Universidade Federal do Rio de Janeiro

Oportunidades em Inovação em Fármacos: INCT-INOFAR

a Brazilian network for drug design, discovery and development

LASSBio
Laboratório de Avaliação e Síntese de Substâncias Bioativas

FAPERJ

CNPq

Eliezer J. Barreiro

Professor Titular

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Projeto CNPq nº 573.564/2008-6 «» FAPERJ nº E-26/170.020/2008

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Summary

- *Prologue: a brief view of scientific research nowadays*
- *The complex drug design, discovery & development process (*D4*)*
- *The pharmaceutical innovation (radical & incremental)*
- *The actual role of the university in the D2 process*
- *The INCT-INOFAR: the mission*
- *The INCT-INOFAR: who are we?*
- *The INCT-INOFAR: what we did and do?*
- *Final remarks & Acknowledgments*

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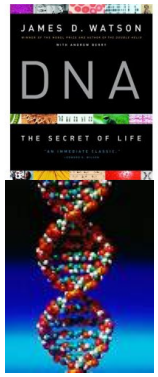
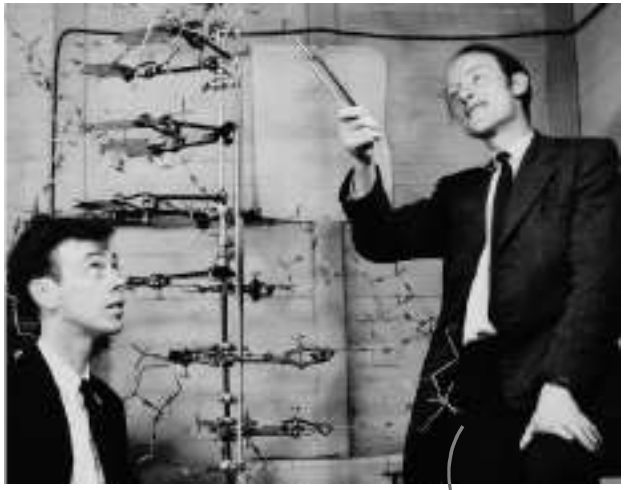
The scientific activity through the ages...

Galileo, Newton, Darwin, & Einstein





The physical Crick & the biologist Watson

JD Watson & FHC Crick, A Structure for Deoxyribose Nucleic Acid, *Nature* **1953**, *171*, 737–738 .

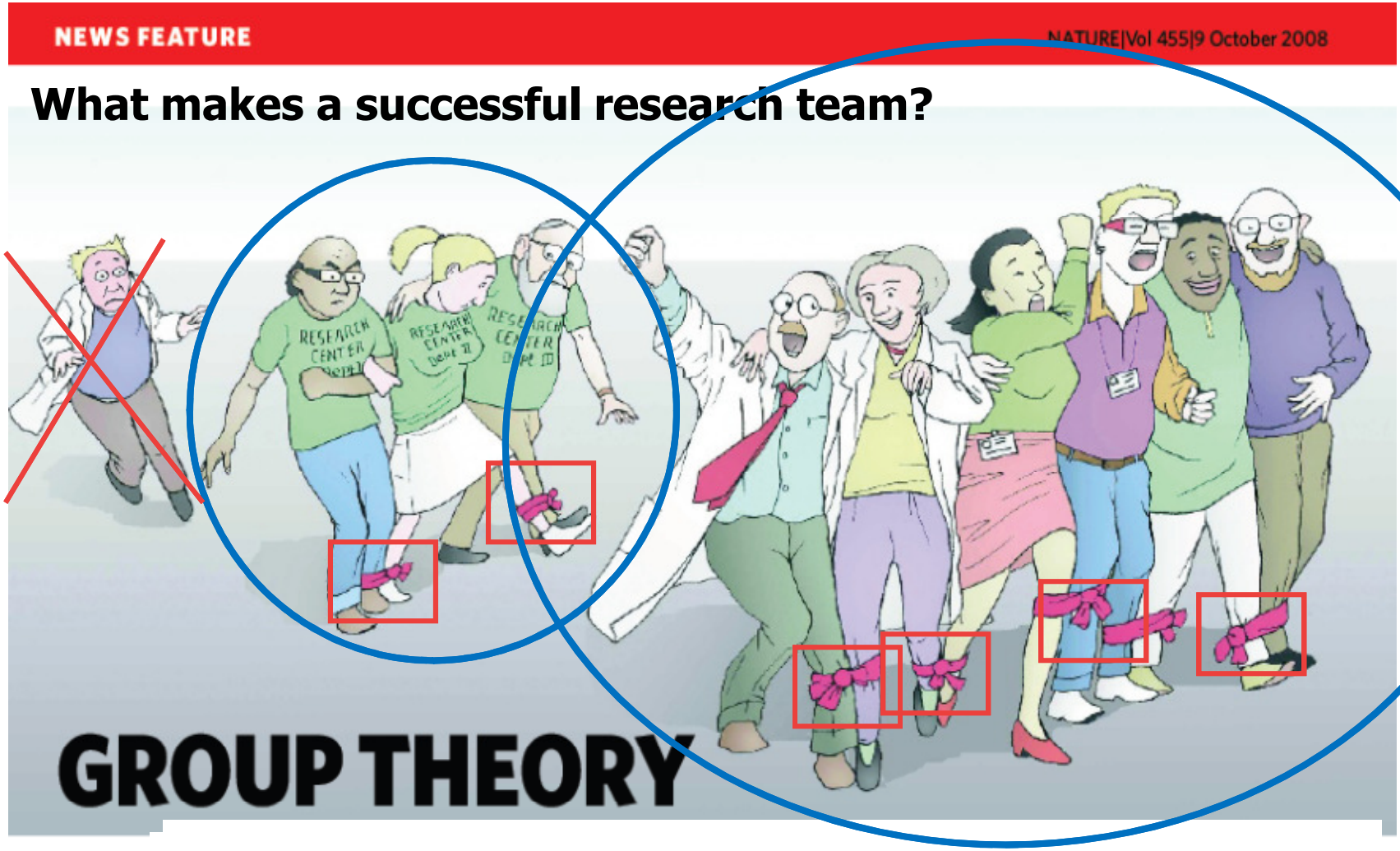
The human genome team

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, Kimmen 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

Science **2001** *291*, 1304-1351 [DOI: 10.1126/science.1058040]

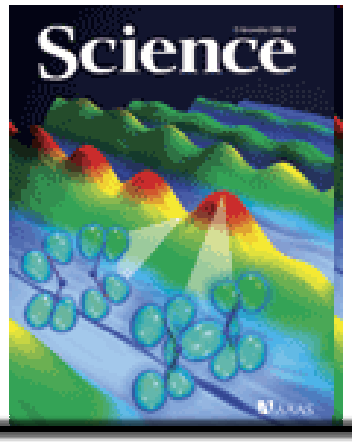
J. Whitfield, *Nature* **2008**, *455*, 720



M Armstrong, GM Murphy Jr, Invertorship & ownership considerations & pitfalls with collaborative research, *ACS Med Chem Lett* **2012**, *3*, 349; W Masona, D J Watts, Collaborative learning in networks, *PNAS* **2012**, *109*, 764; M Williams, Productivity Shortfalls in Drug Discovery: Contributions from the Preclinical Sciences?, *JPET* **2011**, *336*, 3; R Guimera, B Uzzi, J Spiro, L A N Amaral, Team Assembly Mechanisms Determine Collaboration Network Structure and Team Performance, *Science* **2005**, *308*, 697.

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

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

The authors demonstrate that scientific research in interdisciplinary teams has an impact on the quality of work, increasing the production of new knowledge really innovative.

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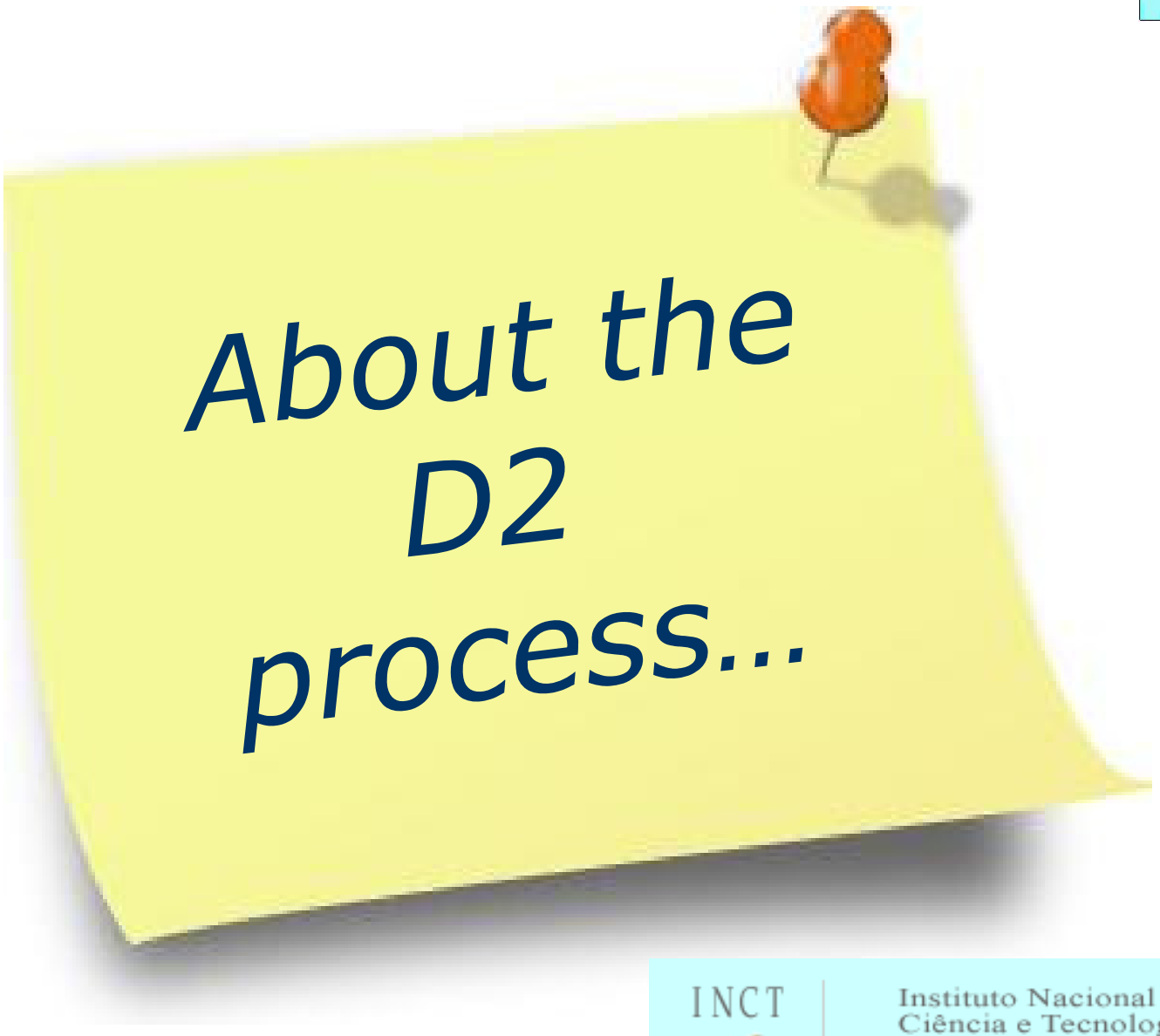

About the D2 process...

