DESHPANDE CENTER IDEASTREAM SYMPOSIUM 2003

Health Care and the New Biology Challenges and Opportunities

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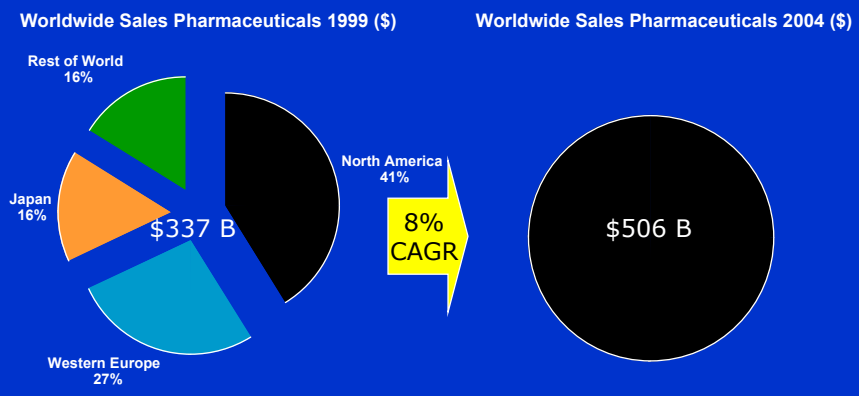
Outline

- The Pharmaceutical Industry Challenges
  - Pipelines, economics, innovation
- Role of New Biology to meet challenges
  - Innovative strategies in drug discovery and disease management
- Summary
  - Requires knowledge management from beginning to end i.e. from basic science to patient care

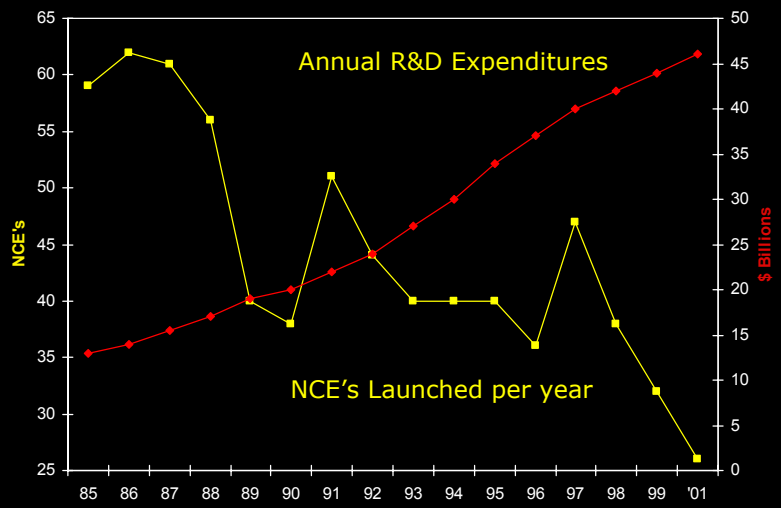
Global Pharmaceuticals



7% decline in total shareholder returns for top 20 Pharma over last two years

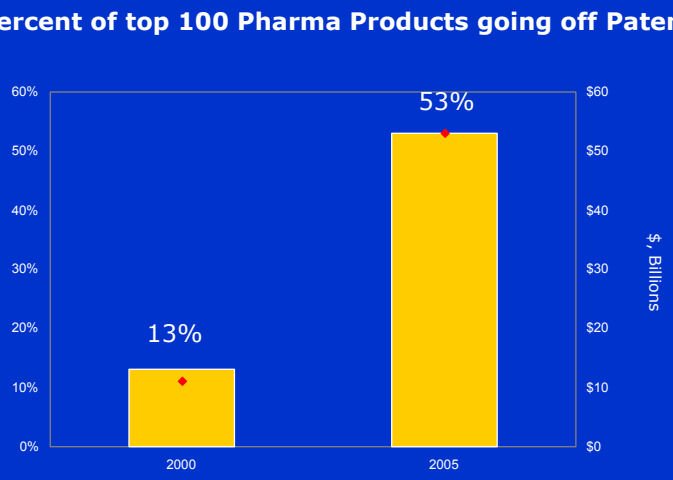
Source: IMS Health

Big Pharma R&D Productivity is Falling



Source: IMS/Price Waterhouse Coopers

Lifeblood Patents are Ending



Source: Price Waterhouse Coopers

Inside the Big Pharma Numbers

➢ Revenues/per company (avg.)	$10 billion
➢ Required Growth	10%/year (> $1B/year)
➢ Average pharma product	$300-400M/year
➢ Product needs	About 3 to 4 per year
➢ Average Product Launches/year	.5

