



Universidade Federal do Rio de Janeiro

O Quadrante Pasteur, a inovação e o desenvolvimento de fármacos



Eliezer J. Barreiro

Professor Titular

**Programa de Desenvolvimento de Fármacos
ICB - UFRJ**

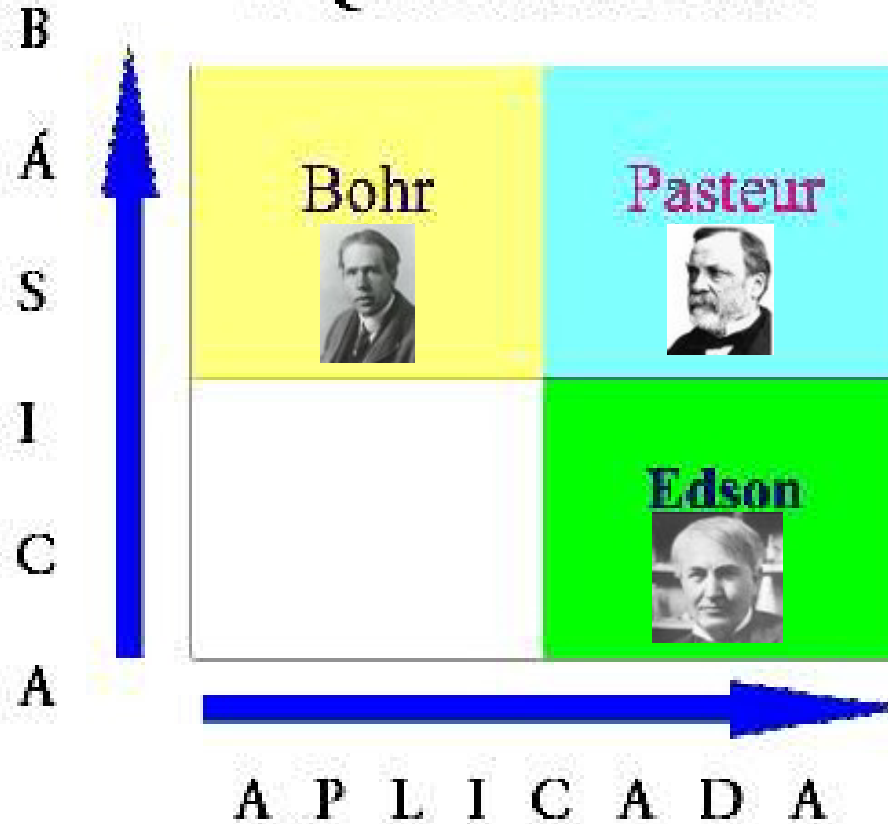
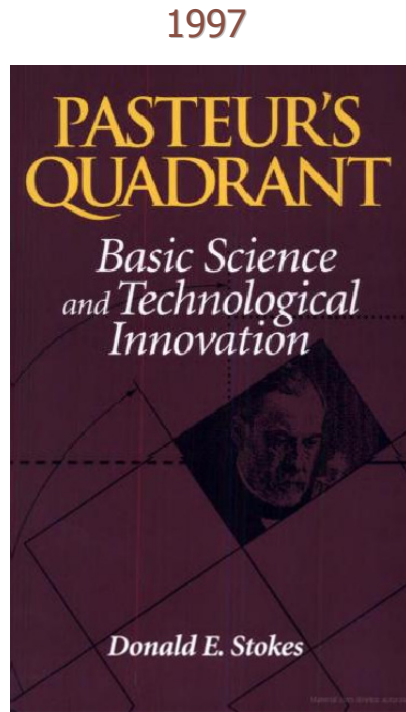
Laboratório de Avaliação e Síntese de Substâncias Bioativas



<http://www.farmacia.ufrj.br/lassbio>

A produção do conhecimento

O Quadrante de Pasteur



1950 - NSF

D. E. Stokes; *Pasteur's Quadrant: Basic Science and Technological Innovation*, Book News, Inc., Portland, EUA, 1999.

Avanço do conhecimento & aplicabilidade do conhecimento
X Ciência básica & Ciência aplicada;

Slide 2

EJB1

The production of knowlegde

Eliezer J Barreiro; 02/05/2010



Nature **409**, 397-401 (18 January 2001) | doi:10.1038/35053187

feature

Pasteur's Quadrant and malnutrition

George L. Blackburn



Basic science has been the wellspring of advances in technology in everything from cellular phones to nutrient-fortified foods. Biochemistry and food technology afford new techniques that enrich nutritional science and aid in the fight against malnutrition. Bionutrition, the term used to describe the application of these techniques, can be the source of innovations that will help eradicate malnutrition globally.



Quim. Nova, Vol. 28, Suplemento, S95-S99, 2005

O QUADRANTE DE RUETSAP E A ANTI-CIÊNCIA, TECNOLOGIA E INOVAÇÃO

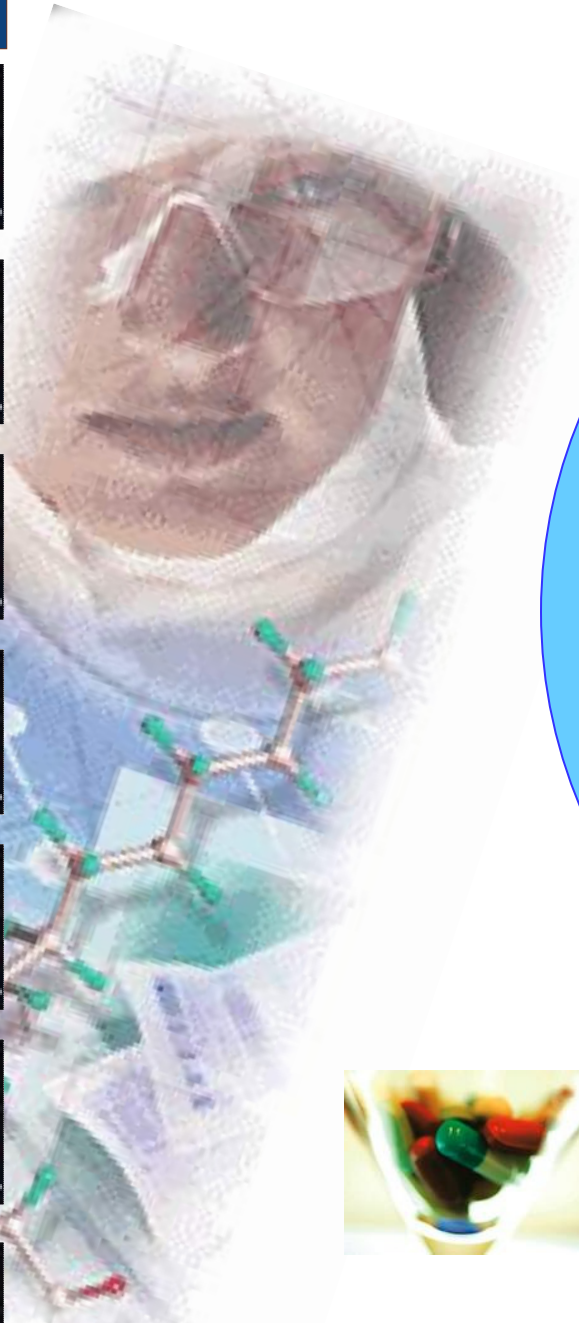
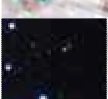
Francisco Radler de Aquino Neto

Instituto de Química, Universidade Federal do Rio de Janeiro, Cid. Univ. Ilha do Fundão, 21949-900 Rio de Janeiro - RJ





Ciência & Tecnologia



INOVACÃO

Inovação

Desenvolvimento

Inovação



■ A **inovação** é atributo da competitividade empresarial
(Patel & Pavitt, 1994)

➡ Produtos inovadores são industriais;

Capacidade de **inovação**

➤ Elevada: EUA, Jpn, Fr, UK, IT

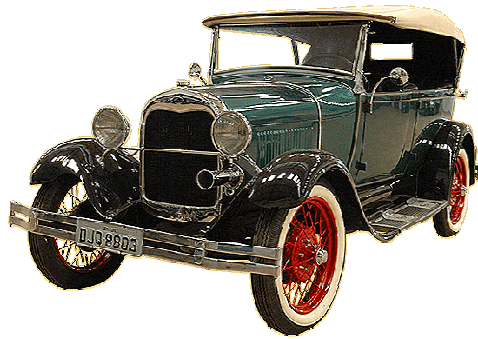
➤ Incompleta: **Br**, Ar, Mex, In, Ch, Ru