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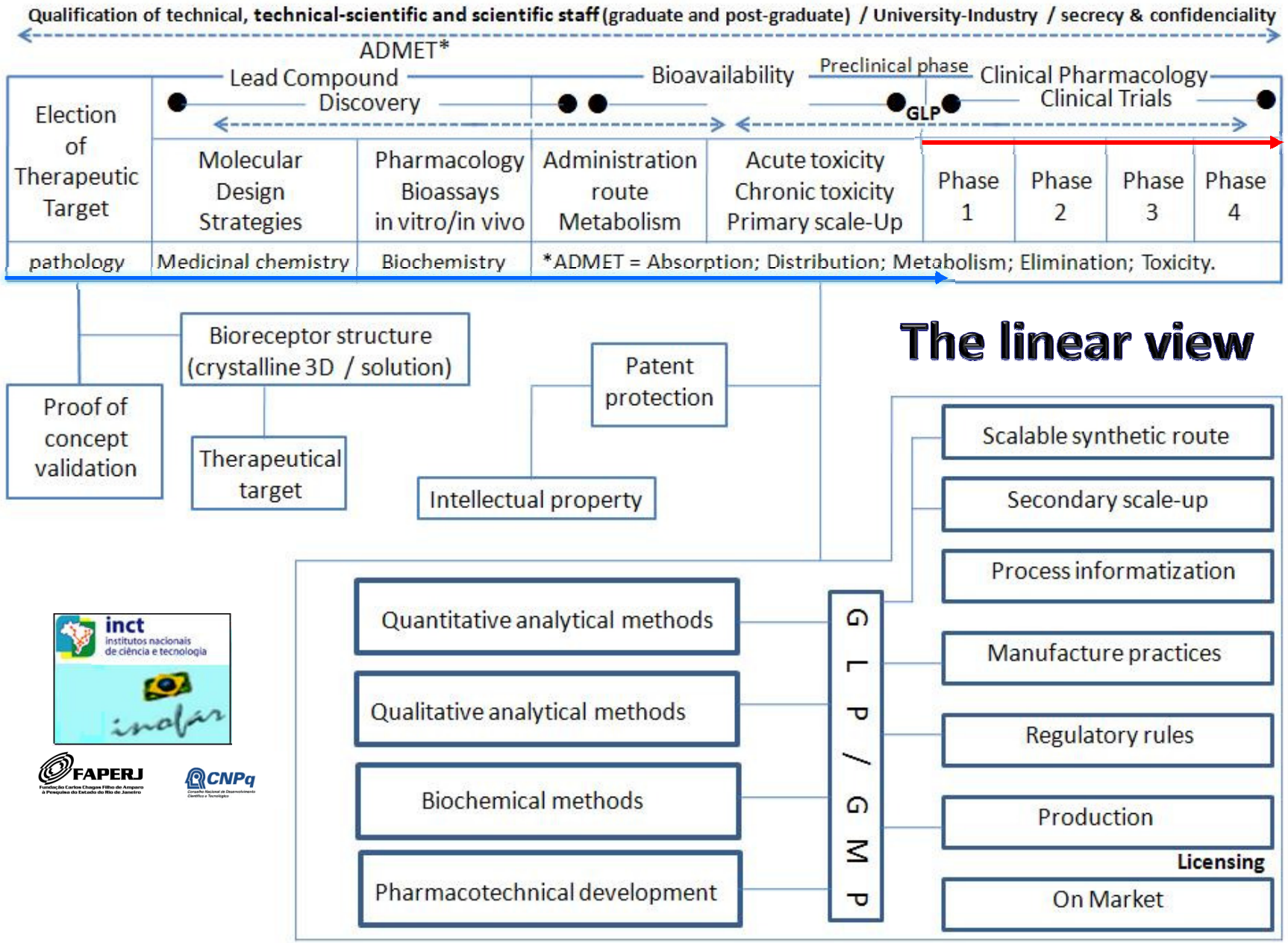
The drug discovery & development process



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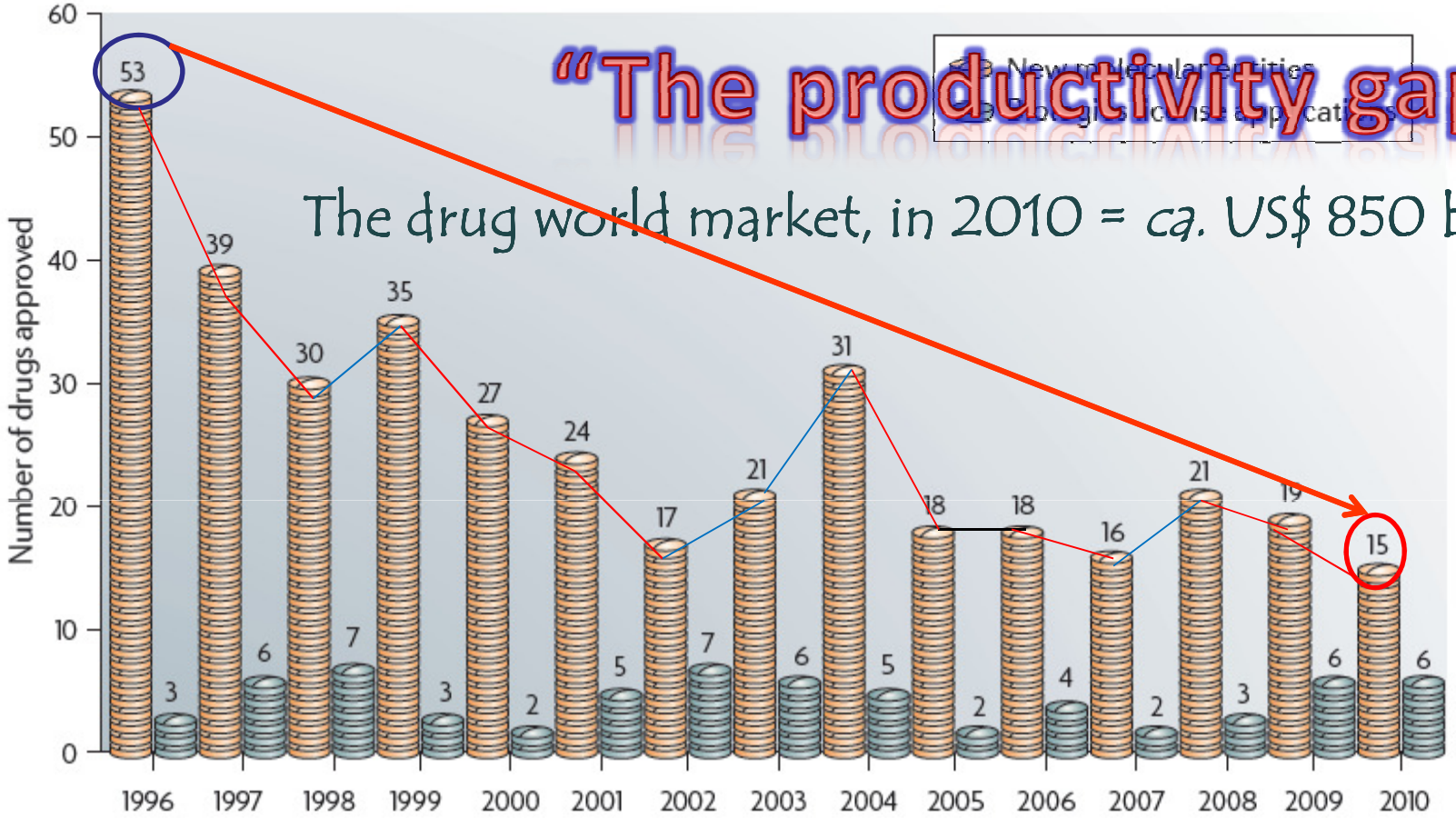
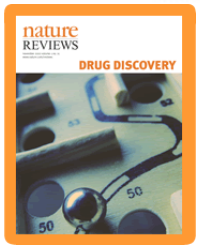
The *Big-Pharma* ...

JW Scannell *et al.*, Diagnosing the decline in pharmaceutical R&D efficiency, *Nature Rev. Drug Discov*. **2012,** *11*, 191; F Pammolli *et al*., The productivity crisis in pharmaceutical R&D, *Nature Rev. Drug Discov.* **2011**, *10*, 428; S M Paul *et al*. How to improve R&D productivity: the pharmaceutical industry's grand challenge, *Nature Rev. Drug Discov.* **2010**, *9*, 203; B Hughes, Harnessing open innovation, *Nature Rev. Drug Discov*. **2009**, *8*, 344; B Munos, Lessons for 60 years of pharmaceutical innovation, *Nature Rev. Drug Discov*. **2009**, *8*, 959.

The Big Pharma innovation crisis...





* A. Mullard, 2010 FDA drug approvals, *Nature Rev. Drug Discov*. **2011**, *10*, 82.

"In the 10-year period between 1999 and 2008, the FDA approved 183 small-molecule drugs..."*

* D Swinney & J Anthony, How were new medicines discovered? *Nature Rev. Drug Discov.* **2011**, *10*, 507.

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O mercado farmacêutico mundial atingiu US$ 860 bilhões em 2012.

