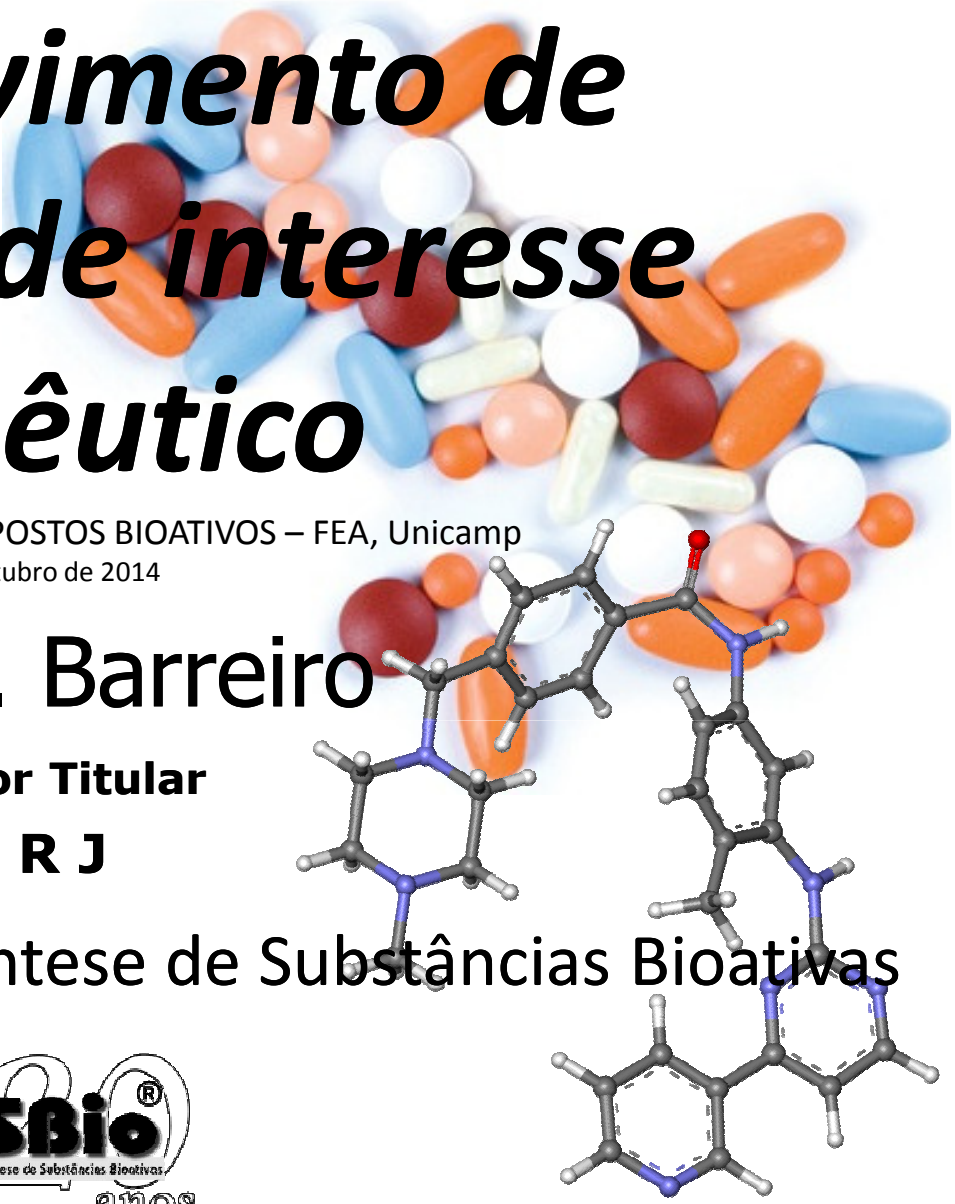
Desenvolvimento de moléculas de interesse terapêutico



I SIMPÓSIO BRASILEIRO DE COMPOSTOS BIOATIVOS – FEA, Unicamp
06-08 de outubro de 2014

Eliezer J. Barreiro

Professor Titular

U F R J

Laboratório de Avaliação e Síntese de Substâncias Bioativas

Instituto Nacional de Ciência e Tecnologia
de Fármacos e Medicamentos
INCT-INOFAR