Tríplice Hélice

(Leydesdorff & Etzkowitz, 1998)

■ Modelo espiral de inovação baseado
na geração e distribuição do conhecimento



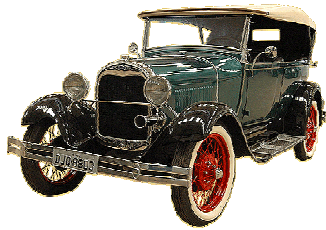
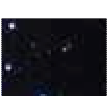


A inovação tecnológica é um processo dinâmico,
talvez o mais dinâmico na atividade industrial;



O dinamismo da inovação tecnológica,
depende da interação
da Ciência & Tecnologia;

- *Inovação incremental*



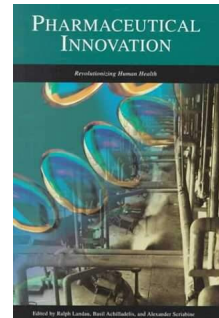
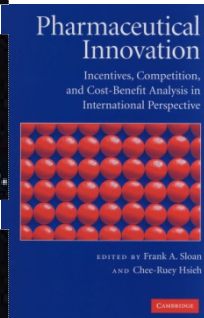
A inovação tecnológica é um processo dinâmico,
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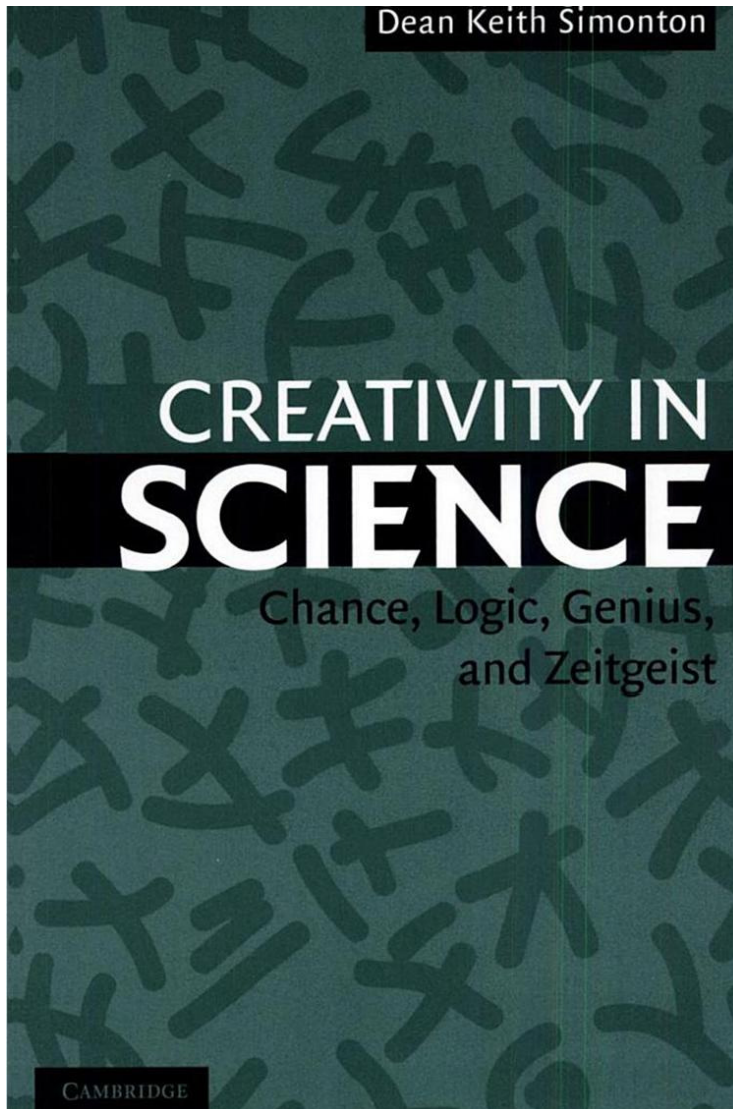
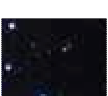
O dinamismo da inovação tecnológica,
depende da interação
da Ciência & Tecnologia;



A inovação é a principal
driving-force da indústria farmacêutica que
descobre moléculas;



.....
Invenção, talento, genialidade & criatividade



Descobertas & invenções



zeitgeist or "spirit of the times"

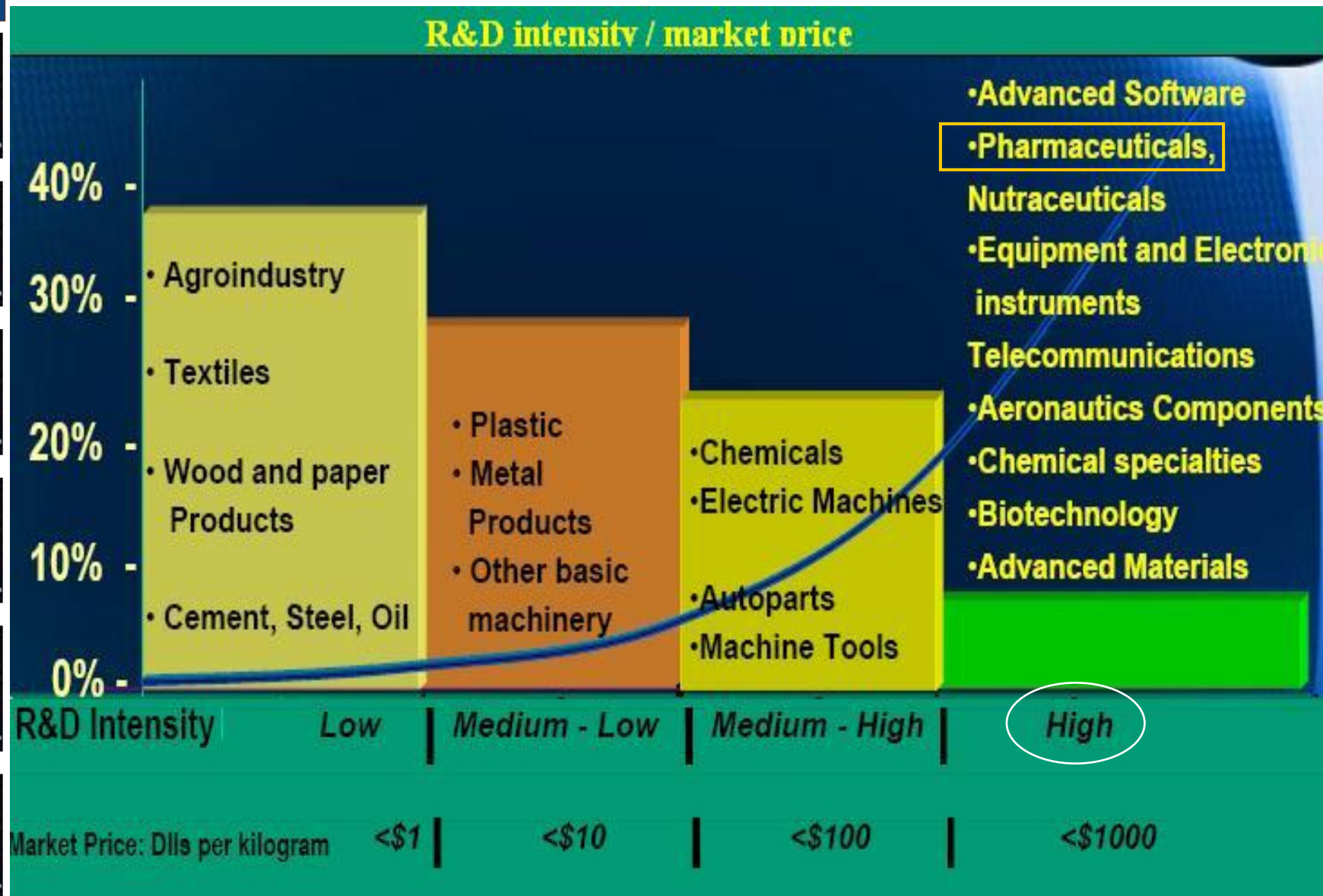
"discoveries and inventions become virtually inevitable (1) as prerequisite kinds of knowledge accumulate in man's cultural store; (2) as the attention of a sufficient number of investigators is focused on a problem – by emerging social needs, or by developments internal to the particular science, or by both"

Robert K. Merton (1961)

The role of genius in scientific advance. *New Scientist*, 12, 306-308



O desenvolvimento de fármacos depende da pesquisa





O desenvolvimento de fármacos ...