World's top 15 pharmaceutical companies by 2016									
	Market Rank				Rx & OTC pharma sales ($bn)				
	2011	2012	2014	2016	2011	2012	2014	2016	CAGR 2011-16
Sanofi	3	1	1	1	47.9	51.6	55.4	58.4	4%
Novartis	2	2	2	2	49.5	49.9	52.2	54.8	2%
Pfizer	1	3	3	3	54.1	49.8	49.7	51.9	(1%)
GlaxoSmithKline	5	6	5	4	39.3	41.2	45.6	50.9	5%
Roche	6	4	4	5	39.1	44.1	46.3	49.0	5%
Merck & Co	4	5	6	6	42.1	41.9	41.4	43.4	1%
Johnson & Johnson	8	8	7	7	24.8	26.5	29.4	31.5	5%
AstraZeneca	7	7	8	8	32.0	29.2	27.5	25.7	(4%)
Teva	12	10	10	9	17.4	20.3	22.5	24.4	7%
Abbott Laboratories	9	9	9	10	22.5	23.5	23.7	24.3	2%
Bayer	11	12	11	11	18.9	19.7	21.7	23.4	4%
Takeda	14	13	12	12	17.0	18.2	18.7	20.2	3%
Bristol-Myers Squibb	13	16	17	13	17.1	14.2	15.4	18.9	2%
Novo Nordisk	17	17	15	14	12.3	13.6	16.4	18.9	9%
Eli Lilly	10	11	14	15	21.5	20.1	17.6	17.9	(4%)

Source: EvaluatePharma

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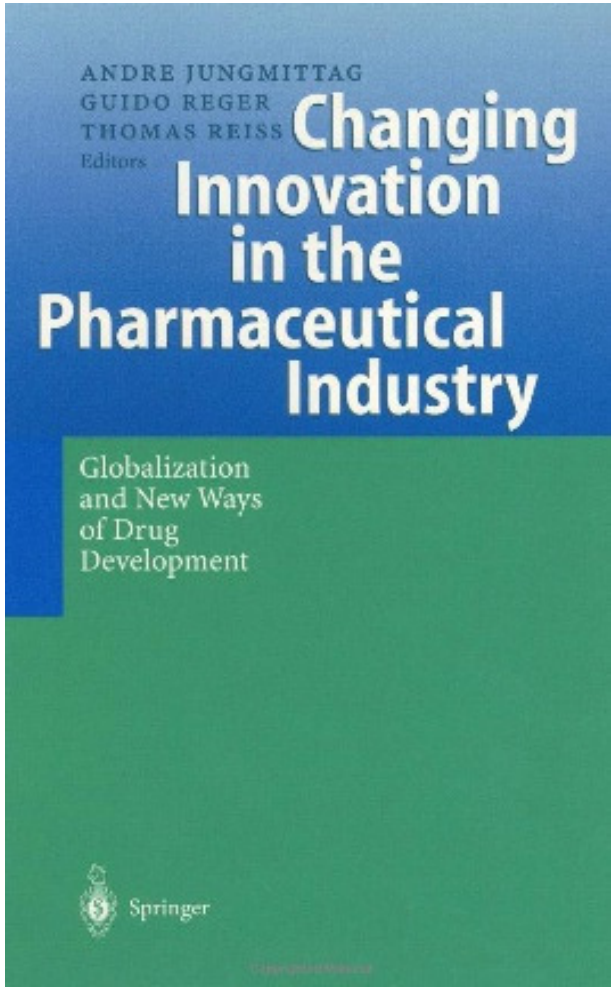

Technological innovation is a process most dynamic in industrial activity.
This dynamism is accentuated in <u>pharmaceutical innovation</u> which, more than any other, depends on the effective and productive interaction between <u>Science & Technology</u>.

The blockbuster sindrome...

IN FOCUS NEWS

2011

PHARMACEUTICALS

Traditional drug-discovery model ripe for reform

Academic researchers set to play much greater role in pharmaceutical development.

BY DANIEL CRESSEY

With drug pipelines running dry and a slew of blockbuster medicines about to lose patent protection, the voices arguing that the traditional drug-development process is too expensive and inefficient to survive are getting louder.

Employing thousands of in-house scientists to develop drug candidates from scratch has turned into a billion-dollar gamble that simply isn't delivering enough profitable products to market. Bernard Munos, founder of the Inno-Think pharmaceutical policy research group in Indianapolis, Indiana, is not alone in believing that the next three years "will probably see an implosion of the old model" of drug discovery.

So what comes next? Cutbacks, certainly: witness Pfizer's dramatic announcement early last month that it will soon close its research site at Sandwich, UK, and slice roughly US$1.5 billion from its proposed 2012 research and development spend (see *Nature* 470, 154; 2011).

HULTON-DEUTSCH/CORBIS

The kit may have improved, but the in-house drug discovery model has changed relatively little.

Nature 2011, 471, 17

" without a dramatic improvement in R&D productivity, the pharmaceutical industry cannot sustain ... innovation ..."
D Swinney & J Anthony, How, were new medicines discovered?, *Nature Rev. Drug Discov.* 2011, *10*, 507.

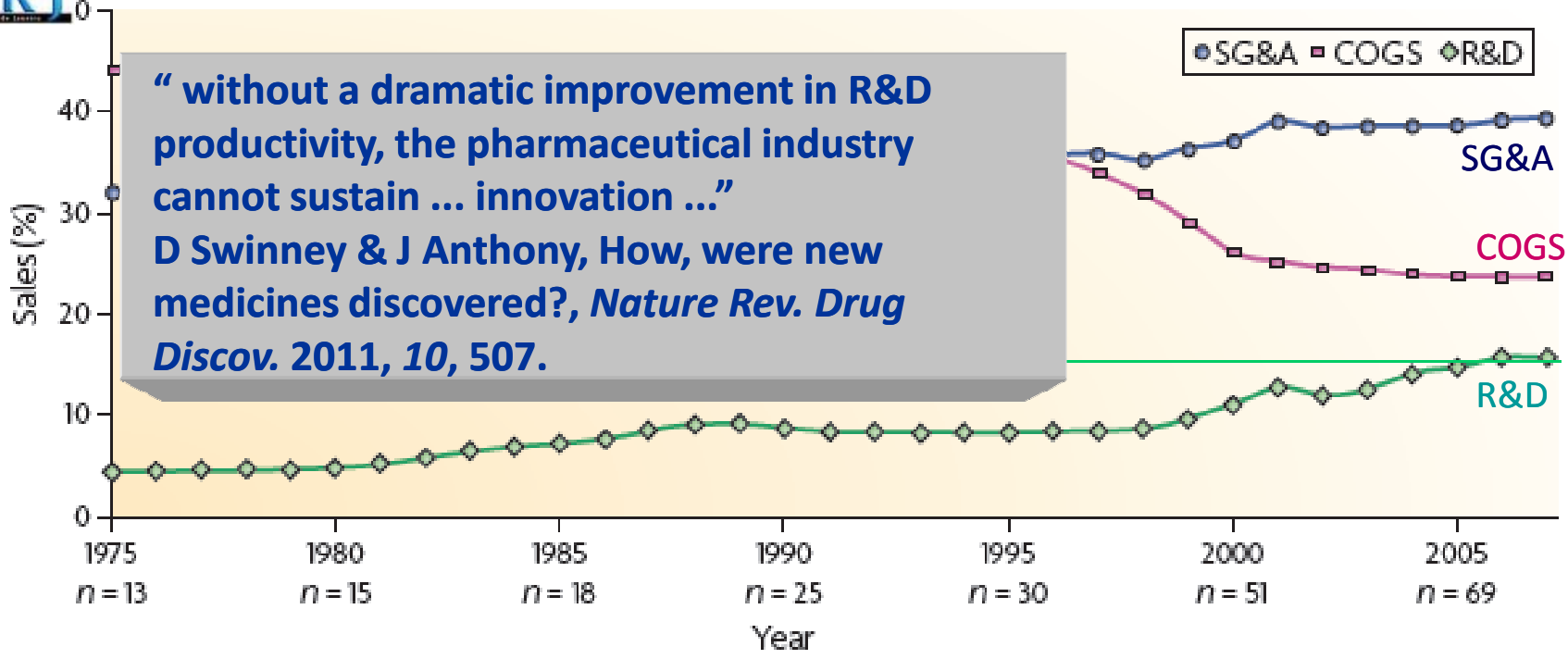

Figure 1 | **Trends in resource allocation to SG&A, R&D and COGS in the pharmaceutical industry: 1975–2007.** The figure plots median percentage of sales (smoothed). Investment in SG&A (sales, general and administrative costs) is shown in blue circles, COGS (costs of goods sold) is shown in pink squares and R&D (research and development) is shown in green diamonds.

- R&D. Research and development expenditures include raw materials and professional services used in R&D projects, salaries of R&D personnel, depreciation of infrastructure and cost of utilities committed for R&D purposes. R&D expenditures do not include costs of knowledge or formulas acquired from other companies.
- SG&A. Sales, general and administrative expenditures include costs of sales, promotions, customer support and training, marketing, advertising campaigns, public relations, distribution, sponsorships, general corporate activities and compensation of senior executives.
- COGS. Costs of goods sold include manufacturing costs such as raw materials, subcontractors, salaries of production labour, depreciation of machines, production lines and infrastructures, utilities, maintenance costs and other manufacturing costs.

D Weiss, P Naik, R Weiss, The 'big pharma' dilemma: develop new drugs or promote existing ones?, *Nature Rev. Drug Discov.* **2009**, *8*, 533.

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The drug discovery process...

2000

2004

...is completely scientific-based !.

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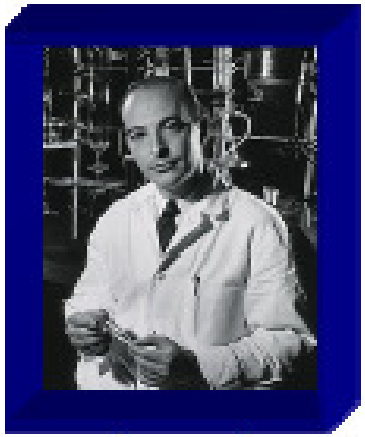
Nobel Prize, 1959



Arthur Kornberg
1918-2007

The Two Cultures: Chemistry and Biology[1]

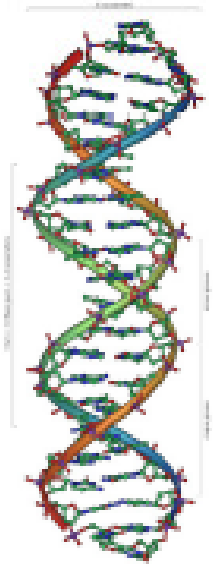
Arthur Kornberg
Department of Biochemistry, Stanford University, Stanford, California 94305

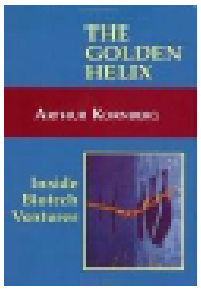
Received July 14, 1987

1959

1987

"Much of life can be understood in rational terms if expressed in the language of chemistry... the historical roots of **chemistry** *and* **biology** *are intertwined in many places...*





Pharmaceutical chemistry *was until recently the bastion of organic chemistry... in the search for alternative or superior drugs for the treatment of various diseases..."*