Universidade Federal do Rio de Janeiro

Fármacos

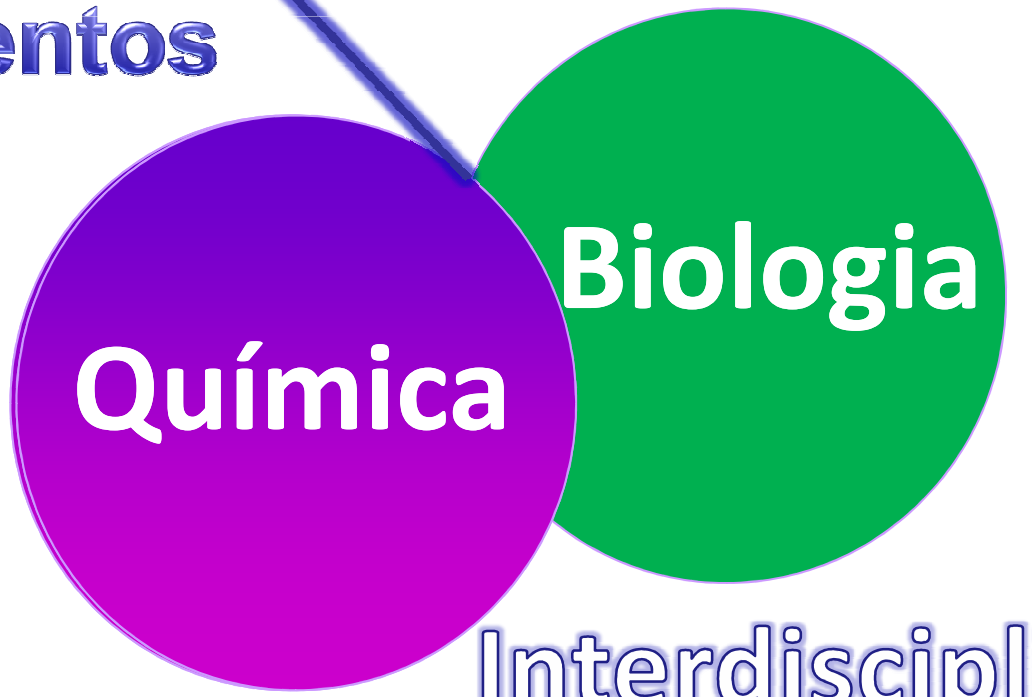
Pesquisa científica

Fitofármacos
Biofármacos
Fitoterápicos

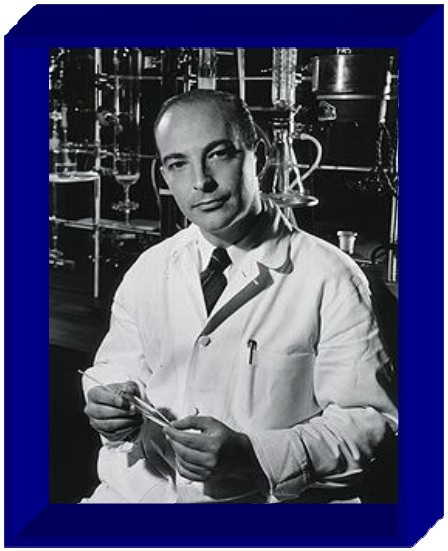
Science **2004**, *303*, 1713
Editor D. Kennedy

Medicamentos

Indústria farmacêutica



Interdisciplinar



Arthur Kornberg
1918-2007

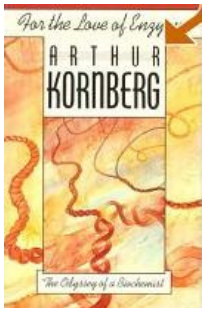
Prêmio Nobel, 1959

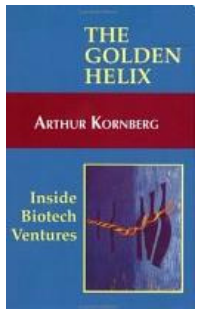
The Two Cultures: Chemistry and Biology[1]