- *Science* **2000**, 287, 1951 (J. Uppenbrink, J. Mervis)



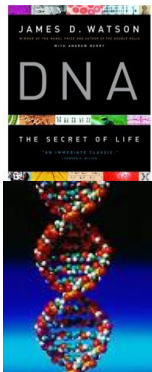
...depende da pesquisa científica



A pesquisa científica através dos tempos...



Galileo, Newton, Darwin, & Einstein



O físico Crick & o biólogo Watson



A equipe do genoma humano...





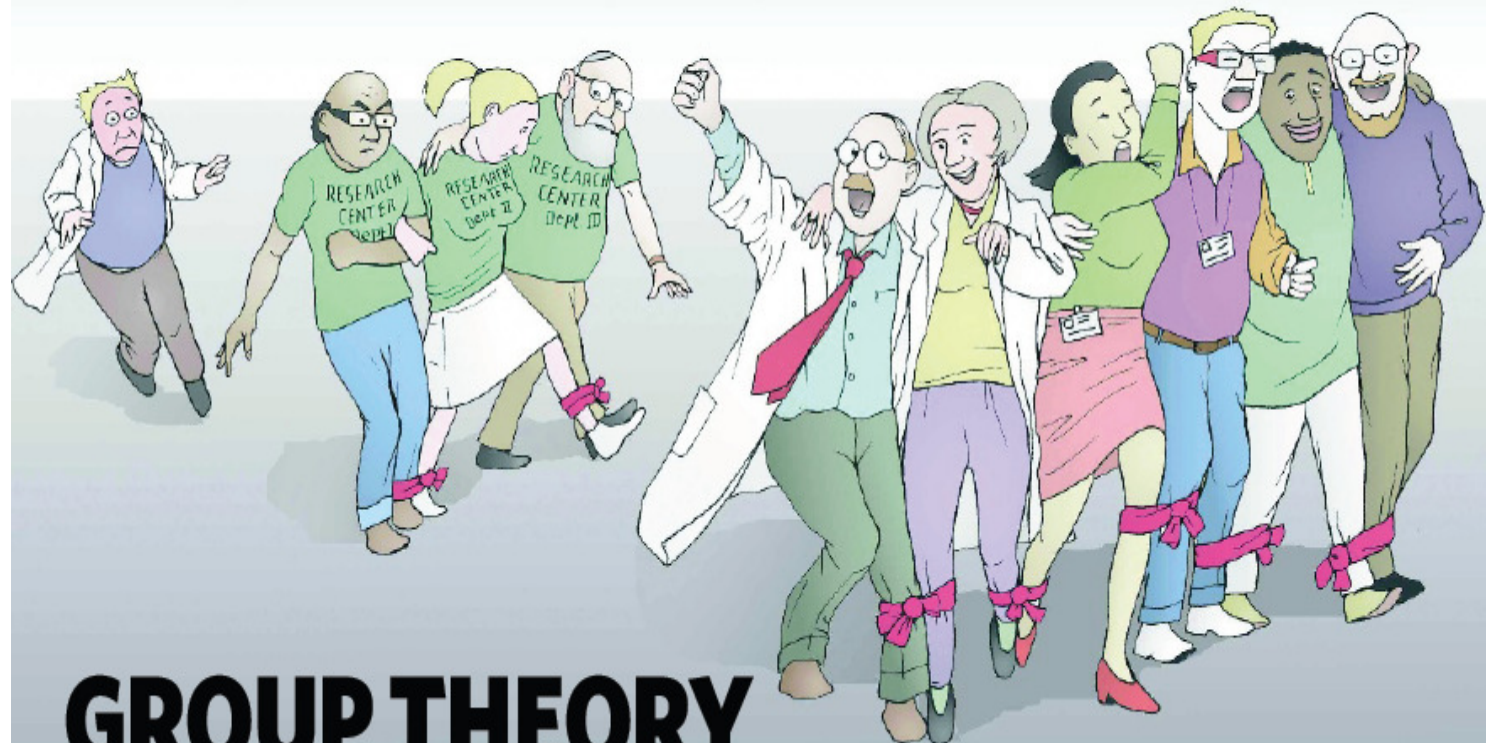
The Sequence of the Human Genome

J. Craig Venter, Mark D. Adams, Eugene W. Myers, Peter W. Li, Richard J. Mural, Granger G. Sutton, Hamilton O. Smith, Mark Yandell, Cheryl A. Evans, Robert A. Holt, Jeannine D. Gocayne, Peter Amanatides, Richard M. Ballew, Daniel H. Huson, Jennifer Russo Wortman, Qing Zhang, Chinnappa D. Kodira, Xiangqun H. Zheng, Lin Chen, Marian Skupski, Gangadharan Subramanian, Paul D. Thomas, Jinghui Zhang, George L. Gabor Miklos, Catherine Nelson, Samuel Broder, Andrew G. Clark, Joe Nadeau, Victor A. McKusick, Norton Zinder, Arnold J. Levine, Richard J. Roberts, Mel Simon, Carolyn Slayman, Michael Hunkapiller, Randall Bolanos, Arthur Delcher, Ian Dew, Daniel Fasulo, Michael Flanigan, Liliana Florea, Aaron Halpern, Sridhar Hannenhalli, Saul Kravitz, Samuel Levy, Clark Mobarry, Knut Reinert, Karin Remington, Jane Abu-Threideh, Ellen Beasley, Kendra Biddick, Vivien Bonazzi, Rhonda Brandon, Michele Cargill, Ishwar Chandramouliswaran, Rosane Charlab, Kabir Chaturvedi, Zuoming Deng, Valentina Di Francesco, Patrick Dunn, Karen Eilbeck, Carlos Evangelista, Andrei E. Gabrielian, Weiniu Gan, Wangmao Ge, Fangcheng Gong, Zhiping Gu, Ping Guan, Thomas J. Heiman, Maureen E. Higgins, Rui-Ru Ji, Zhaoxi Ke, Karen A. Ketchum, Zhongwu Lai, Yiding Lei, Zhenya Li, Jiayin Li, Yong Liang, Xiaoying Lin, Fu Lu, Gennady V. Merkulov, Natalia Milshina, Helen M. Moore, Ashwinikumar K Naik, Vaibhav A. Narayan, Beena Neelam, Deborah Nusskern, Douglas B. Rusch, Steven Salzberg, Wei Shao, Bixiong Shue, Jingtao Sun, Zhen Yuan Wang, Aihui Wang, Xin Wang, Jian Wang, Ming-Hui Wei, Ron Wides, Chunlin Xiao, Chunhua Yan, Alison Yao, Jane Ye, Ming Zhan, Weiqing Zhang, Hongyu Zhang, Qi Zhao, Liansheng Zheng, Fei Zhong, Wenyan Zhong, Shiaoping C. Zhu, Shaying Zhao, Dennis Gilbert, Suzanna Baumhueter, Gene Spier, Christine Carter, Anibal Cravchik, Trevor Woodage, Feroze Ali, Huijin An, Aderonke Awe, Danita Baldwin, Holly Baden, Mary Barnstead, Ian Barrow, Karen Beeson, Dana Busam, Amy Carver, Angela Center, Ming Lai Cheng, Liz Curry, Steve Danaher, Lionel Davenport, Raymond Desilets, Susanne Dietz, Kristina Dodson, Lisa Doup, Steven Ferriera, Neha Garg, Andres Gluecksmann, Brit Hart, Jason Haynes, Charles Haynes, Cheryl Heiner, Suzanne Hladun, Damon Hostin, Jarrett Houck, Timothy Howland, Chinyere Ibegwam, Jeffery Johnson, Francis Kalush, Lesley Kline, Shashi Koduru, Amy Love, Felecia Mann, David May, Steven McCawley, Tina McIntosh, Ivy McMullen, Mee Moy, Linda Moy, Brian Murphy, Keith Nelson, Cynthia Pfannkoch, Eric Pratts, Vinita Puri, Hina Qureshi, Matthew Reardon, Robert Rodriguez, Yu-Hui Rogers, Deanna Romblad, Bob Ruhfel, Richard Scott, Cynthia Sitter, Michelle Smallwood, Erin Stewart, Renee Strong, Ellen Suh, Reginald Thomas, Ni Ni Tint, Sukyee Tse, Claire Vech, Gary Wang, Jeremy Wetter, Sherita Williams, Monica Williams, Sandra Windsor, Emily Winn-Deen, Keriellen Wolfe, Jayshree Zaveri, Karena Zaveri, Josep F. Abril, Roderic Guigó, Michael J. Campbell, Kimmie V. Sjolander, Brian Karlak, Anish Kejariwal, Huaiyu Mi, Betty Lazareva, Thomas Hatton, Apurva Narechania, Karen Diemer, Anushya Muruganujan, Nan Guo, Shinji Sato, Vineet Bafna, Sorin Istrail, Ross Lippert, Russell Schwartz, Brian Walenz, Shibu Yooseph, David Allen, Anand Basu, James Baxendale, Louis Blick, Marcelo Caminha, John Carnes-Stine, Parris Caulk, Yen-Hui Chiang, My Coyne, Carl Dahlke, Anne Deslattes Mays, Maria Dombroski, Michael Donnelly, Dale Ely, Shiva Esparham, Carl Fosler, Harold Gire, Stephen Glanowski, Kenneth Glasser, Anna Glodek, Mark Gorokhov, Ken Graham, Barry Gropman, Michael Harris, Jeremy Heil, Scott Henderson, Jeffrey Hoover, Donald Jennings, Catherine Jordan, James Jordan, John Kasha, Leonid Kagan, Cheryl Kraft, Alexander Levitsky, Mark Lewis, Xiangjun Liu, John Lopez, Daniel Ma, William Majoros, Joe McDaniel, Sean Murphy, Matthew Newman, Trung Nguyen, Ngoc Nguyen, Marc Nodell, Sue Pan, Jim Peck, Marshall Peterson, William Rowe, Robert Sanders, John Scott, Michael Simpson, Thomas Smith, Arlan Sprague, Timothy Stockwell, Russell Turner, Eli Venter, Mei Wang, Meiyuan Wen, David Wu, Mitchell Wu, Ashley Xia, Ali Zandieh, and Xiaohong Zhu