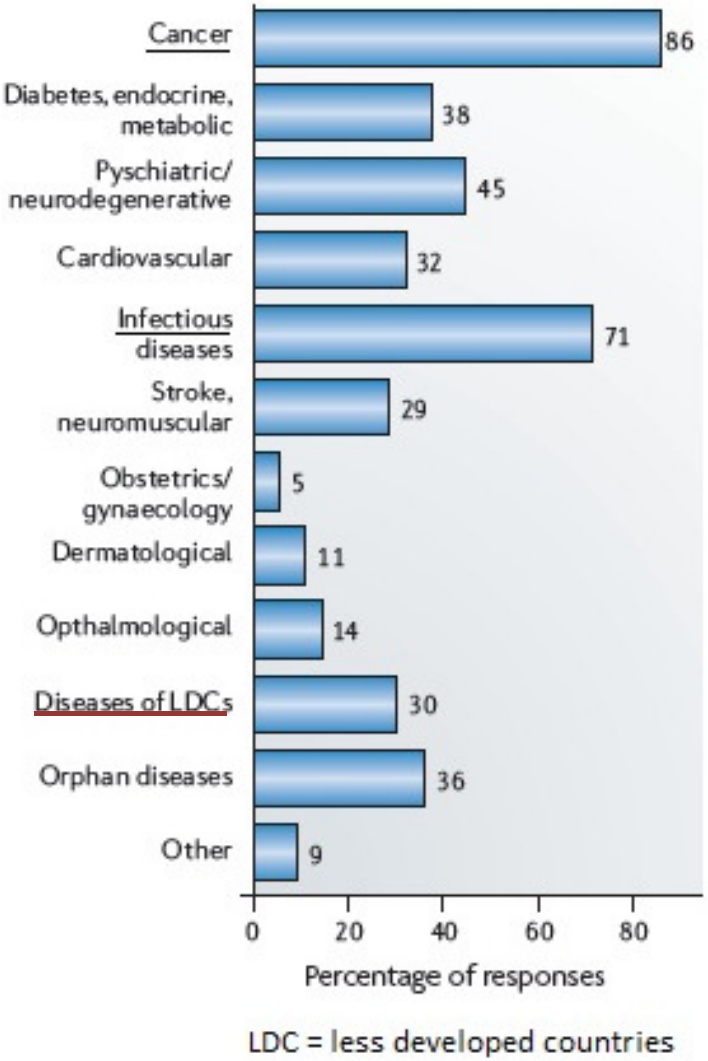
A. Kornberg, **Science and medicine at the millennium,** *Braz J Med Biol Res,* **1997**, *30*, 1379

Biochemistry 1987, *26*, 6888-6891

Interdisciplinarity

US academic drug discovery

Stephen Frye, Marina Crosby, Teresa Edwards and Rudolph Juliano

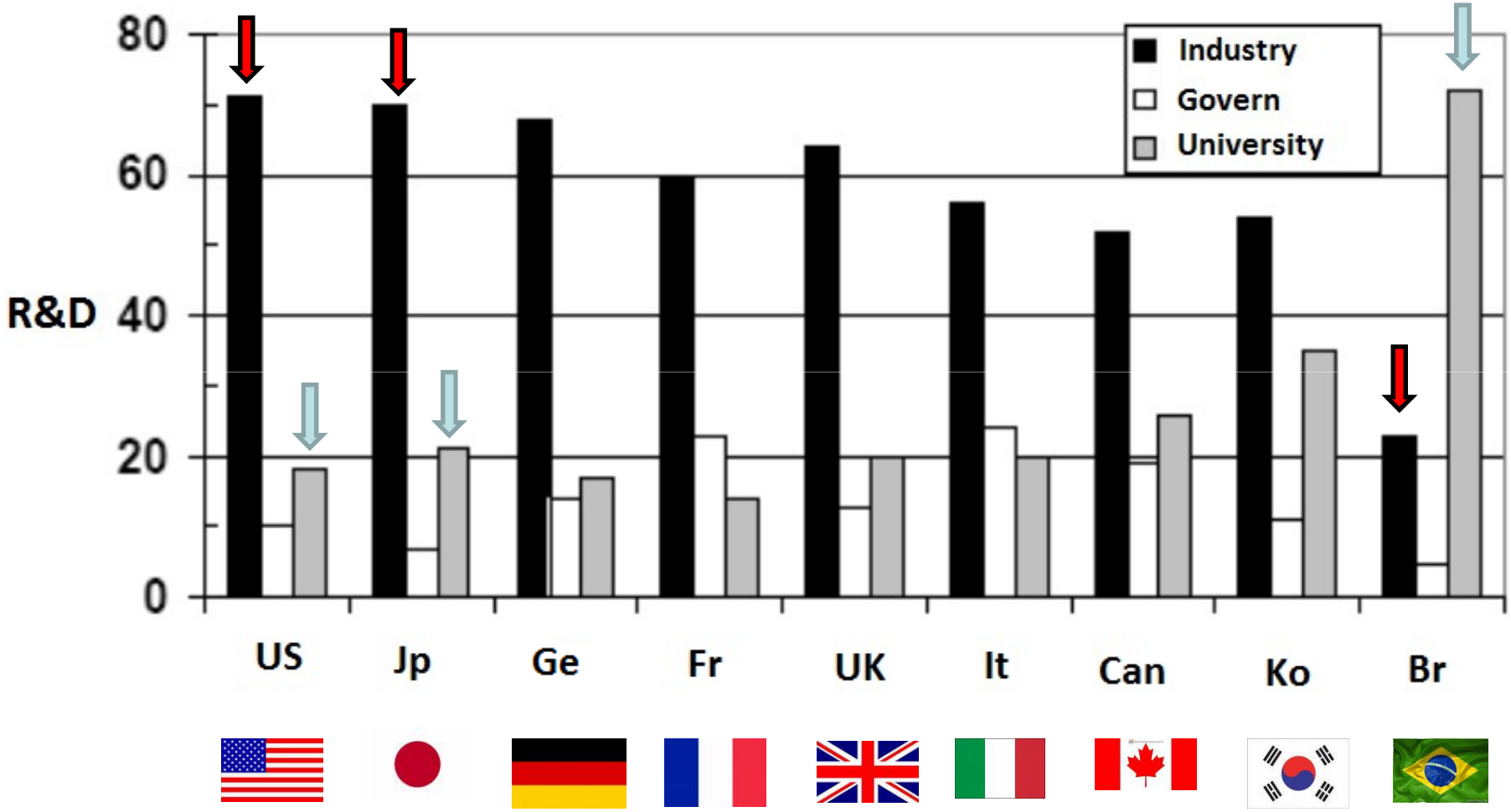


Nature Rev. Drug Discov. **2011**, *10*, 409

The authors identified 78 AI's involved in academic drug discovery (ADD): cancer (86%), infectious diseases (71%) and CNS (45%), metabolic & endocrine diseases (38%), orphan diseases (36%), cardiovascular (32%), diseases of less developed countries (30%)

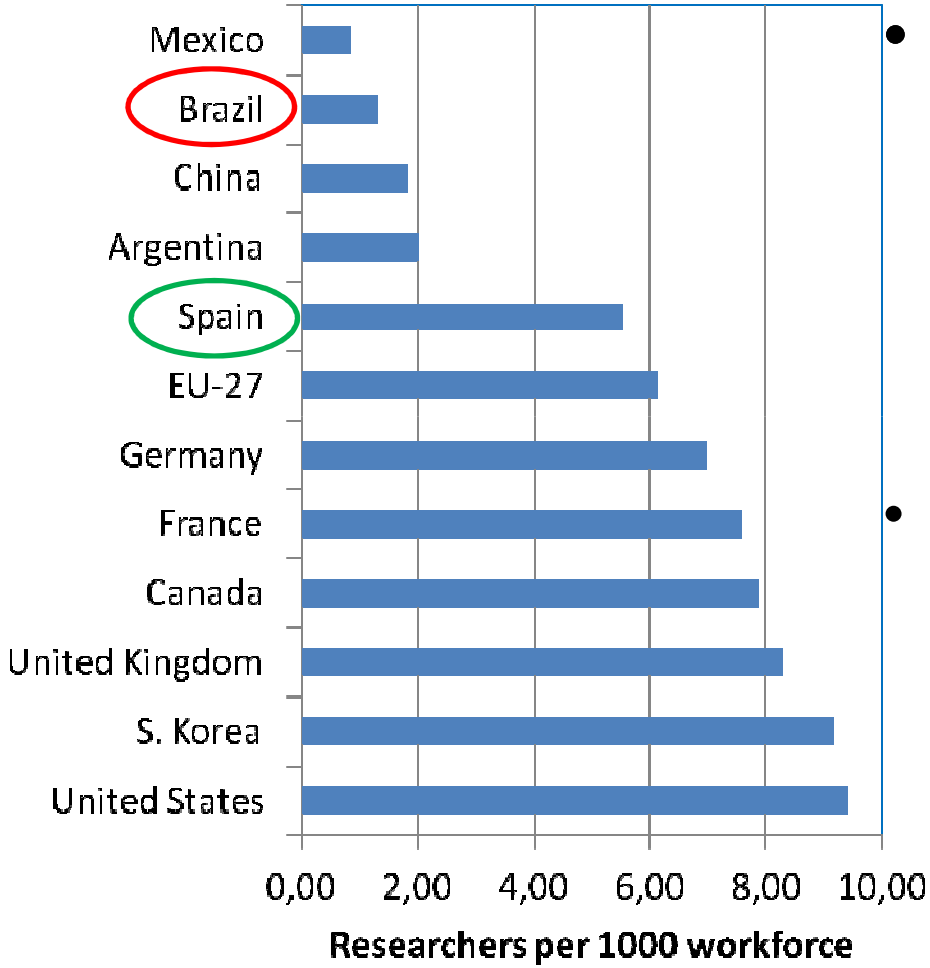
ADD → **Several targets: PK's, GPCR's**

The scientific manpower



Source: 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)

Densidade de pesquisadores no Brasil



- 133 mil pesquisadores no Brasil
  - 57% em universidades
  - 37% em empresas
    - PINTEC 2010 mostra diminuição do número de pesquisadores em empresas
- Pesquisadores ativos
  - Brasil tem
    - 1/3 da Espanha;
    - menos de 1/4 da Coréia

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The mission of INCT-INOFAR

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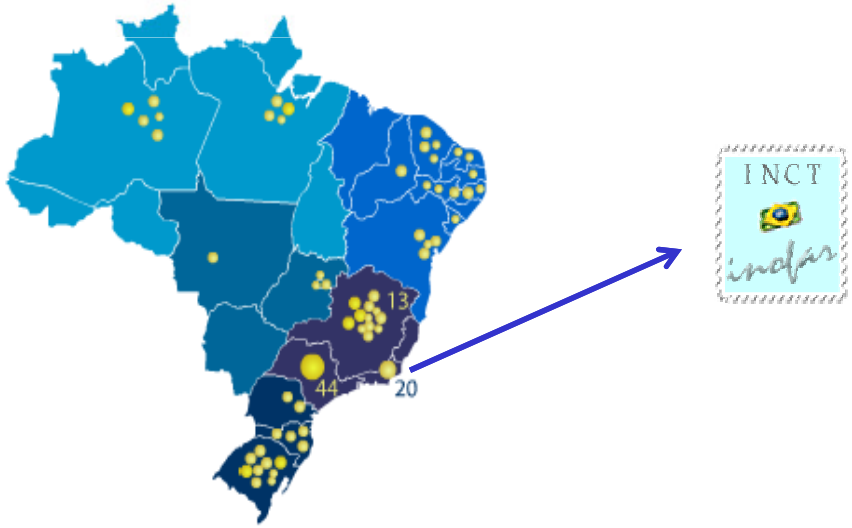
Apresentação



The National Institutes of Science and Technology (INCT's) program has ambitious and large goals in terms of mobilizing national effort of the best research groups in Brazil, acting at frontier and strategic areas of science to contribute for sustainable development of the country.