Arthur Kornberg

Department of Biochemistry, Stanford University, Stanford, California 94305

Received July 14, 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…

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

Biochemistry **1987,** *26,* 6888-6891

Universidade Federal do Rio de Janeiro

ISBN: 9788582711170

3ª Edição

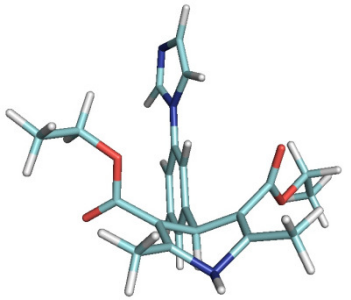
2015

Capítulo 1

Química Medicinal:

as bases moleculares

da ação dos fármacos



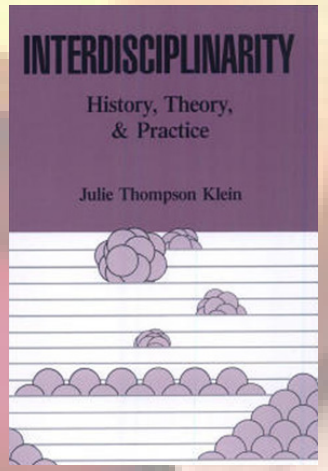
Universidade Federal do Rio de Janeiro

m e d
Química Medicinal
chem

Universidade Federal do Rio de Janeiro

A **interdisciplinaridade**

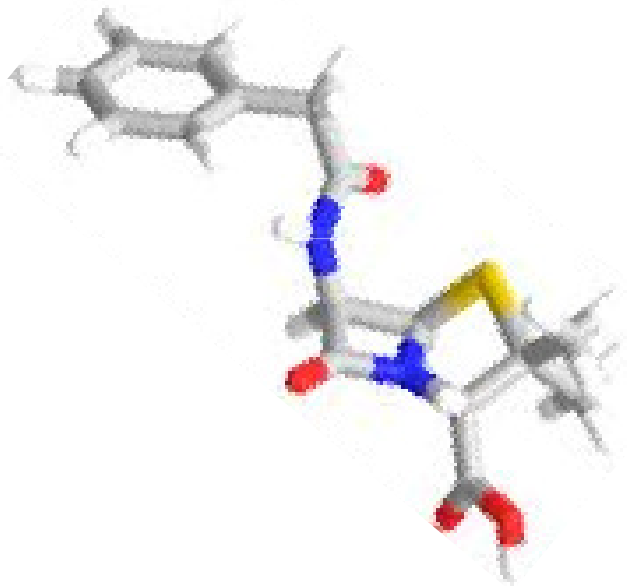
exige arranjos institucionais & temporais inovadores para seu pleno exercício!

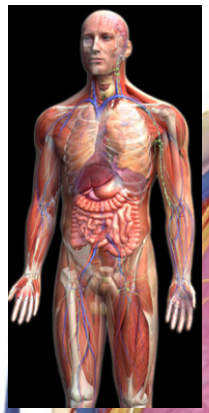


O desenvolvimento de fármacos é interdisciplinar e complexo!

Universidade Federal do Rio de Janeiro

Os medicamentos foram uma das maiores invenções do século 20 !





Os fármacos são moléculas pequenas,

inteligentes & valiosas!

Cadeia de Inovação em Fármacos & Medicamentos

Universidade Federal do Rio de Janeiro

DESENVOLVIMENTO FÁRMACOS

Etapa de Pesquisa

Seleção do Alvo Molecular; Desenvolvimento dos ensaios farmacológicos *in vitro* e *in vivo*; Desenho de ligantes; Síntese; Identificação e Otimização do Protótipo.

Etapa de Desenvolvimento

Inicial: Realização dos ensaios pré-clínicos.
Tardia: Realização dos ensaios clínicos (Fase I, Fase II e Fase III).

