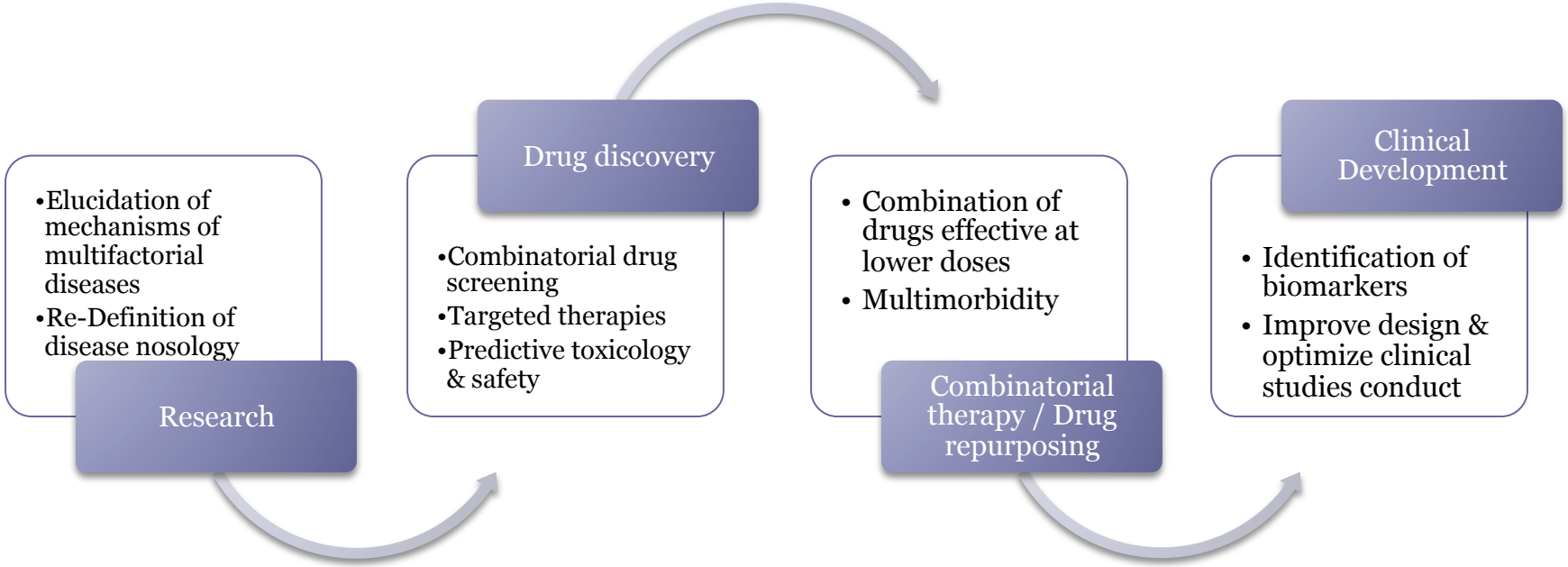
Affordable Costs

Public-Private Collaboration

- Biosensors & portable monitoring devices
- Non-invasive in vivo measurements
  - Cellular
  - Tissue
  - Organ levels
- Modeling & Simulations Platforms
  - Relevant level

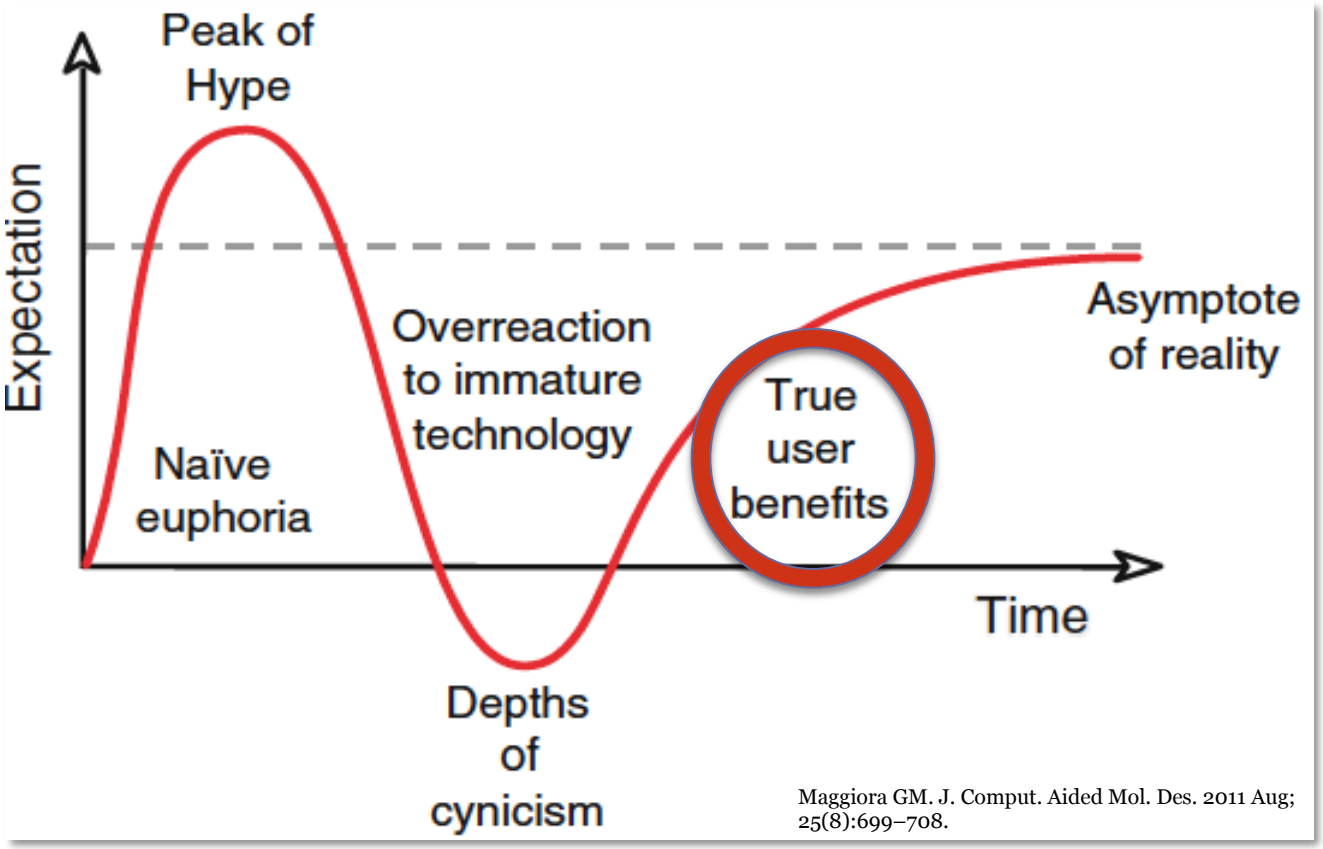
Conclusion

HPC supported Systems Medicine can help cure Pharma R&D



Higher Rate of Success

The "Technology Cycle"



Maggiora GM. J. Comput. Aided Mol. Des. 2011 Aug; 25(8):699–708.

Thank you for your attention!