What makes a successful team?



GROUP THEORY

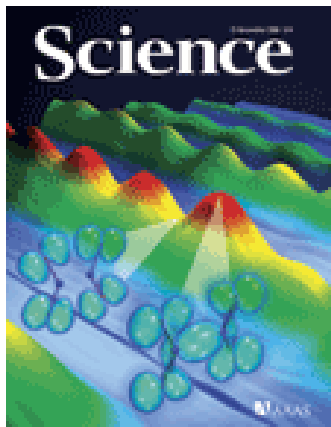
What makes a successful team? **John Whitfield** looks at research that uses massive online databases and network analysis to come up with some rules of thumb for productive collaborations.

Em tempos da interdisciplinaridade...

Multi-University Research Teams: Shifting Impact, Geography, and Stratification in Science



Benjamin F. Jones,^{1,2*} Stefan Wuchty,^{3*} Brian Uzzi^{1,3,4*}



SCIENCE VOL 322 21 NOVEMBER 2008 1259

¹Kellogg School of Management, Northwestern University, Evanston, IL 60208, USA. ²National Bureau of Economic Research, Cambridge, MA 02138, USA. ³Northwestern Institute on Complexity (NICO), Northwestern University, Evanston, IL 60208, USA. ⁴Haas School of Business, University of California at Berkeley, Berkeley, CA 94720, USA.

.....
A pesquisa científica contemporânea se faz em ambiente de rede.

Slide 14

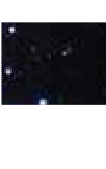
EJB13

Para completude em sua atuação com plena formação de M&D,I a PG precisa interagir além de sua própria arena, sem ir de lado mas com decisão.