Big Pharma Restructures

Circa 2002

Acquires Innovation

Merck/Rosetta
Abbott/Vysis

Acquires for Size

SmithKline Beecham/Glaxo = GSK
BMS/DuPont Merck Pharma
J&J/ALZA
Abbott/Knoll (BASF)
Pfizer (P & U)

Big Pharma
Needs to do something?
Lilly
SP
Wyeth
Pfizer

Grows Up

Genentech
Millenium
Amgen/Immunex

More Focus

Aventis/AventisCrop Science (Bayer)
P&U/Monsanto (IPO)
P & U acquired by Pfizer
Roche sells Vitamin business (DSM)

Divests out of Pharma

BASF (Knoll to Abbott)
DuPont (DuPont/Merck to BMS)

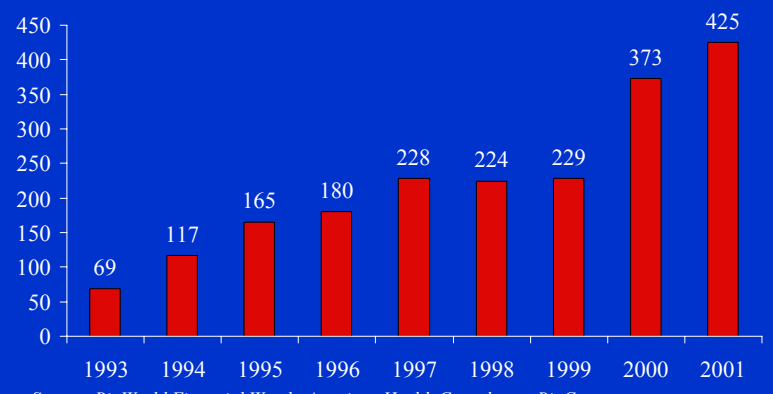
In Process:

Bayer spins-out/sells Pharma?—$15-20B (GSK, Roche)
Novartis acquires 20% of Roche; more to come?

Source: Burrill & Co.

Strategy Two: Collaborations

Number of New Biotech— Big Pharma Collaborations 1993–2000



Source: BioWorld Financial Watch, American Health Consultants, BioCentury

Summary Pharma Trends

- **Enormous Pressure on Big Pharma**
  - **Slowing growth**
  - **Falling R&D and clinical productivity**
  - **Core blockbuster patents ending**
  - **Strategy one: consolidation**
    - **Control of distribution, marketing, and sales**
  - **Strategy two: expanding science and technology base to source innovations leading to new products**
    - **Collaborations at academic centers of excellence and industrial partners**

Challenges to Pharmaceutical Development

- **"The easy drugs have been done"**
  - Acute diseases or chronic diseases with simpler symptom profiles
  - Simple endpoints (blood pressure, serum cholesterol level) are being exploited
- **New drugs will require new technologies and new approaches for disease and unraveling patient stratification and staging**
  - Examples include: cancer, diabetes, infectious diseases, sepsis, MS, autoimmune disorders and diseases
  - **Becomes the real challenge for the New Biology**

Opportunities for Pharmaceutical Development

- Unprecedented number of new chemical entities to investigate
  - Products of biotechnology revolution
- New technologies for investigating complex biological systems
- New technologies for measuring drug effects
- New technologies for predicting outcomes; *In silico*
- Creative approaches to development and manufacturing
- ***Integrating New Technologies Effectively will be KEY***