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English

CNPq FAPERJ

Project CNPq 573.564/2008-6

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- Home
- INCT-INOFAR
- Team
- Scientific adviser board (SAB)
- Research groups
- Research people
- Useful articles
- Publications
- Meetings
- Videos

The Mission

- Organize the Brazilian scientific capacity in an effective drug discovery network;
- Support multi-institutional research projects in drug discovery & design;
- Contribute to Brazilian radical & incremental innovation in new & generic drugs;
- Studies in total synthesis of generic drugs & advanced synthetic intermediates and starting materials;
- Contribute to continuous high qualification of students in medicinal chemistry & pharmacology;


Who are we?

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Governance committee

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Estudos de metabolismo

Análise Estrutural

Toxicidade em animais

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Formulações galênicas

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Projeto CNPq nº 573.564/2008-6 «» FAPERJ nº E-26/170.020/2008

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Radical *Inn*ovation

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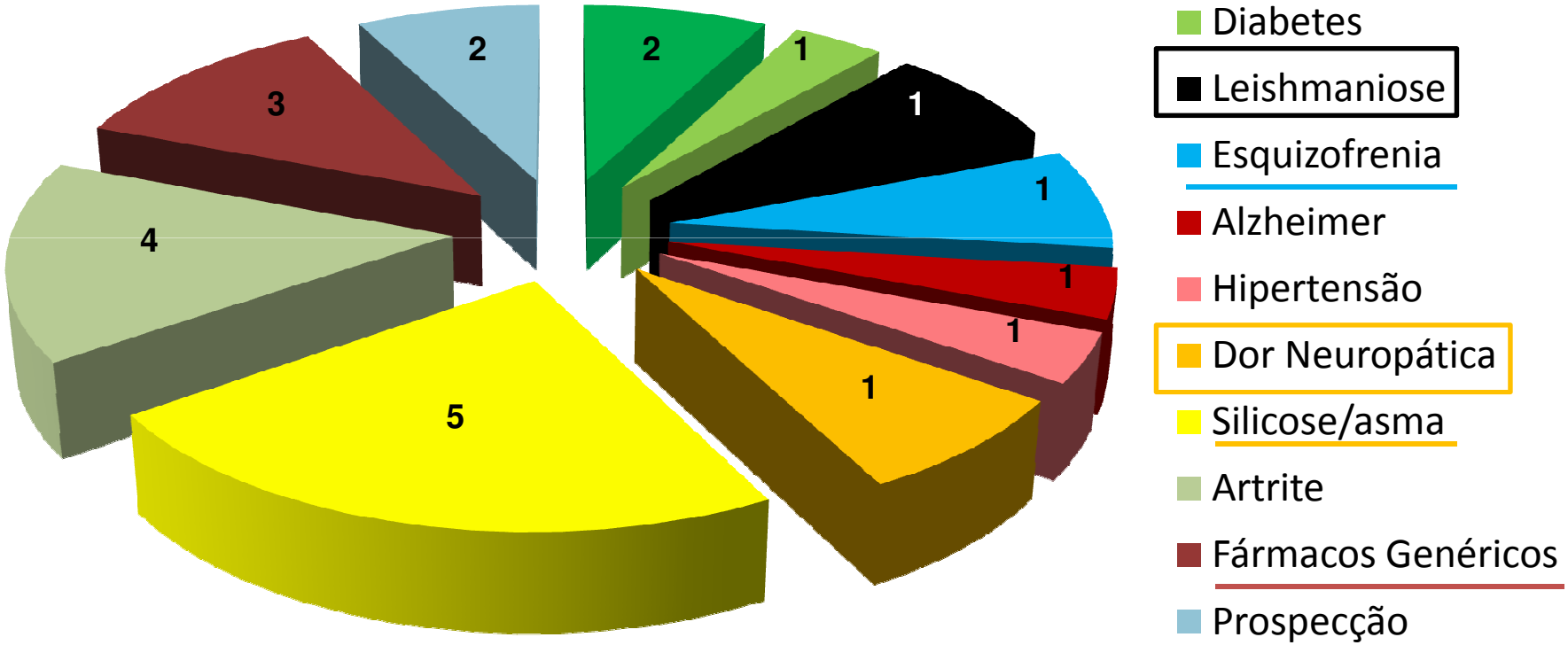
Sub-projetos



* Em destaque os subprojetos classificados como prioritários e *pipeline*

Radical Innovation

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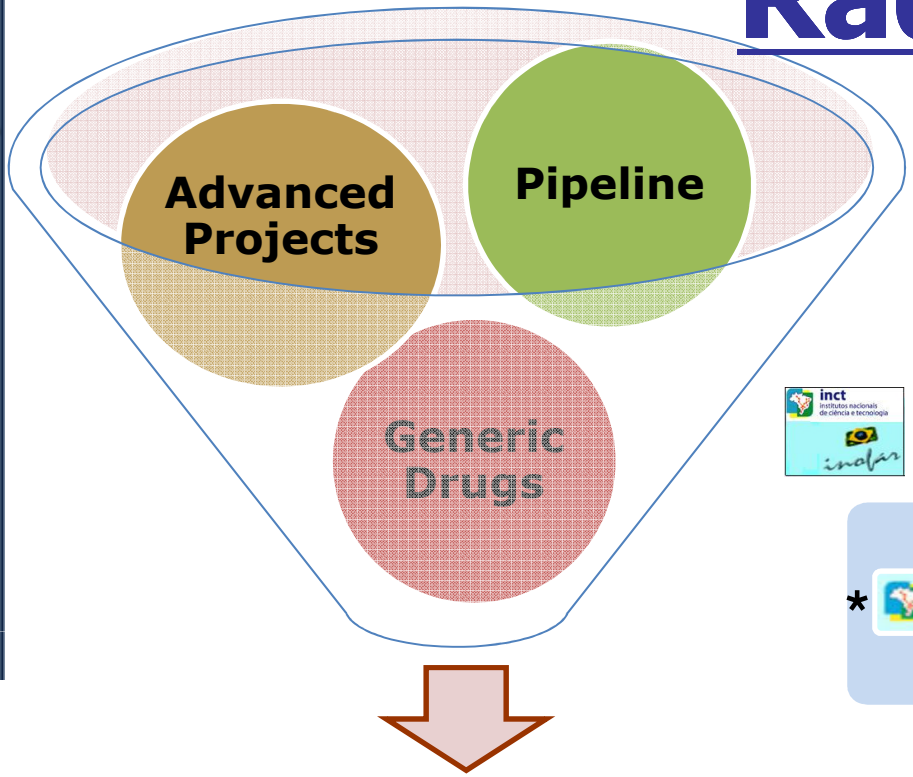

* Discovery of new antitumor drug candidates, analogs to combrestatin A4
(PCT/BR2013/000095)

* Evaluation of leishmanicide activity of a series of semicarbazone and hydrazine-*N*-acylhydrazone derivatives
(INPI BR102012 0190958)

* Pharmacological and toxicological evaluation of new drugs for the prevention and treatment of myocardiopathy and neuropathy caused by diabetes mellitus
(INPI BR102013 0126462)

03 projects classified as advanced*
03 projects classified as pipeline
03 generic drugs synthesized;
02 new generic synthesis in study;
02 projects discontinued ⇒ toxicity
01 project discontinued for lack of novelty;
03 academic projects concluded
projects with academic status;

Radical *Innovation*

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Study of the potential anti-inflammatory effect of LASSBio 897 compound, in silicosis and asthma models

Prof. Patrícia Machado R. Silva & Prof. Marco Aurélio Martins

FIOCRUZ – RJ

*Development of new antiasthmatic prototypes (LASSBio-596)**

Prof. Patricia Rieken Macedo Rocco

IBCCF-UFRJ

WO2012054996

Study of N-phenylpiperazine functionalized derivatives as prototypes for the development of new atypical antipsychotics

Prof. Stela Maris Kuze Rates*

FF-UFRGS & LASSBio-UFRJ

---

* 01 Tese de Doutoramento (Gilda Angela Neves, 2009, UFRGS); 02 Dissertações de Mestrado (Andresa H. Betti, 2009, UFRGS; Camila Boque antonio, 2011, UFRGS); 02 doutoramentos em andamento (UFRGS).