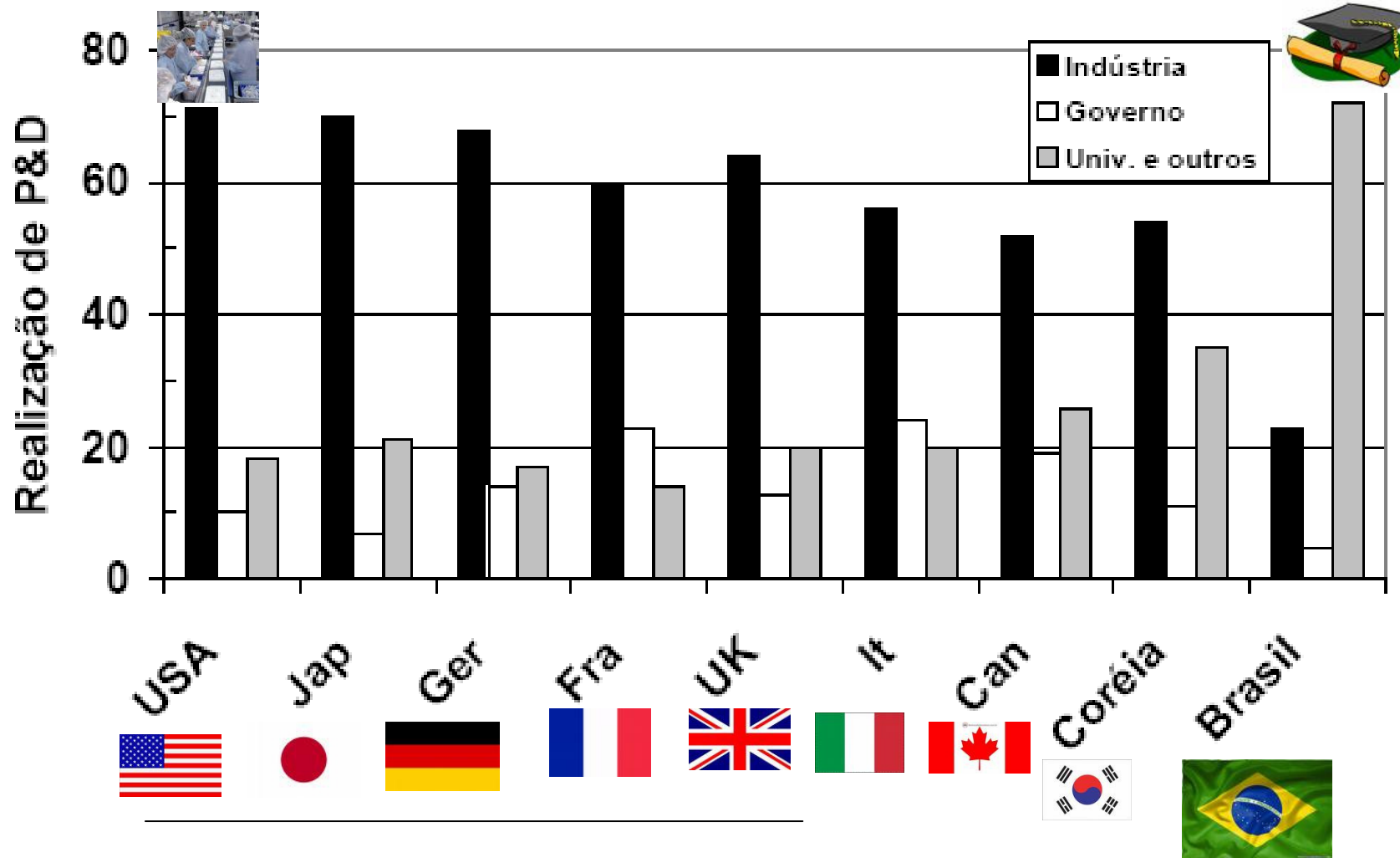
Eliezer J. Barreiro; 04/03/2010

E4

Eliezer; 22/04/2010



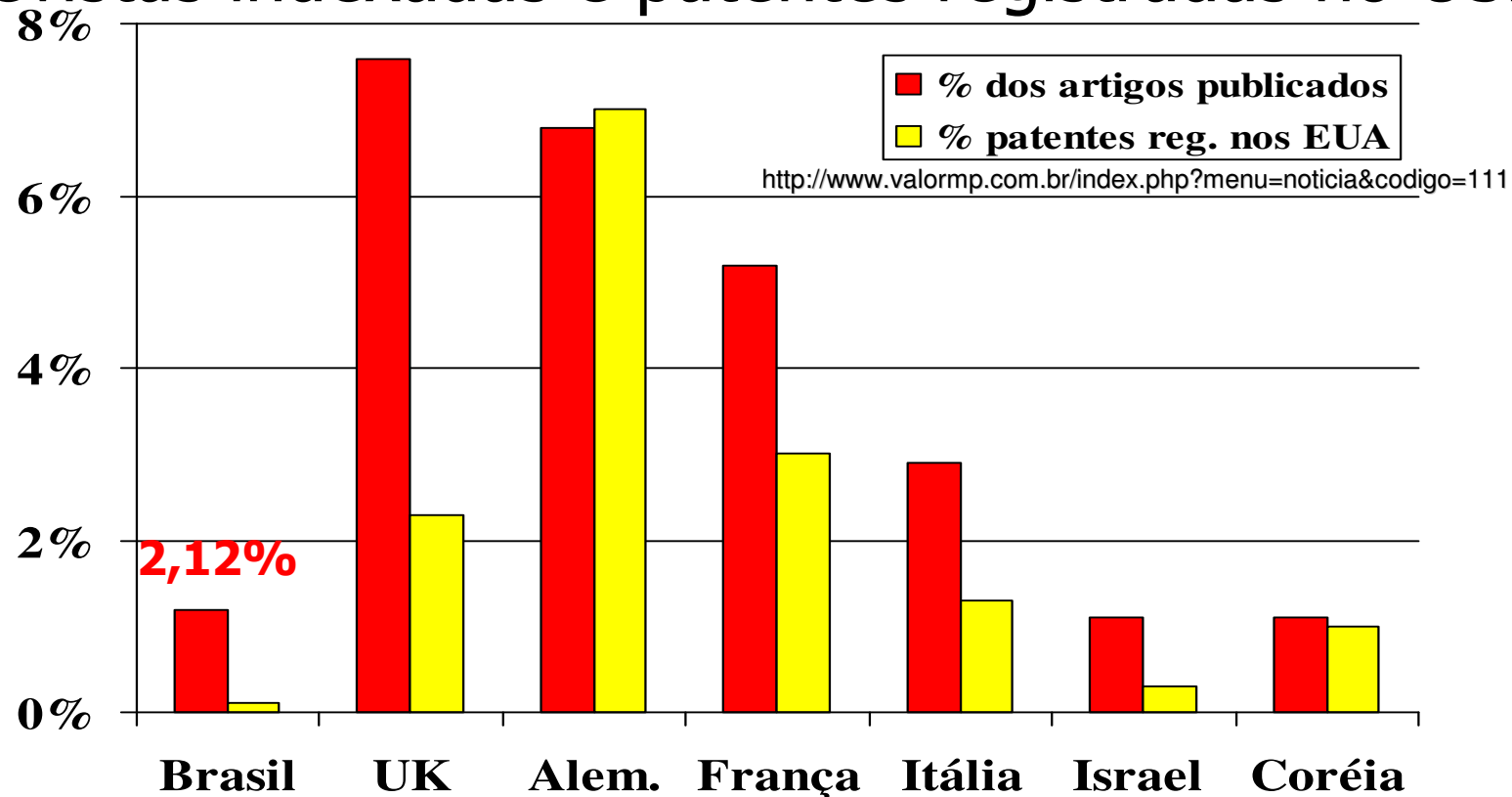
Distribuição dos pesquisadores ativos



Adaptado de C. H. Brito Cruz & C. A. Pacheco, "Conhecimento & Inovação: Desafios do Brasil no Século XXI", em www.inovacao.unicamp.br/report/intc-pacheco-brito.pdf (2/01/2009)



Contribuição do Brasil em artigos publicados em revistas indexadas e patentes registradas no USPTO



O Brasil se encontra no **28º** lugar no *ranking* mundial de patentes e tecnologia, com apenas 101 registros de patentes em 2008 (USPTO), tendo a China 1.536, a Índia 636*. Em contraste, **2,12%** do conhecimento novo mundial foi produzido no País, com **30.415** publicações, em 2008 (**19.487** em 2007; NSI) à frente da **Holanda** (28.443), **Rússia** (27.909), **Suíça** (21.065) e **Suécia** (19.127)&.

*Fonte: Jornal do Commercio - Texto de Jaqueline Porto - 20/07/2009;

& Fonte: O Globo, 06/05/2009;



O desenvolvimento de fármacos...

Science
Translational
Medicine



Online Issue 28 December 2009



O mercado mundial de medicamentos (2009): *ca.* US\$ 785 bi



the Pharmaceutical Century

TEN DECADES OF DRUG DISCOVERY

[Analytical Chemistry](#) | [Chemical & Engineering News](#) | [Modern Drug Discovery](#)
[Today's Chemist at Work](#) | [E-Mail Us](#) | [Electronic Readers Service](#)

1800s to 1919

We live today in a world of drugs. Drugs for pain, drugs for disease, drugs for allergies, drugs for pleasure, and drugs for mental health. Drugs that have been rationally designed; drugs that have been synthesized in the factory or purified from nature. Drugs fermented and drugs engineered. Drugs that have been clinically tested. Effective. Safe.



~~Binômio doença-doente~~



zoom

"We live today in a world of **drugs**. Drugs for **pain**, drugs for **disease**, drugs for **allergies**, drugs for **pleasure**, and drugs for **mental health**. Drugs that have been **rationally designed**; drugs that **have been synthesized** or **purified from nature**. Drugs **fermented** and drugs **engineered**. Drugs that have been clinically tested. Effective. Safe."

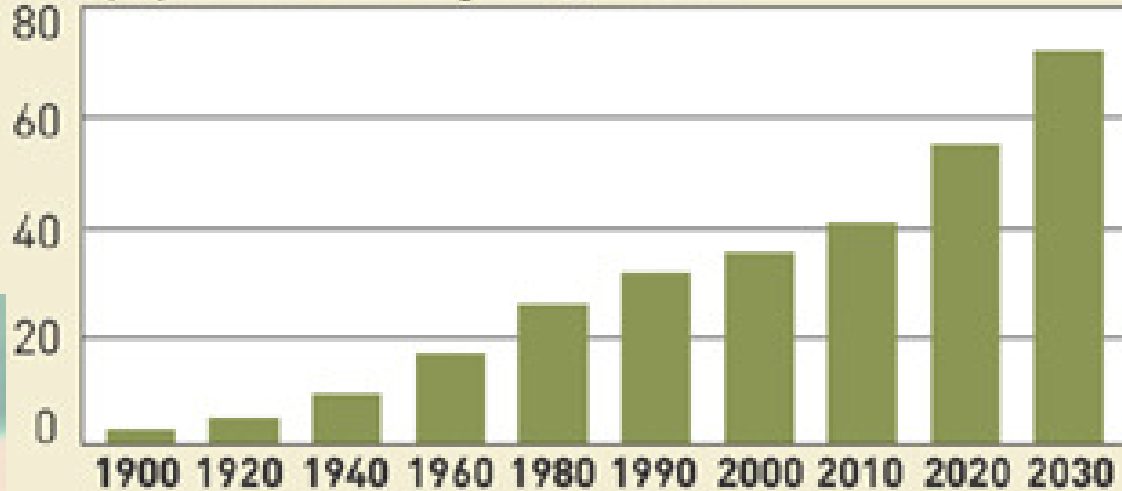


"New style drugs"

ELDER BOOM

Thanks to baby boomers, the U.S. population over 65 will swell between 2010 and 2030