Etapa Regulatória

ANVISA; EMEA, FDA, etc

Etapa de Comercialização

Marketing e vendas

DURAÇÃO MÉDIA

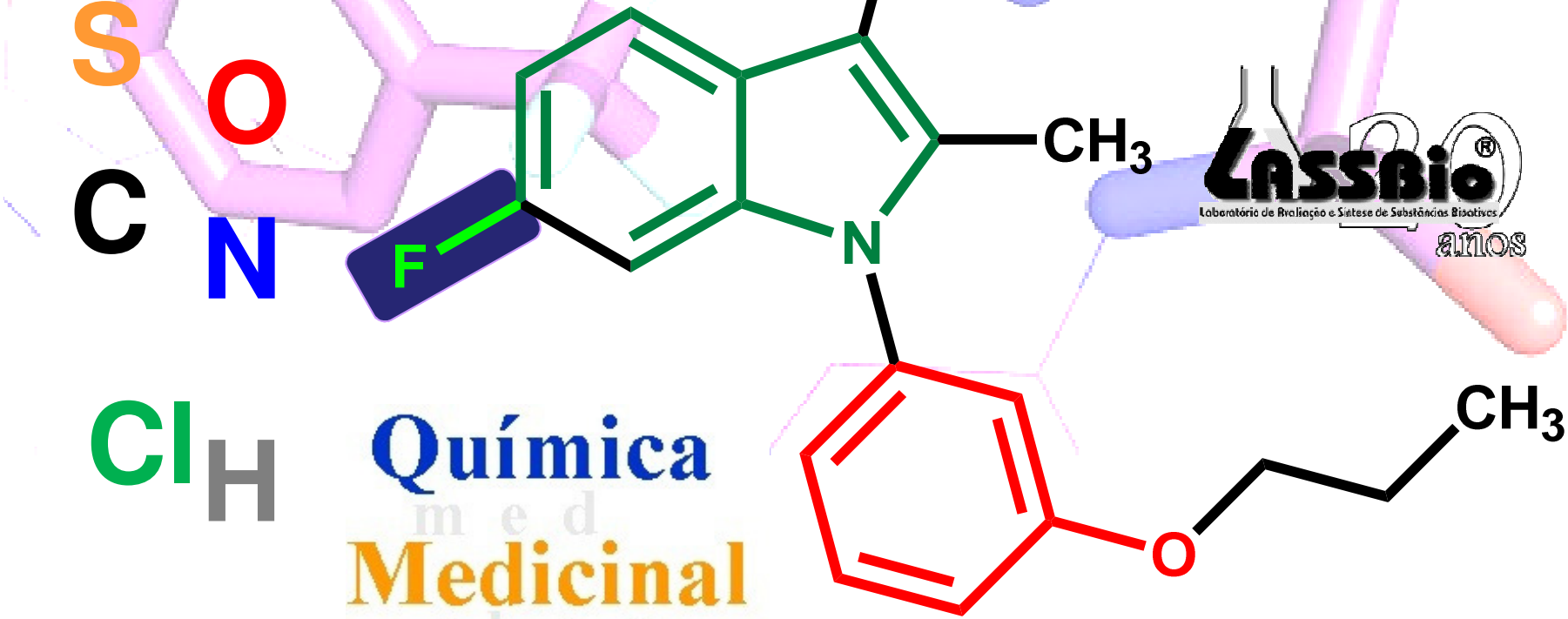
Como inventar uma molécula?

Bioativa....(?)

Our Job!

S O C N Cl H

Química med Medicinal chem



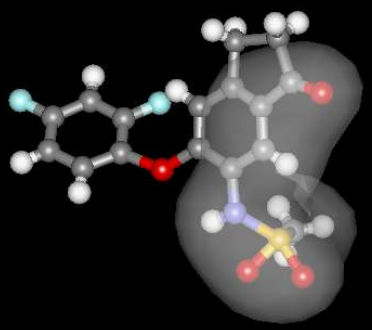
LASSBio® Laboratório de Avaliação e Síntese de Substâncias Bioativas 20 anos

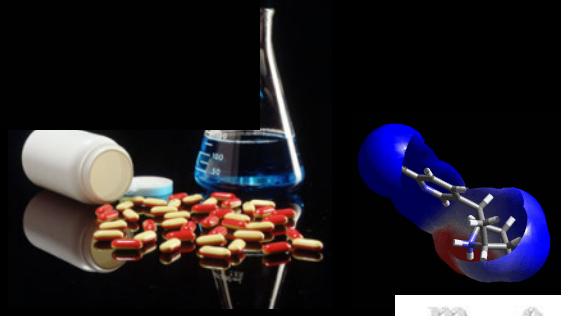
Universidade Federal do Rio de Janeiro

Universidade Federal do Rio de Janeiro

UFRJ

Atualmente, os novos fármacos, capazes de atuarem em qualquer alvo-terapêutico, são *descobertos/inventados* por planejamento racional.