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Thaiana C F Mendes, Fernanda Antunes, Margarete M Trachez, Nailton M Nascimento Jr, Carlos A M Fraga, Eliezer J Barreiro, Gisele Zapata-Sudo, Roberto T Sudo,

Antihyperalgesic effects of a novel muscarinic agonist (*LASSBio-873*) in spinal nerve ligation in rats

Clinical and Experimental Pharmacology and Physiology, 40, 404–411 (2013)

Novo mecanismo de ação para controle da dor neuropática

Clinical and Experimental Pharmacology and Physiology (2013) **40**, 395–397 doi: 10.1111/1440-1681.12123

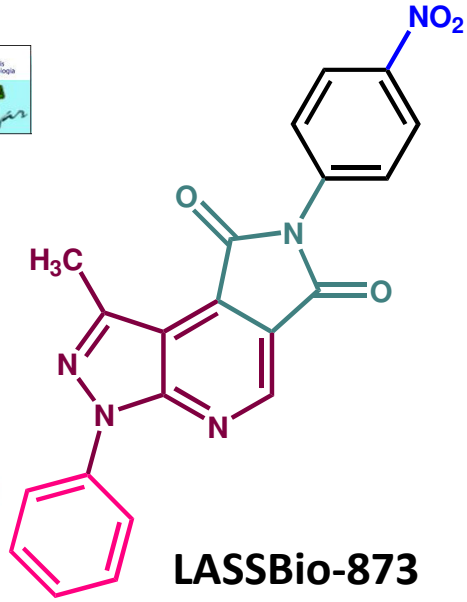
Muscarinic agonists in the treatment of neuropathic pain: a novel finding

EDITORIAL

Table 1 Antinociceptive effects of opioids, antidepressants, anticonvulsants, cannabinoid and muscarinic agonists in neuropathic pain models

Class	Compounds	Antinociception	Acute or chronic SNL	Route of administration	Reference
Opioids	Morphine	Yes	Acute	i.p.	4
	Morphine	Partial	Acute	i.t.	5
Tricyclic antidepressants	Amitriptyline	Yes	Chronic	i.p., i.t.	6
	Desipramine	Yes	Chronic	i.p.	7
	Desipramine	Yes	Acute	s.c.	8
Anticonvulsants	Gabapentin	Partial	Acute	i.t.	5
	Gabapentin	Yes	Chronic	i.t.	9
	Gabapentin	Yes	Chronic	i.t.	10
Cannabinoid agonist	MDA7 (CB_2 agonist)	Yes	Acute	i.p.	12
	MDA19 (CB_2 agonist)	Yes	Acute	i.p.	13
	A-836339 and AM1241 (CB_2 agonists)	Yes	Acute	intra-DRG, i.t.	14
Muscarinic agonist	LASSBio-873	Yes	Acute, chronic	p.o.	15

SNL, spinal nerve ligation; DRG, dorsal root ganglion.



LASSBio-873

Portal DockThor

Um Servidor Web Gratuito para Docking Proteína-Ligante

Isabella A. Guedes, Eduardo Krempser, Diogo Marinho, Camila S. de Magalhães & Laurent E. Dardenne

Laboratório Nacional de Computação Científica – LNCC/MCTI

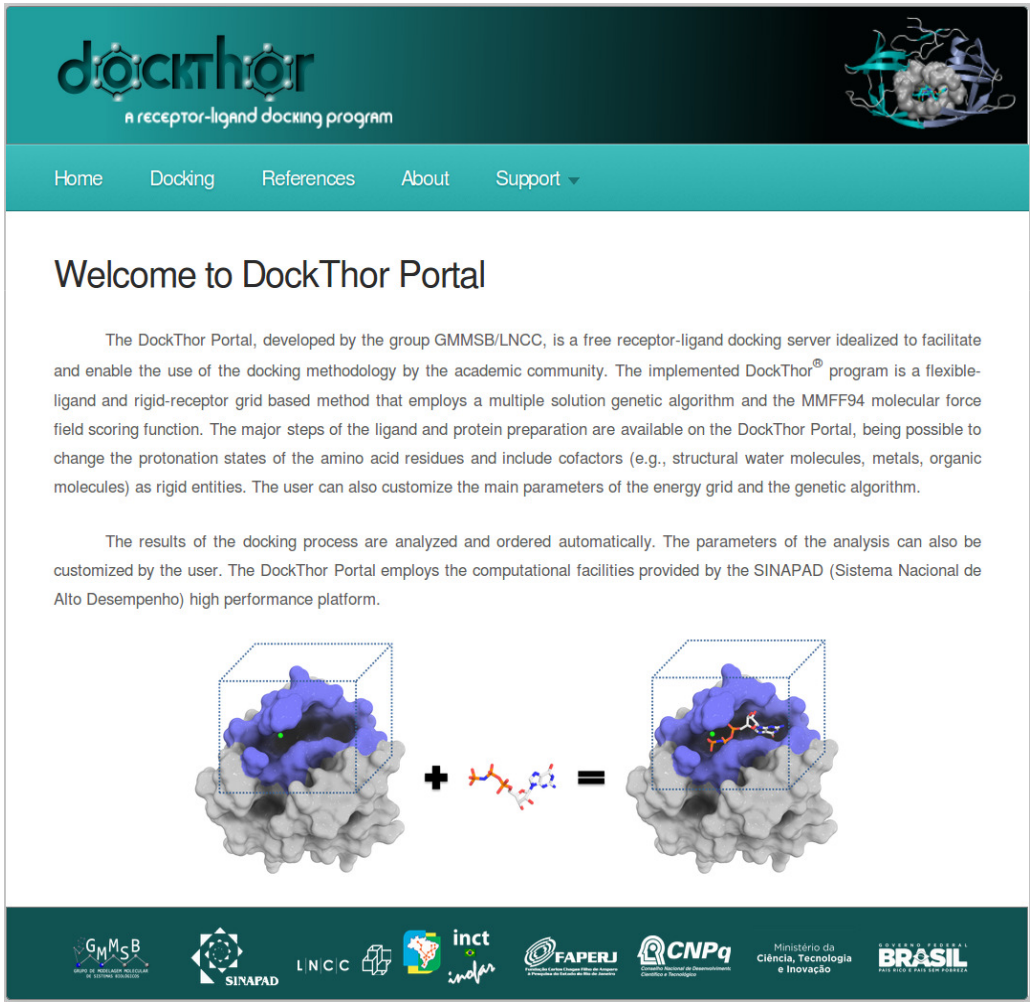
Universidade Federal do Rio de Janeiro

INPI Software Registration Number 13318-3

www.dockthor.lncc.br

DockThor Portal is a free ligand-receptor docking server developed by the GMMSB/LNCC group with the aim of facilitate and enable the use of the program by the academic community using the computational facilities provided by the SINAPAD high performance platform.

dockthor@lncc.br



Incremental *Innovation*

Generic drugs*

In Brazil the market of generic drugs is *ca*. US$ 18 bi (2011)

Active pharmaceutical ingredients (API's)

"The art is to select [generics] that will be winners *versus* ones where there will be enormous competition."

M McCoy, Generic Drugs, *C&EN* **2002** (#13) *80*, 23

Incremental *Innovation*

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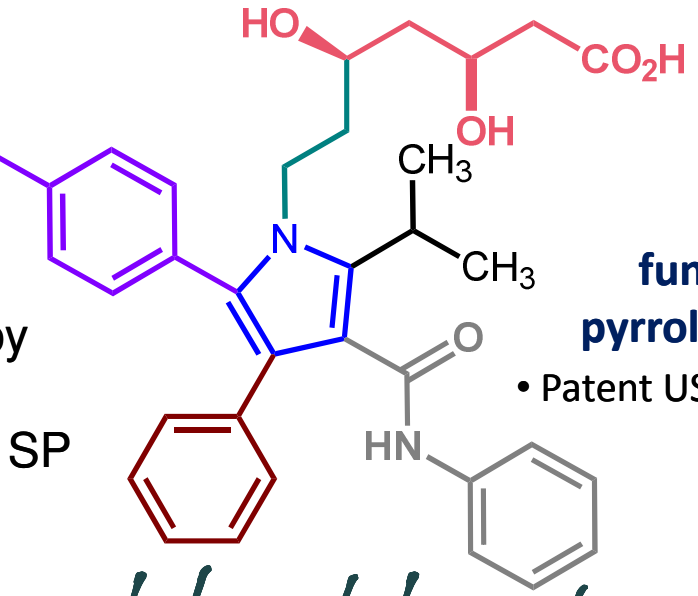
• Atorvastatin

1991 Lipitor™



functionalized pyrrolheptenoic acid

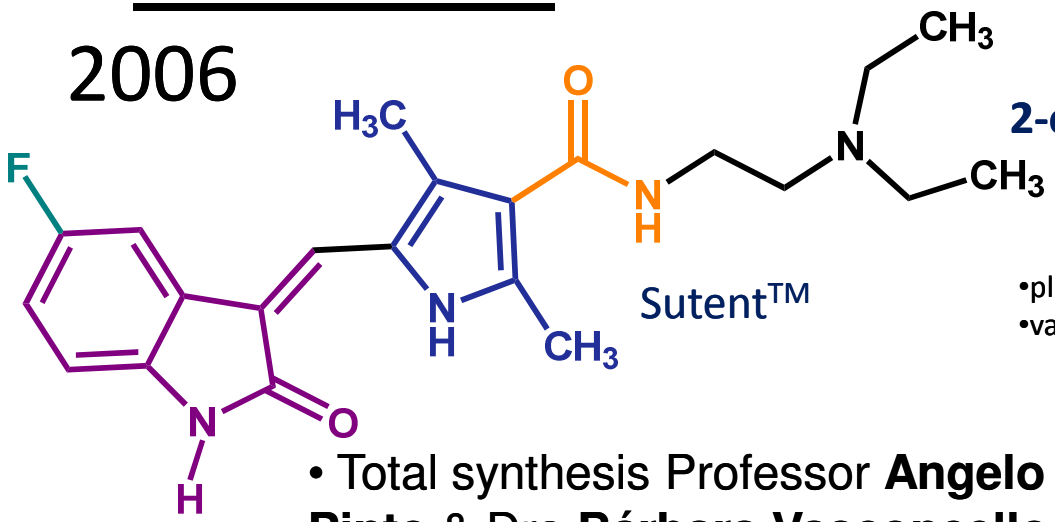
• Patent US 5273995 Pfizer (1991)

•HMGCoAR

• New stereoselective synthesis by Professor **Luiz Carlos Dias** & Dr **Adriano S. Vieira**, UNICAMP, SP (2010) – INPI Patent, 2011 (BR)

• Sunitinib *super blockbuster-drug*

2006



Sutent™

functionalized 2-oxo-1*H*-indol -1*H*-pyrrole-3-carboxamide

*Patent US 7211600 (2001)

•platelet-derived growth factor receptor (PDGF-Rs)
•vascular endothelial growth factor receptor (VEGFRs),

• Total synthesis Professor **Angelo da Cunha Pinto** & Dra **Bárbara Vasconcellos da Silva** UFRJ, RJ (**2011**) (BR)

Total sales of tinibs in US market:

ca.US$ 18,5 bi (2009)

República Federativa do Brasil
Ministério do Desenvolvimento, Indústria
e do Comércio Exterior
Instituto Nacional da Propriedade Industrial

(21) **PI0806985-9 A2**

BRPI0806985A2

(22) Data de Depósito: 16/10/2008
(43) Data da Publicação: 21/09/2010
(RPI 2072)