U.S. population over age 65, millions



SOURCE: Census Bureau



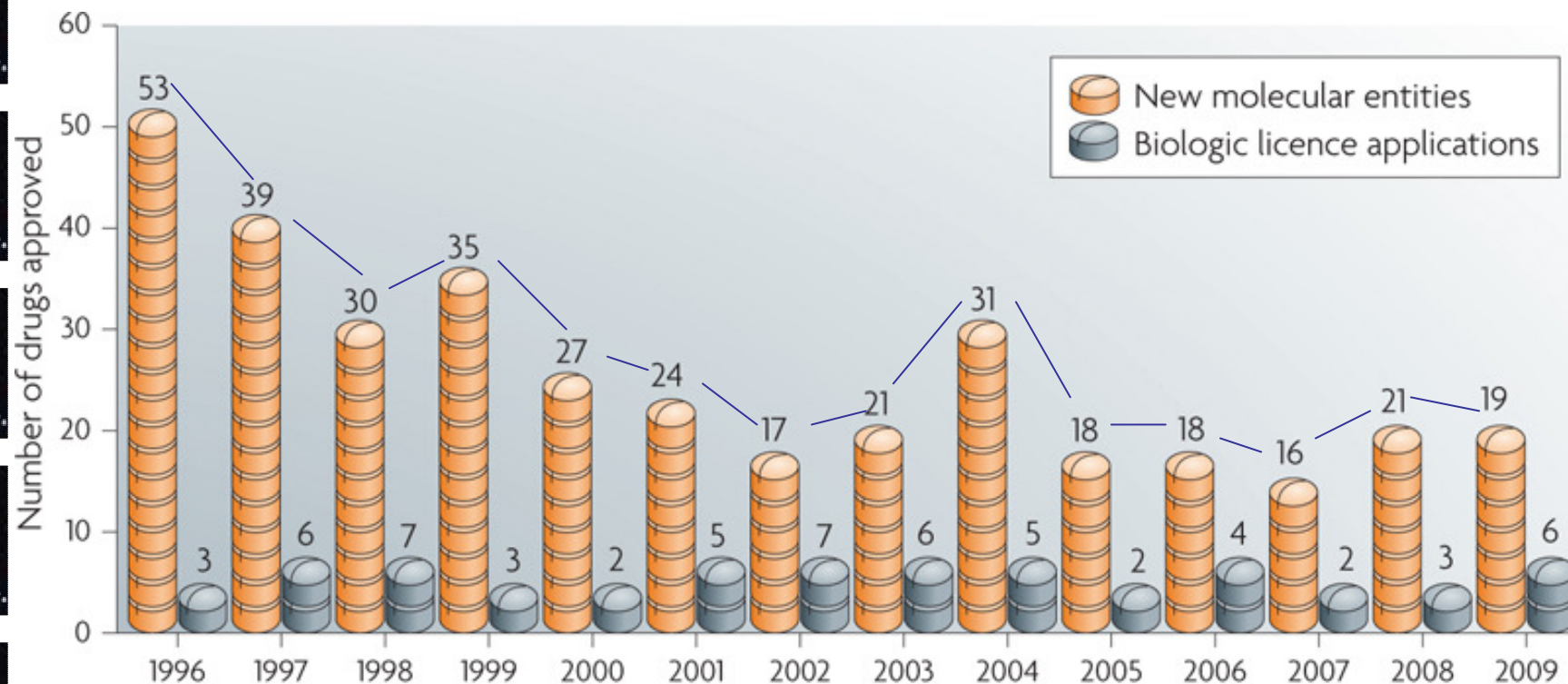
À esquerda rato transgênico "envelhecido" com 100 anos-humanos.

the Pharmaceutical Century

TEN DECADES OF DRUG DISCOVERY



Os fármacos inovadores estão mais r(c)aros...



Ou: as inovações já não são assim tão inovadoras!



Nature Reviews | Drug Discovery



DECEMBER 7, 2009
C&EN
 CHEMICAL & ENGINEERING NEWS

CHEMICAL SECURITY
 Antiterrorism det-
 moves to Senate I
 TRIBOLC
 Molecular wear and tea
 unusual systems I

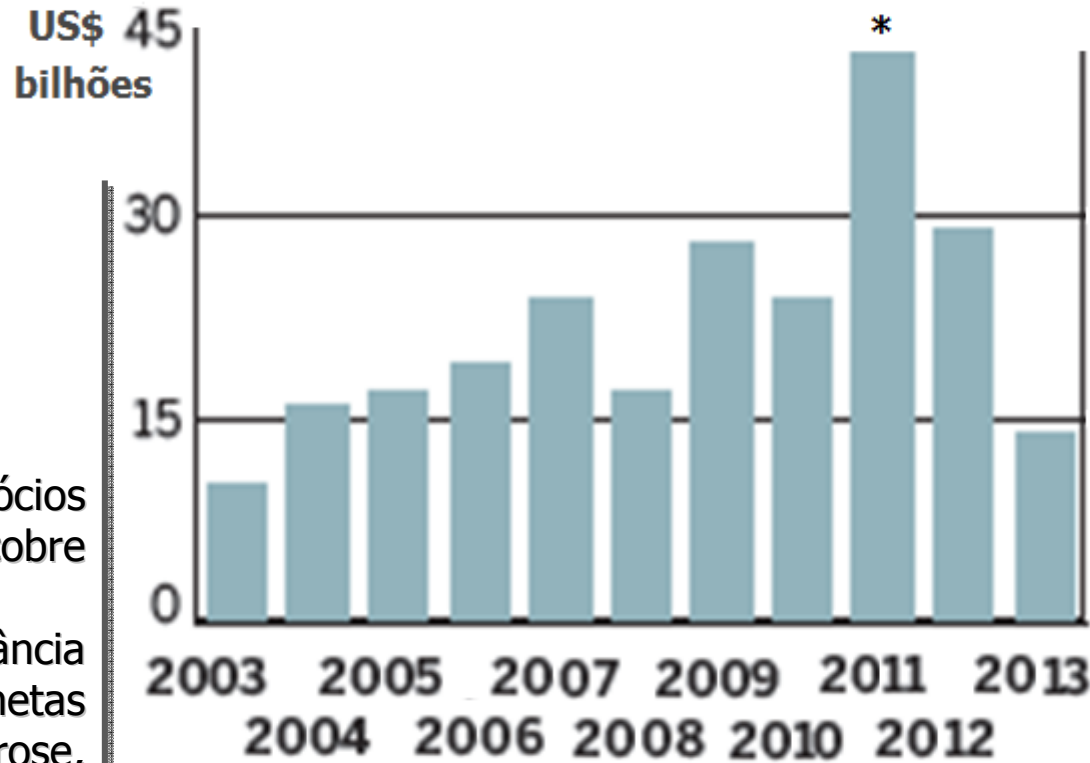


PHARMA REFORMULATES
 Pushing plans to fortify pipelines, profits p.13
PUBLISHED BY THE AMERICAN CHEMICAL SOCIETY

As estratégias de negócios mudam na IF que descobre moléculas:

Novas fusões, alternância geográfica, ajustes de metas terapêuticas (osteoporose, sistema respiratório, trombose, esclerose múltipla, altismo, câncer), participação no mercado de medicamentos genéricos (ca. US\$ 80 bi em 2009; Aventis & Medley, BR)

A IF global observará reduções nos oito principais mercados (EUA, Jpn, Fr, Ale, It, Ch, Sp, UK)



* Três blockbusters perderão proteção patentária: e.g. atorvastatina, clopidogrel & seretide

