Publicly-funded Biomedical R&D and Private Sector Innovation

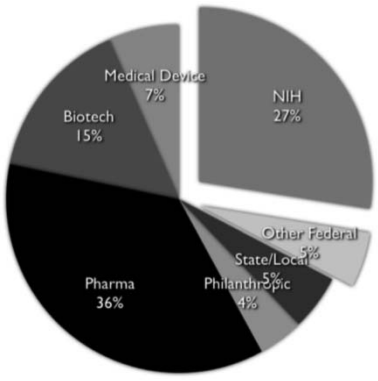
Pierre Azoulay
Massachusetts Institute of Technology
Sloan School of Management

@pierre_azoulay

NAS Innovation Policy Forum
December 15th, 2016

MIT MANAGEMENT SLOAN SCHOOL

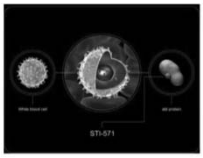
Both the public and private sector spend a lot of money on biomedical R&D

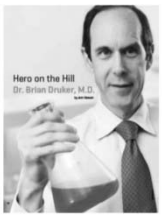


- ***The US spends over $100 billion on biomedical R&D each year***
- ***The public sector plays a significant role***
  - *The NIH alone spends $30 billion*
  - *Half of all patents for FDA-approved drugs cite NIH-funded research*

MIT MANAGEMENT SLOAN SCHOOL

Gleevec: A retrospective look



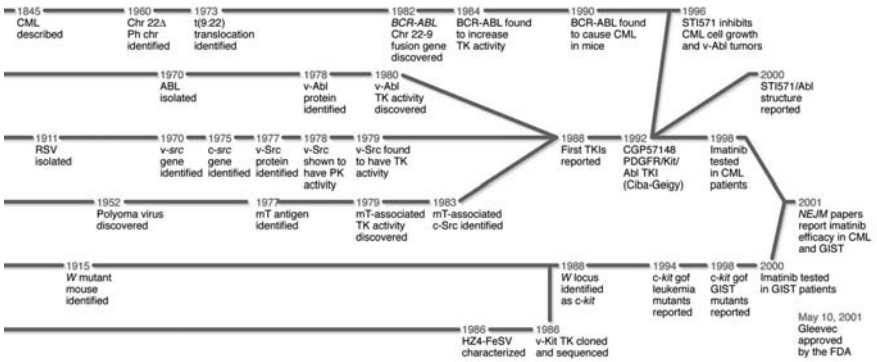


The New England Journal of Medicine

EFFICACY AND SAFETY OF A SPECIFIC INHIBITOR OF THE BCR-ABL TYROSINE KINASE IN CHRONIC MYELOID LEUKEMIA

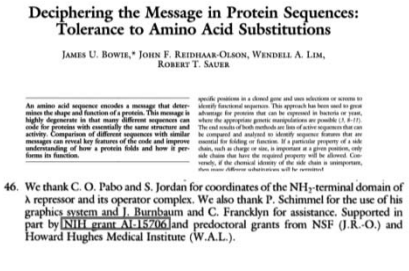
MIT MANAGEMENT SLOAN SCHOOL

The long road to imatinib [Gleevec]



MIT MANAGEMENT SLOAN SCHOOL

Mapping the chain of biomedical R&D



Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions

JAMES U. BOWIE,* JOHN F. REIDHAAR-OLSON, WENDELL A. LIM, ROBERT T. SAUER

An amino acid sequence encodes a message that determines the shape and function of a protein. This message is highly degenerate in that many different sequences can code for proteins with essentially the same structure and activity. Comparison of different sequences with similar messages can reveal key features of the code and improve understanding of how a protein folds and how it performs its function.

specific positions in a cloned gene and uses selections or screens to identify functional sequences. This approach has been used to great advantage for proteins that can be expressed in bacteria or yeast, where the appropriate genetic manipulations are possible (*5, 8–11*). The end results of both methods are lists of active sequences that can be compared and analyzed to identify sequence features that are essential for folding or function. If a particular property of a side chain, such as charge or size, is important at a given position, only side chains that have the required property will be allowed. Conversely, if the chemical identity of the side chain is unimportant, then many different substitutions will be permitted

46. We thank C. O. Pabo and S. Jordan for coordinates of the NH_2-terminal domain of λ repressor and its operator complex. We also thank P. Schimmel for the use of his graphics system and J. Burnbaum and C. Francklyn for assistance. Supported in part by NIH grant AI-15706 and predoctoral grants from NSF (J.R.-O.) and Howard Hughes Medical Institute (W.A.L.).