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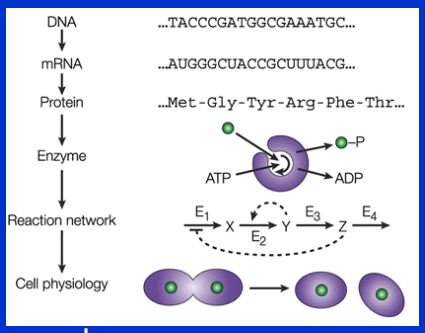
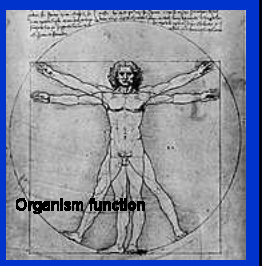
Human Health Depends on Well-Functioning Complex Assemblies





Omics

- **Genomics, Proteomics, Metabolomics, Phenomics, Epigenomics, Ligandomics, etc.**
- **Definition: Study of entities in aggregate, *e.g.* the entire complement of RNA, DNA or other molecule in a cell, tissue or organism**
- **Databases of molecular data generated**
- **Valuable tools for analyzing cells**

Science (1998) 282:627.
Nature Biotech. (2000) 18:127.

Current Scientific & Technological Advances

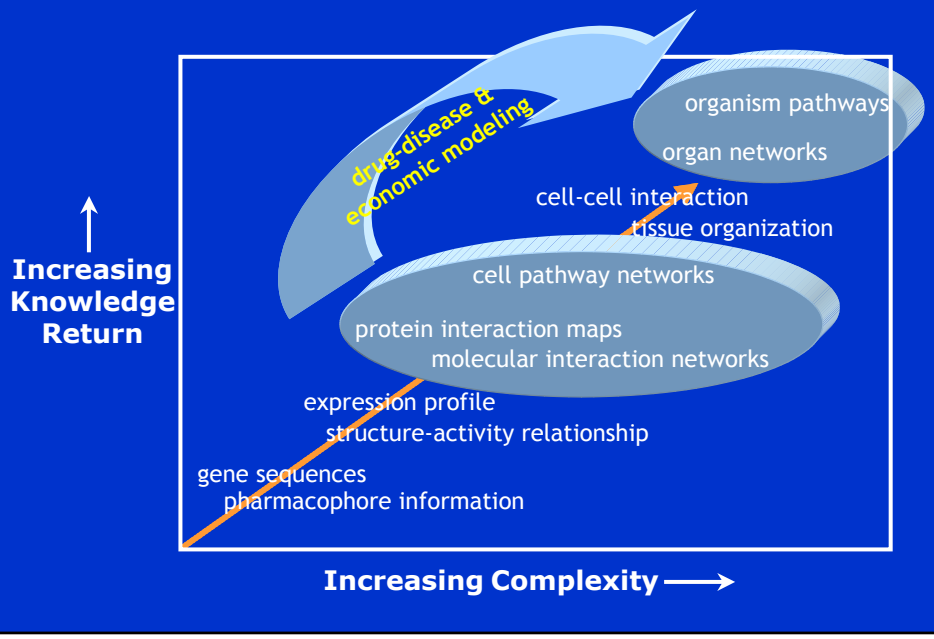
Data Generation

- **High-Throughput** and **Parallel** techniques
- **Miniaturization** to facilitate high-throughput and parallel experiments
- **Prediction / Modeling**

Knowledge Generation

- More testing ***in silico***
- **Information Technology**
  - Information management
  - Bioinformatics