Fonte: SJ Ainsworth, *C&EN* 2009 (07/12) 13-21



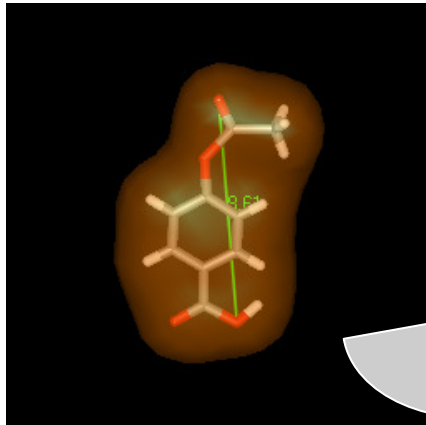
Everyone is *searching* for drugs



Editorial overview
Alan Cuthbert

Current Opinion in Pharmacology 2004, 4, 487

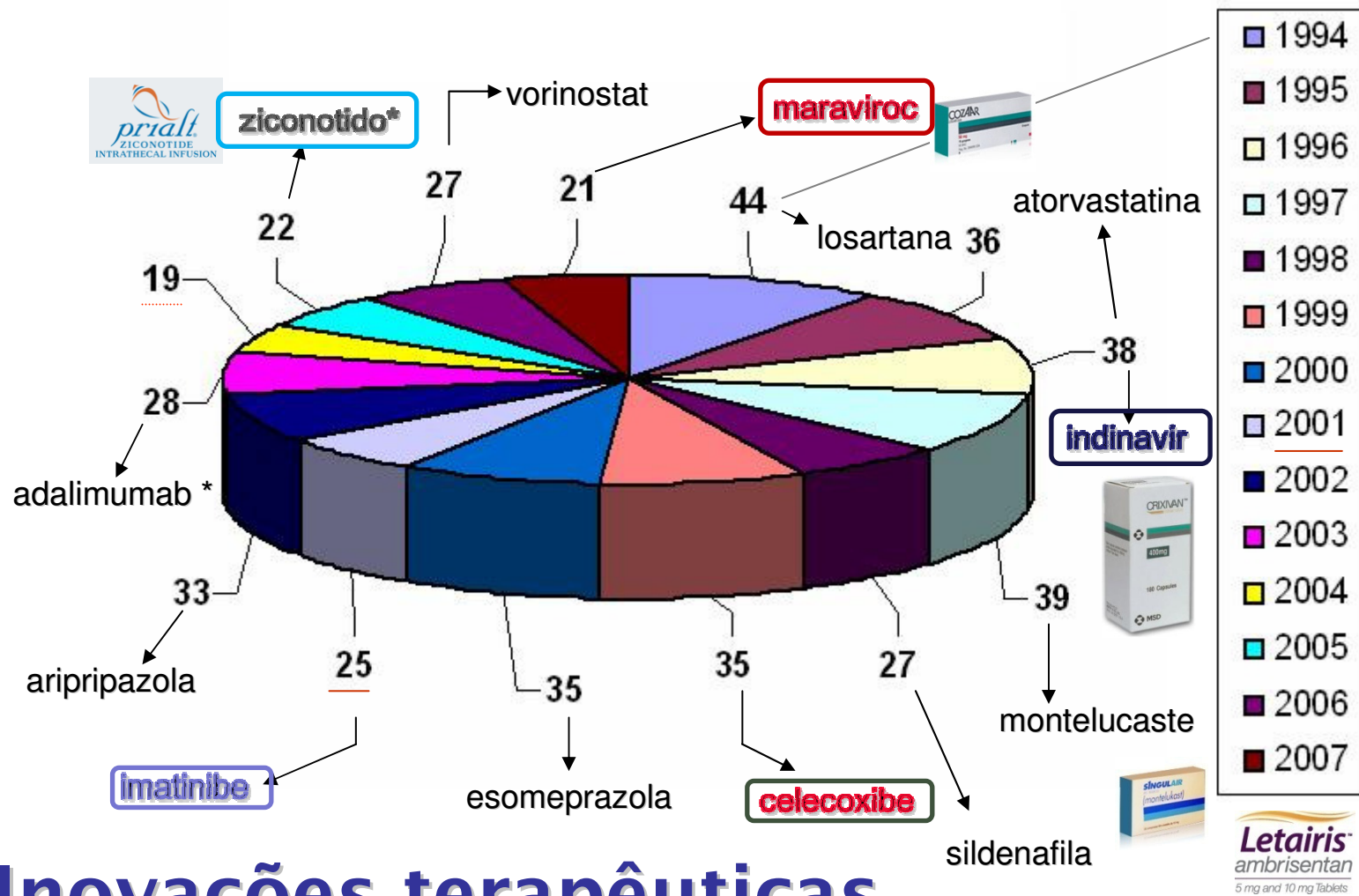
**Big-pharma
&
small
molecules**





Novos fármacos lançados por ano

(1994 – 2007)

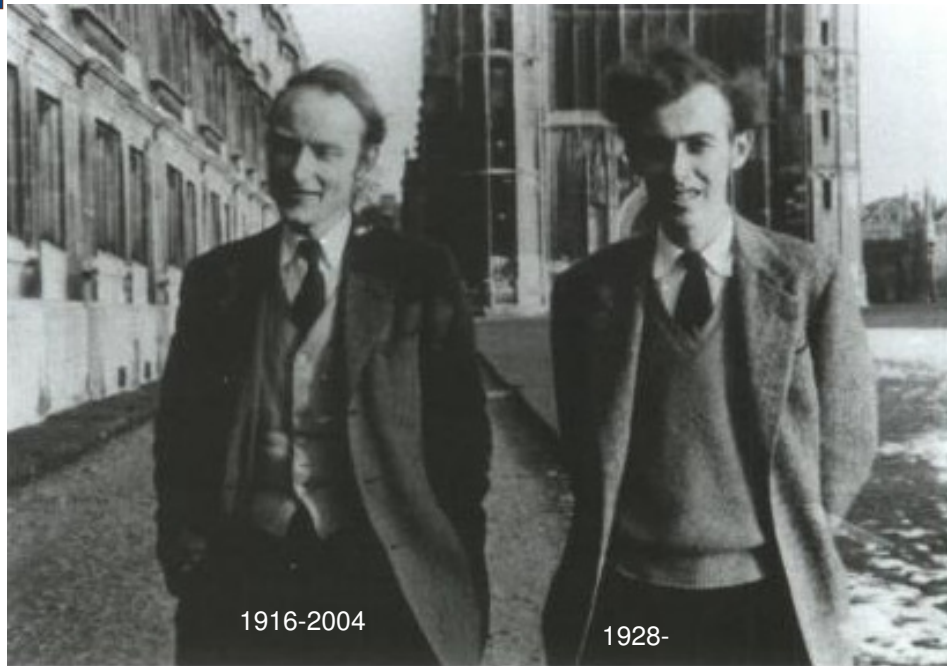


Inovações terapêuticas

ca. 30 novos fármacos lançados / ano

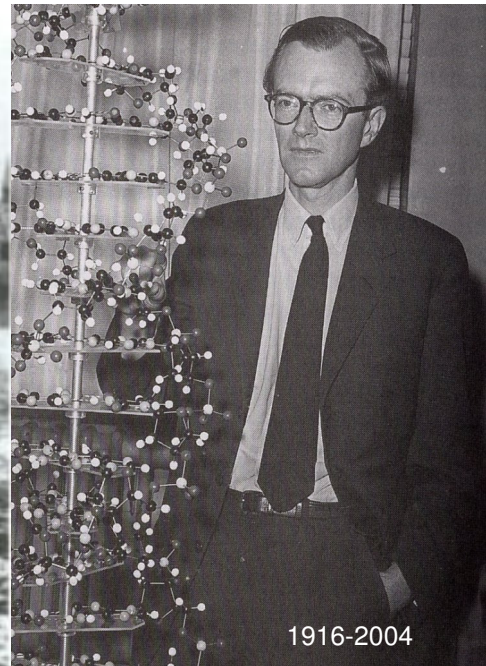
Letairis[®]
ambrientan
5 mg and 10 mg Tablets

Prêmio Nobel de Fisiologia/Medicina



1916-2004

1928-



1916-2004

1962



Francis Crick and James Watson in Cambridge, England, 1953
(Courtesy of the James D. Watson Special Collection, Cold Spring Harbor Laboratory Archives.
From Watson J.D. 1968, *The Double Helix*. Atheneum Press, New York.)