(12) **United States Patent**
Li et al.

(10) **Patent No.: US 6,867,006 B2**
(45) **Date of Patent: Mar. 15, 2005**

(54) **ANTIBODIES TO HUMAN CHEMOTACTIC PROTEIN**

(75) Inventors: **Haodong Li**, Gaithersburg, MD (US); **Steven M. Ruben**, Olney, MD (US); **Granger Sutton, III**, Columbia, MD (US)

(73) Assignee: **Human Genome Sciences, Inc.**, Rockville, MD (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 230 days.

(21) Appl. No.: **10/141,965**

(22) Filed: **May 10, 2002**

WO	WO 96/38559	12/1996
WO	WO 96/40762	12/1996
WO	WO 97/1559x	5/1997
WO	WO-98/44118	10/1998

OTHER PUBLICATIONS

Beall, C.J., et al., "Conversion of Monocyte Chemoattractant Protein-1 into a Neutrophil Attractant by Substitution of Two Amino Acids," *J. Biol. Chem.* 267:3455–3459, American Society for Biochemistry and Molecular Biology, Inc. (1992).

Berkhout, T.A., et al., "Cloning, in Vitro Expression, and Functional Characterization of a Novel Human CC Chemokine of the Monocyte Chemotactic Protein (MCP) Family (MCP-4) That Binds and Signals through the CC Chemokine Receptor 2B," *J. Biol. Chem.* 272:16404–16413, American Society for Biochemistry and Molecular Biology, Inc. (Jun. 1997).

Bowie, J.U., et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science* 247:1306–1310, American Association for the Advancement of Science (1990).

***Step 1*: NIH Grants → Publications**

***Step 2*: Publications → Patents**

MIT MANAGEMENT SLOAN SCHOOL

NIH Funding Rules

NIH National Institutes of Health
Turning Discovery Into Health

Funding

Scientific Merit

MIT MANAGEMENT SLOAN SCHOOL

Findings

- ***In the long-run, the odds that a drug patent "builds on" NIH-funded research is 30-40%***
  - *But the long run is indeed very long (10-15 years)*
  - *50% of the effect "leaks out" of the intended research area of the grant*
- ***NIH funding for a research area causes a net increase in private sector patenting in that area***
- ***Elasticities of private sector patenting with respect to public funding of around 0.5***
  - *$10M leads to a net increase of 2.3 patents.*
  - *$10M generates $3.5-$27.8 m in PDV of drug sales.*

MIT MANAGEMENT SLOAN SCHOOL

Back-of-the-envelope calculation for an estimate of the private returns

- ***$ Return to NIH funding***
  - *E(V) = # Marginal Patents × p × E(Π)*
  - *p is the probability that each marginal patent is pivotal for an FDA-approved drug*
  - *Π is the present discounted sales for the average FDA-approved drug*
- ***Caveats***
  - *Not all biomedical patents in our sample are for drugs*
  - *Estimates exclude value of non-drug innovations: medical devices, clinical protocols, etc.*
  - *p is hard to estimate*
  - *The distribution of Π is very skewed*

MIT MANAGEMENT SLOAN SCHOOL

Magnitudes

$10 million in NIH funding leads to....

$$\frac{\text{0.034 more patents associated with FDA approved drugs}}{\text{8 Avg. patents per drug}}$$

(Assumed patents are pure substitutes for the drug)

$\times$\$3.47 billion average PDV of sales

(Taken from the literature, DiMasi, Grabowski, and Vernon (2004))

= \$14.7 million in sales for drugs.

MIT MANAGEMENT SLOAN SCHOOL