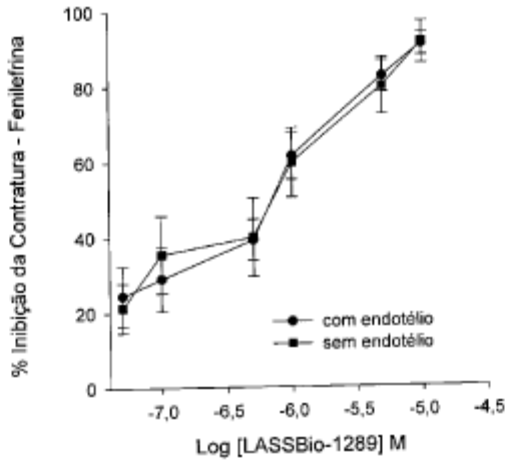
(51) Int.Cl.:
C07D 409/14
A61K 31/381
A61P 9/10
A61P 9/12
A61P 15/10
A61P 21/02

(54) Título: **DERIVADOS N-ACILIDRAZÔNICOS, PROCESSO DE PRODUÇÃO DE COMPOSTOS N-ACILIDRAZÔNICOS, COMPOSIÇÕES FARMACÊUTICAS CONTENDO OS MESMOS, USOS E MÉTODOS DE TRATAMENTO**

(73) Titular(es): Universidade Federal do Rio de Janeiro

(72) Inventor(es): Arthur Eugen Kümmerle, Carlos Alberto Manssour Fraga, Eliezer Jesus de Lacerda Barreiro, Gisele Zapata Sudo, Hellen Jannisy Vieira Beiral, Roberto Takashi Sudo

(57) Resumo: DERIVADOS N-ACILIDRAZÔNICOS, PROCESSO DE PRODUÇÃO DE COMPOSTOS N-ACILIDRAZÔNICOS, COMPOSIÇÕES FARMACÊUTICAS CONTENDO OS MESMOS, USOS E MÉTODOS DE TRATAMENTO. A presente invenção se refere aos compostos N-aciiidrazônicos, capazes de promover relaxamento da musculatura lisa vascular a partir da ativação da biossíntese de óxido nítrico (NO), que obedecem à fórmula geral (1): bem como, a presente invenção também se refere a seu processo de obtenção, composições farmacêuticas contendo os mesmos, seus usos e métodos de tratamento de disfunções relacionadas a síntese do NO em mamíferos humanos e não humanos, bem como, no tratamento de distúrbios musculares.



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Drug Discovery Today • Volume 14, Numbers 1/2 • January 2009 07 October 2009 vol 1, issue 1, 95-101 REVIEWS

Open innovation

Drug discovery: new models for industry–academic partnerships

Cathy J. Tralau-Stewart, Colin A. Wyatt, Dominique E. Kleyn and Alex Ayad

Drug Discovery Centre and Business Development, Imperial College London SW7 2AZ, UK

The re-focusing of pharmaceutical industry research away from early discovery activities is stimulating the development of novel models of drug discovery, notably involving academia as a 'front end'. In this article the authors explore the drivers of change, the role of new entrants (universities with specialised core facilities) and novel partnership models. If they are to be sustainable and deliver, these new models must be flexible and properly funded by industry or public funding, rewarding all partners for

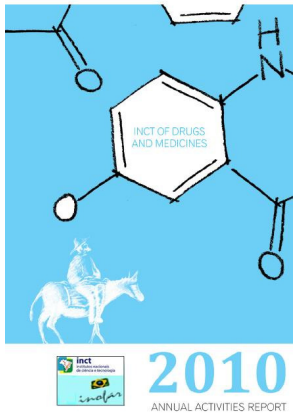
---

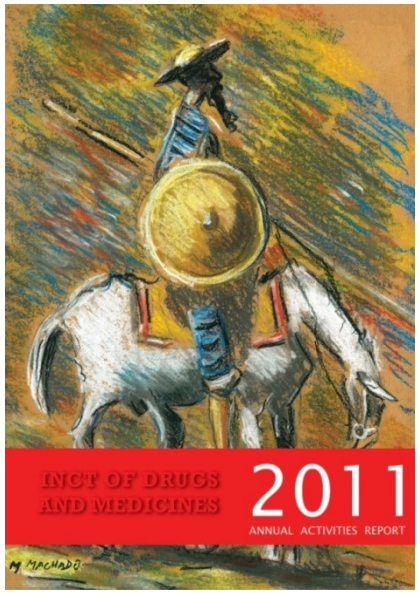
AJ Stevens *et al.,* The role of public-sector research in the discovery of drugs and vaccines. *N. Engl. J. Med.* **2011**, *364*, 535; R Kneller, The importance of new companies for drug discovery: origins of a decade of new drugs. *Nature Rev. Drug Discov.* **2010**, *9*, 867; MR Barnes *et al*., Lowering industry firewalls: pre-competitive informatics iniciatives in drug discovery, *Nature Rev. Drug Discov.* **2009**, *8*, 701; PG Wyatt, The emerging academic drug-discovery sector. *Future Med. Chem.* **2009**, *1*, 1013.

Avanço do estado da arte

Annual Activities Report

(Relatórios públicos)





www.inct-inofar.ccs.ufrj.br/download/aar/2009.pdf
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www.inct-inofar.ccs.ufrj.br/download/aar/2012.pdf

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Outreach activities of INCT-INOFAR

www.inct-inofar.ccs.ufrj.br

CNPq FAPERJ

Cartilhas

Cartilha sobre o Uso Correto dos Antibióticos - INCT-INOFAR

» **Versão site Anvisa**
» **Versão Impressa** *(.pdf)*
» **Versão Vídeo**

Cartilha "*Mandamentos do Uso Correto de Medicamentos*"

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» ***Download Cartilha Animada***

INCT

Divulgação Científica e Educação em Saúde

INCT-INOFAR lança publicação para divulgar suas ações de popularização da Ciência e Saúde

ESCOLA DE VERÃO em Química Farmacêutica & Medicinal

Atividade de extensão universitária

RVQ **Revista Virtual de Química 2012, vol. 4, número 1**

Universidade Federal do Rio de Janeiro

The INCT-INOFAR team

INCT-INOFAR, 6th Evaluation Meeting

Rio de Janeiro, RJ (BR)

May 15 & 16 , 2012

Final remarks & *Acknowledgements*

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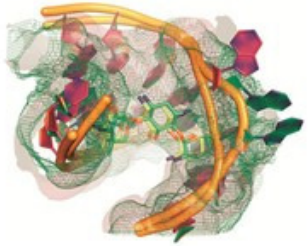
Concluding remarks

ACS Medicinal Chemistry Letters



Drug Discovery in an Academic Setting: Playing to the Strengths

Donna M. Huryn*

Department of Pharmaceutical Sciences, University of Pittsburgh, 712 Salk Hall, 3501 Terrace Street, Pittsburgh, Pennsylvania 15261, United States

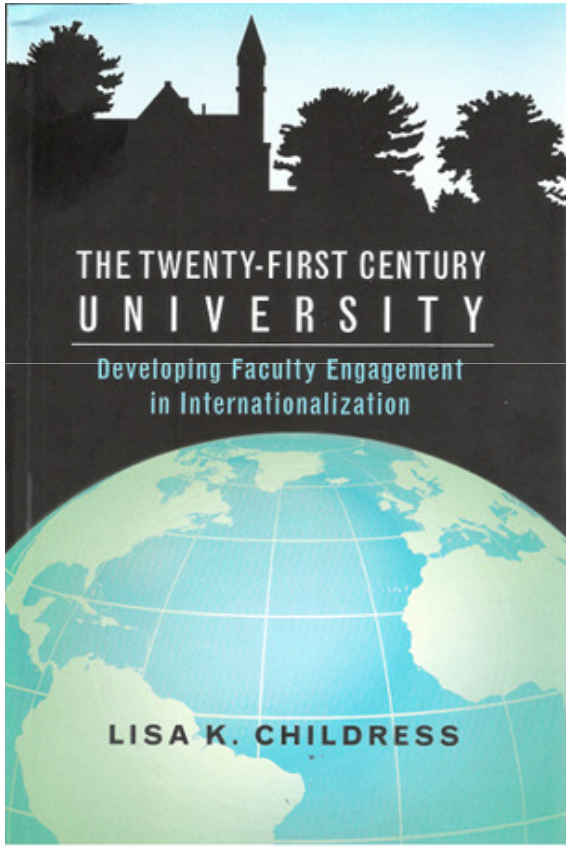
The Penn Center for Molecular Discovery

medicinal chemistry

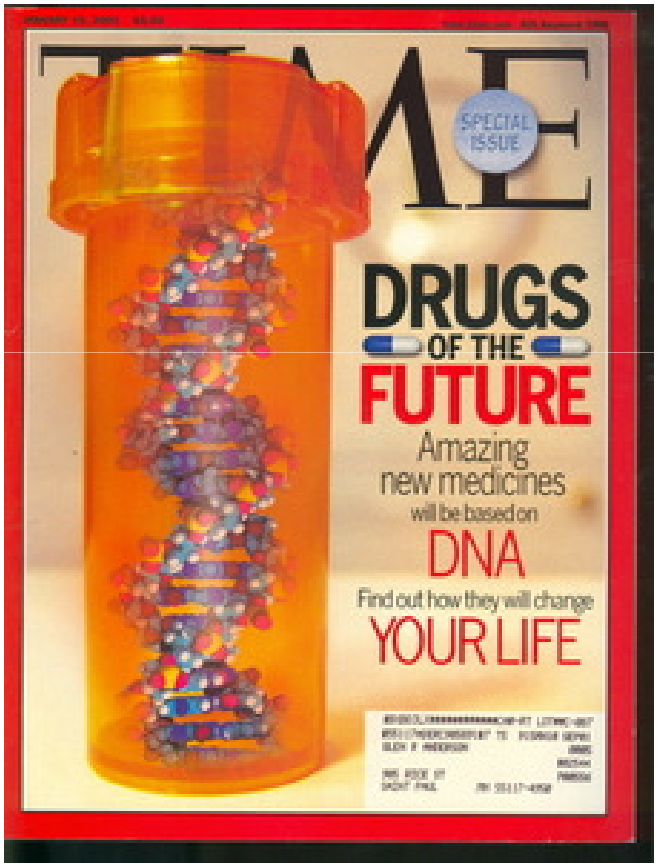
" Without a doubt, a university has a number of unique characteristics that could contribute to making it an ideal enviroment where drug discovery & medicinal chemistry activities can thrive....There is no doubt that academia can play an important role in drug discovery"

ACS Med. Chem. Lett. **2013**, *4*, 313

The twenty-first century university



The George Washington University



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http://ejb-eliezer.blogspot.com

De fármacos e suas descobertas

Pretende-se tratar de temas, opiniões, comentários sobre a Ciência dos Fármacos, seu uso seguro e benefícios. Aspectos da formação qualificada de universitários e pós-graduandos nas Ciências dos Fármacos também são de interesse.

sábado, 6 de julho de 2013

As estruturas químicas e os recursos para desenhá-las

*Relendo um artigo de divulgação científica publicado este ano, me deparei com alguns argumentos centrais do autor, sobre o avanço tecnológico que se observou na difusão da informação, com inúmeros novos recursos, além das redes sociais, capazes de distribuí-la eficiente e rapidamente. Não sei bem porque, fiz um link com a evolução que acompanhei no desenho das estruturas químicas de compostos orgânicos desde aquelas dos triterpenos tetracíclicos do tipo damarano de minha dissertação de mestrado, concluída em 1973, até as últimas, representadas em recente publicação oriunda do **LASSBio**. Achei que poderia ser interessante como leitura, o registro da evolução dos recursos para o desenho das estruturas químicas dos compostos orgânicos, que testemunhei, daquela época até hoje.*

Total de visualizações de página

27,632

www.ejb-eliezer.blogspot.com

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Obrigado

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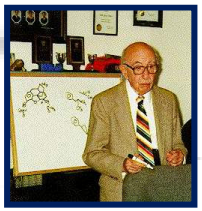
"...The unprecedented increase in human life expectancy, which has almost doubled in a hundred years, is mainly due to drugs and to those who discovered them."