Investigating Complex Systems Increases Knowledge Return



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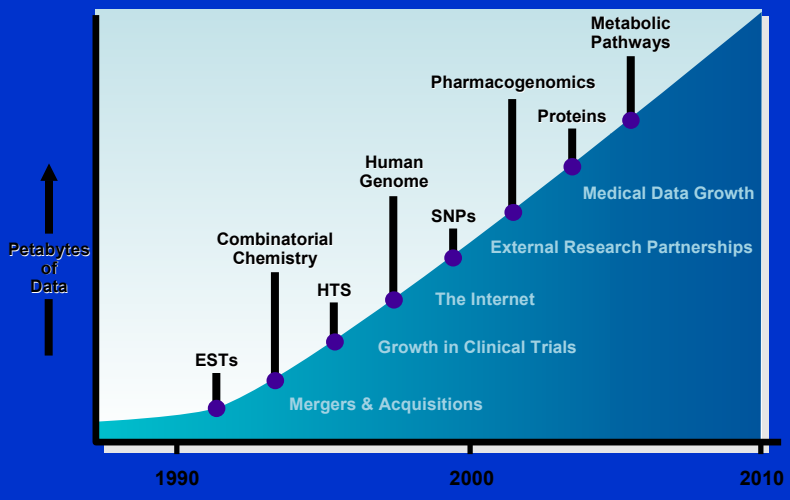
Challenges for Pharmaceutical Innovation from Current Advances

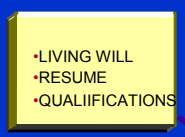
- Effective acquisition and integration of technological advances
- Conversion of data from genomics, proteomics and other high-throughput data-gathering technologies into medically relevant knowledge – i.e. understanding of complex systems that underlie cell physiology
- Successful application of that knowledge toward improved productivity in drug development

Explosion of Drug Discovery Data
(A tyranny of data)



Adapted from Ned McCulloch IBM

The clinical record will be a complex heterogenous object
(a vision of disease management)

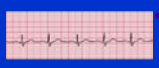


"What protocols were used for tumors which produced similar staining sections, and were from same age group as my patient, and with same "Yakamura" polymorphism in her genes?"

Hospital transaction events

HALO: Heterogeneous Archival Life Object(2 DBs)

Expression Arrays (various tisues)



X-rays, MRI, Grams etc

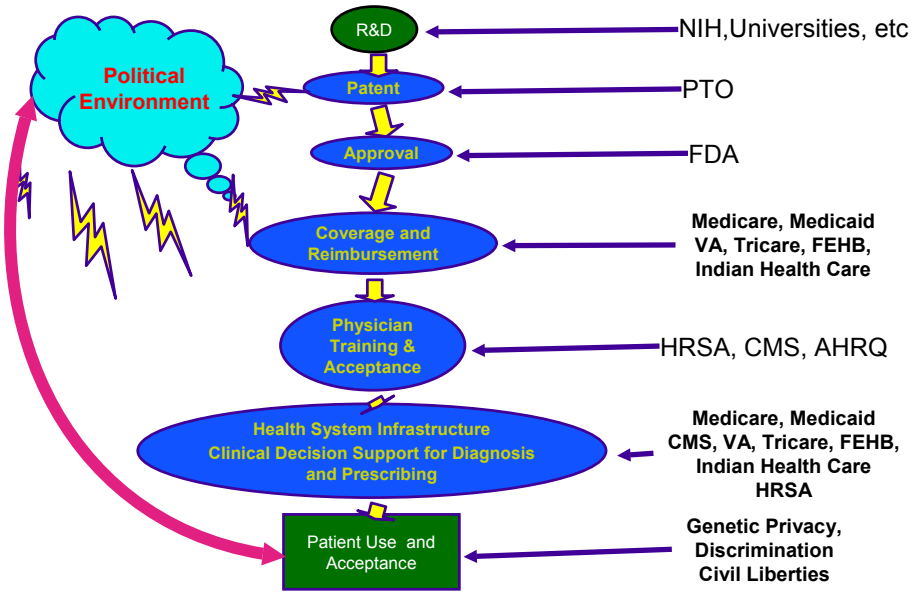
Personal genomics, SNPs

Clinical Record

Analysis lab notes

Adapted from Ned McCulloch IBM

Can Life Sciences Products Get To Patients?



Acknowledgements

Stan Finkelstein,Tom Allen; POPI

Klavs Jensen; Chemical Engineering

Phil Lessard; Biology

Peter Sorger; Biology

ChoKyun Rha; MMBPP

Brigetta Tadmor; CSBi

Robert Mulroy; Merrimack Pharmaceuticals