Maurice H. F. Wilkins

O físico Crick, o biólogo Watson & o médico Wilkins

Interdisciplinaridade

Watson, JD & Crick, FHC, *Nature* 1953, **171**, 737-738

EJB20

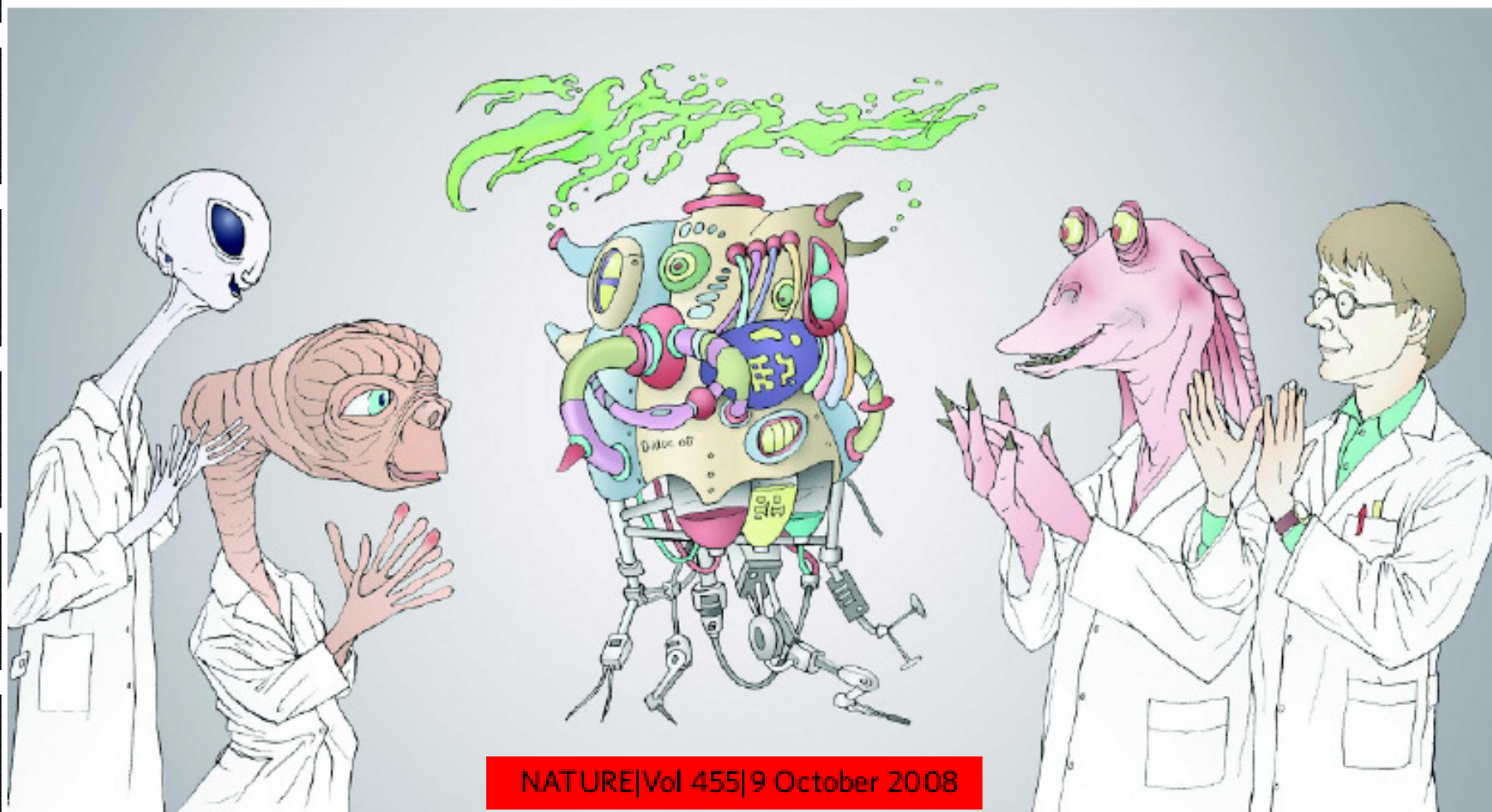
Exemplos de extraordinárias conquistas do conhecimento humano deveram-se às associações de capacidades e competências complementares, essenciais à sua consecução: e.g. DNA em publicação de apenas 2 páginas em prestigioso periódico científico que resultou, décadas depois, na era ômica.

JD Watson & FHC Crick, *Nature*, 1953, 171, 737-738

Eliezer J. Barreiro; 04/03/2010



Sobre a interdisciplinaridade...



A prática do ensino & pesquisa interdisciplinar exige posturas inovadoras



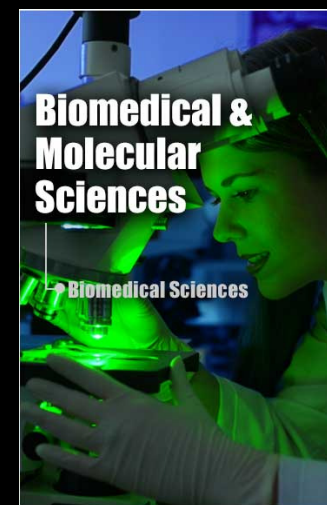
It is an exciting time for chemists to be involved in all aspects of **biomedical research**. The word “**molecular**” has always been an integral part of chemistry, but it has gained a new appreciation from physicians and **biologists**, who have named **emerging fields** **molecular medicine**, **molecular genetics**, **molecular biology**, **molecular bioengineering**, **molecular cardiology**, etc. Clearly, “**chemistry**” or “**molecular science**” has become the **centerpiece of the modern biomedical research**.



Iwao Ojima (Guest Editor)

*Institute of Chemical Biology & Drug Discovery,
State University of New York at Stony Brook*

<http://www.stonybrook.edu/icbdd/>



Accounts of Chemical Research 2008, 41, N° 1

Special Issue on Modern Molecular Approaches to Drug Design and Discovery

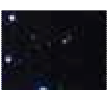


Pôle de recherche interdisciplinaire pour le médicament

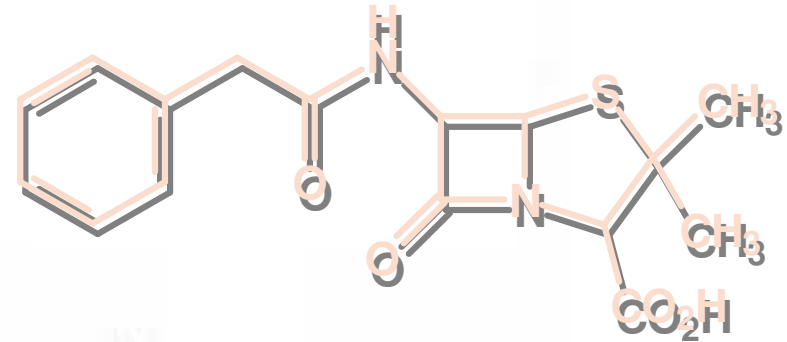


Parc d'Innovation d'Illkirch
Communauté Urbaine de Strasbourg



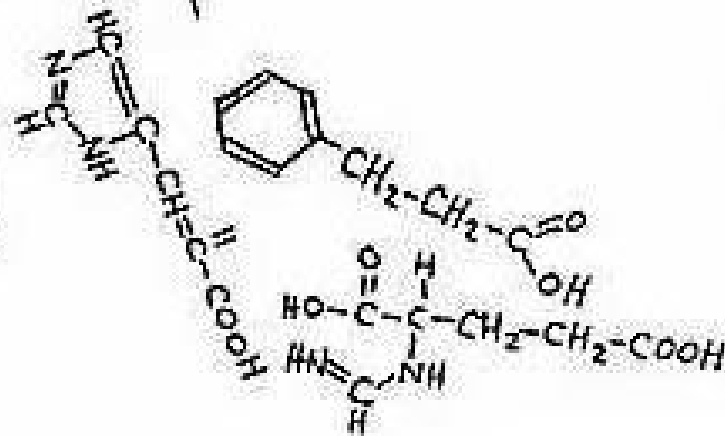


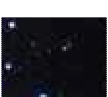
Desperdício molecular...



1928 - 1941

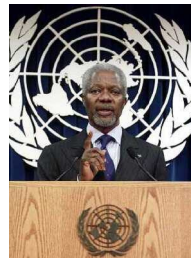
Penicilina





"Science has contributed immensely to human progress and to the development of modern society.

The application of scientific knowledge continues to furnish powerful means for solving many of the challenges facing humanity...."



Kofi Annan

U.N. – Secretary-General

A Challenge to the World's Scientists

Science

Science, 2003, 299, 1485

Contato →

Cursos →

Disciplinas →

Editais de Seleção →

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Orientadores e Linhas de Pesquisa →

Programa de Pós Graduação em Farmacologia e Química Medicinal

29 de abril de 2008

O Instituto de Ciências Biomédicas (ICB) da Universidade Federal do Rio de Janeiro mantém o Programa de Pós-Graduação na modalidade *stricto sensu* que permite obter graus de Mestre e Doutor em Ciências (Farmacologia e Química Medicinal). Os cursos de Mestrado e Doutorado são reconhecidos pela CAPES com conceito 4 e credenciados pelo Conselho Federal de Educação, tendo participações significativas na formação de recursos humanos. O Mestrado e o Doutorado recebem alunos novos regularmente duas vezes ao ano, através de seleções realizadas em fevereiro/março ou julho/agosto.

[SAIBA MAIS] [Único programa da América Latina](#)



instituto nacional de ciência e tecnologia

de Fármacos e Medicamentos

www.inct-inofar.ccs.ufrj.br

A recente criação da PG (M&D) em Farmacologia e Química Medicinal ilustra nova perspectiva de horizonte na PG da UFRJ, pois é a primeira com o perfil desta proposta interdisciplinar na AL.I

Eliezer J. Barreiro; 04/03/2010



Obrigado



UFRJ

Universidade Federal do Rio de Janeiro