Alfred Burger

In "The practice of medicinal chemistry", Wiley, 1970, p 4

Brazil

- *ca*. population of 196.6 million (01/07/2011)
- Immense natural resources (light oil pre-salt, biodiversity plant, conventional natural gas or not, minerals (iron, bauxite)) …
- *ca.* 8% of the world's drinking water
- Since 2006 self-sufficient in oil production
- World leader in the production of alcohol from sugar cane
- Major exporter of soybeans, beef, chicken and sugar
- Has an energy matrix (*ca*. 97%) produced sustainably…
- … has its economy based on commodities ! ! !
- It is necessary to change and take a technological leap.

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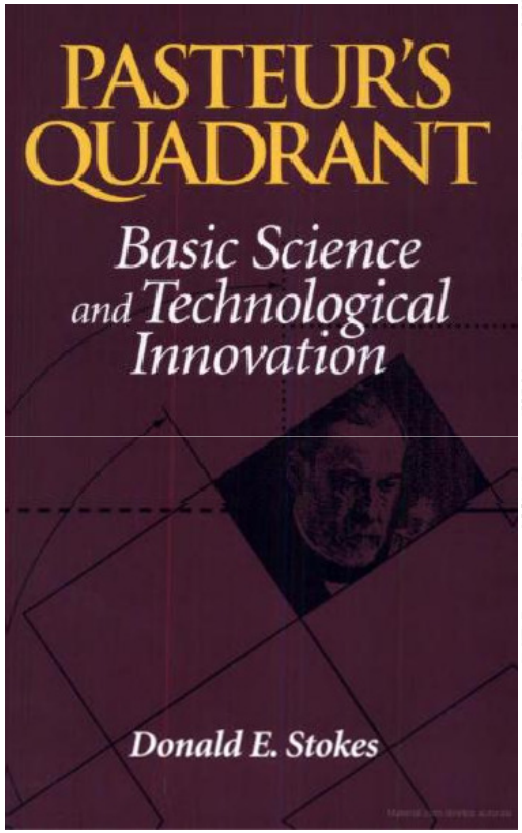
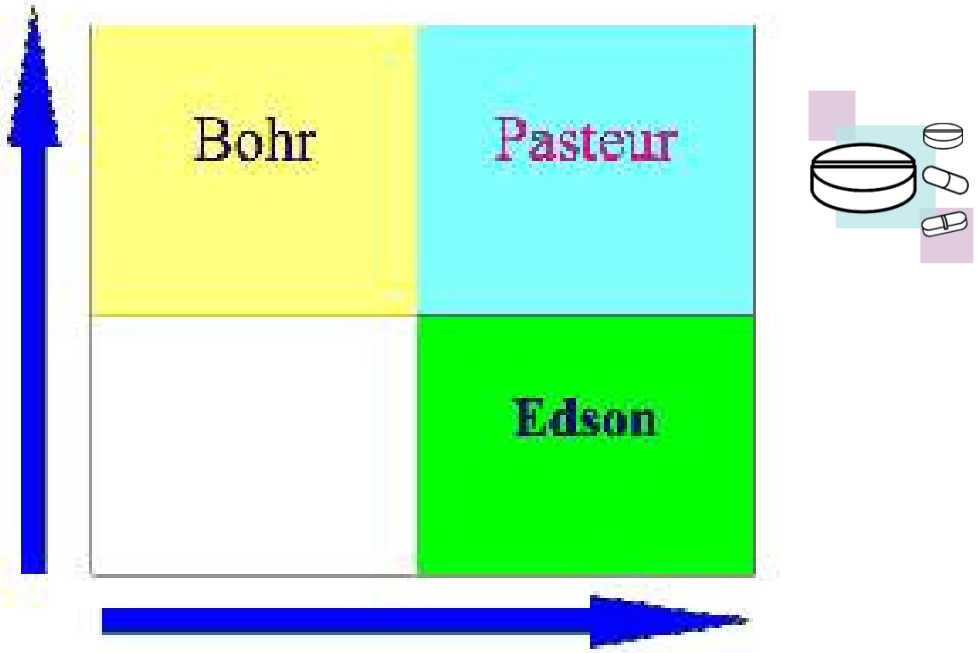
The knowledge generation





D. E. Stokes; Pasteurs Quadrant: Basic Science and Technological Innovation, Book News, Inc., Portland, EUA, 1999.

M. Gibbons *et al*., The new production of knowledge: the dynamics of science & research in contemporary societies, SAGE, London, 1994.

Aspectos da indústria farmacêutica mundial

- a **indústria farmacêutica** é ***intensiva*** em pesquisa➡ **inteligência** estratégica;
- força de trabalho com ***postos*** **qualificados**;
- padrão de **competição** = ***n*ovos fármacos**;
- **inovação tecnológica**, **com** ***investimentos*** **em** pesquisa e **desenvolvimento** (~ 8-10%);
- intensa **atividade** de ***propriedade***

Envisioning a Path to the Future

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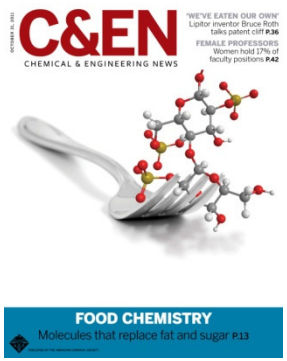
BRIC (SA)

India's Sun Pharma, Vadodara



INDIA PERSEVERES AS DRUG DISCOVERER

Despite setbacks, the country's drug companies continue to pursue **HOMEGROWN COMPOUNDS**

AMRUTHANAND NAIR, C&EN CONTRIBUTING EDITOR, MUMBAI

WWW.CEN-ONLINE.ORG 22 OCTOBER 31, 2011

XX Reunião Anual de Avaliação LASSBio, Barra Nova, Saquarema, RJ, dez 2012.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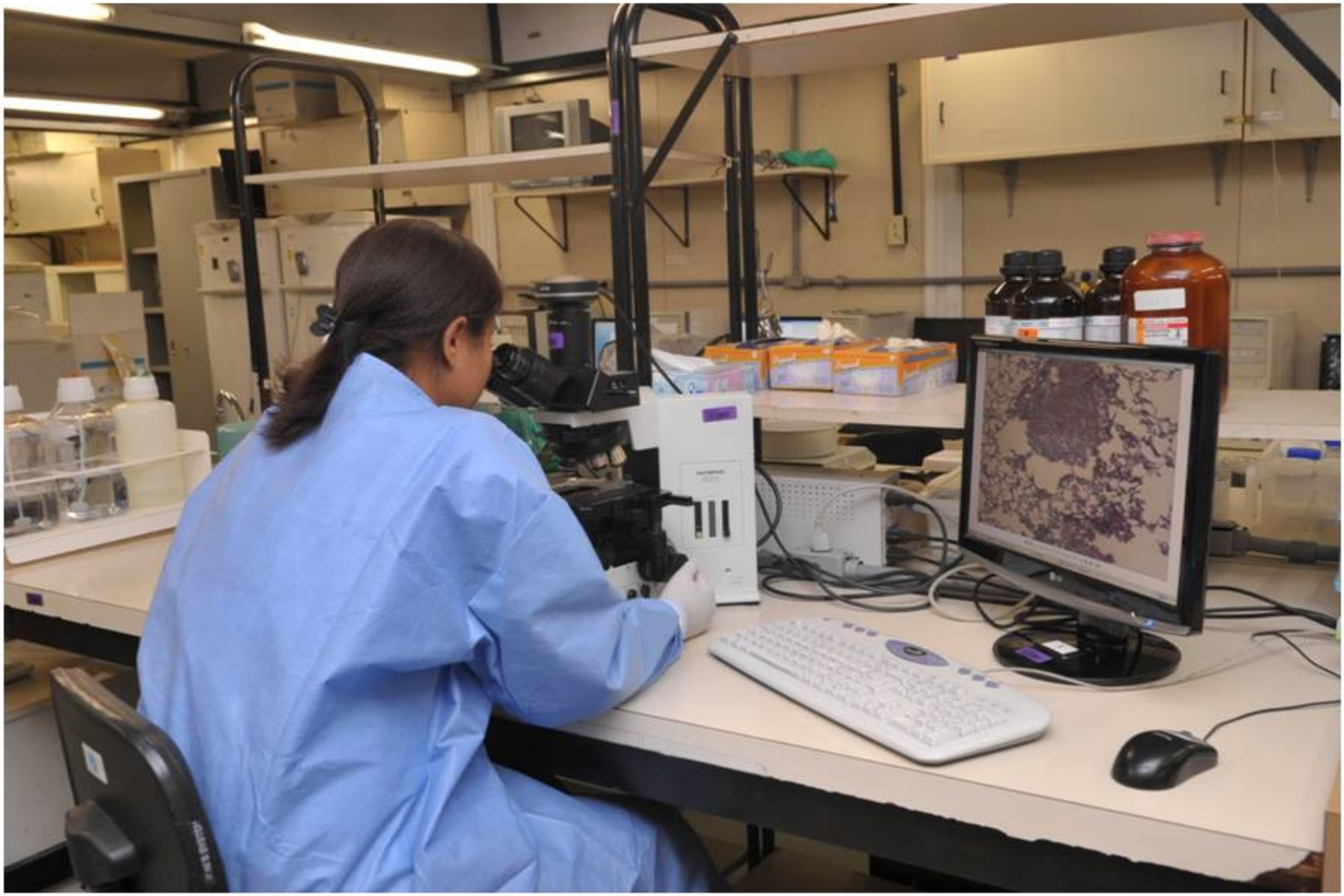

Avaliação histológica e estereologia pulmonar – Laboratório de Inflamação – IOC-FIOCRUZ.