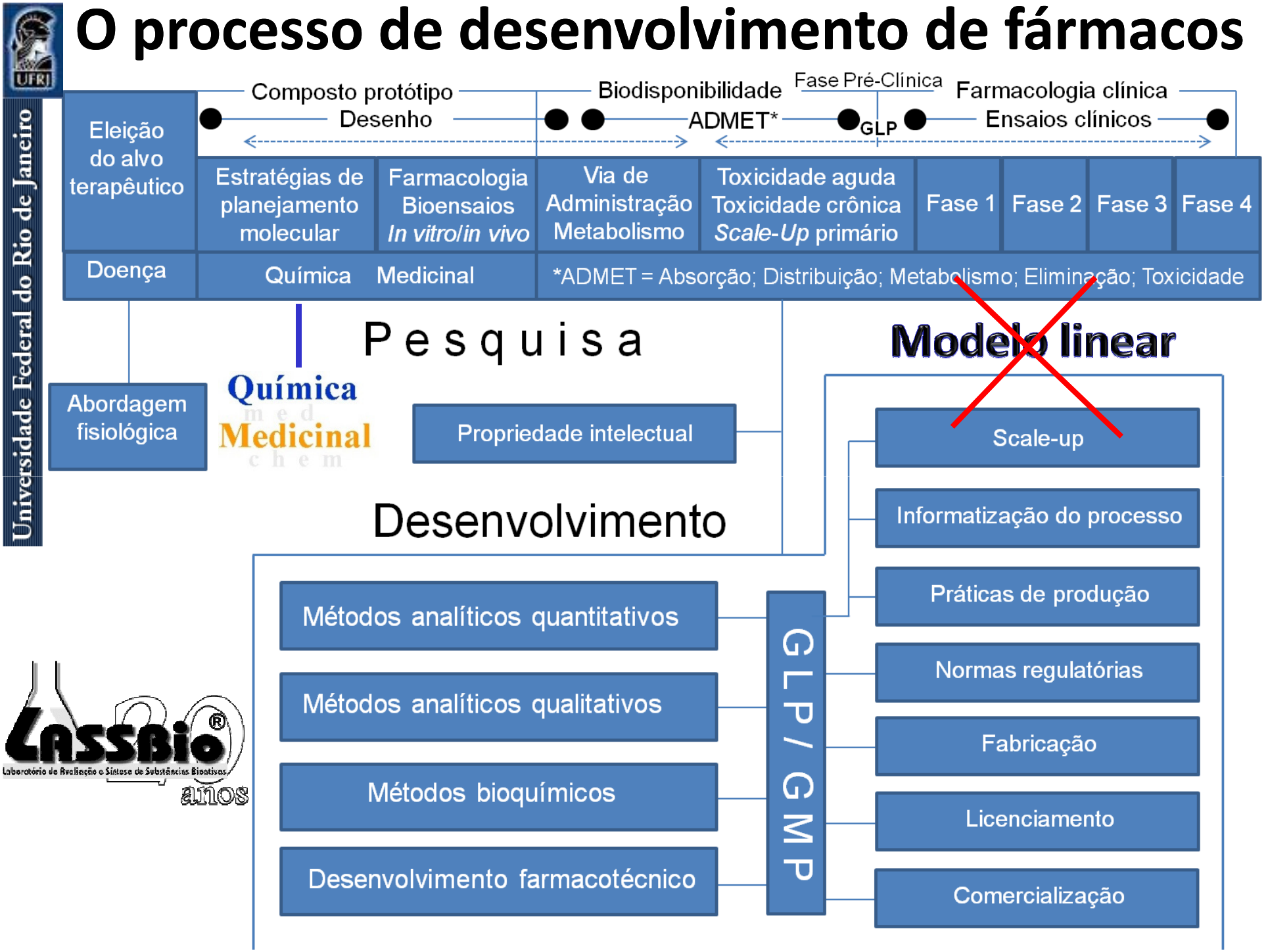




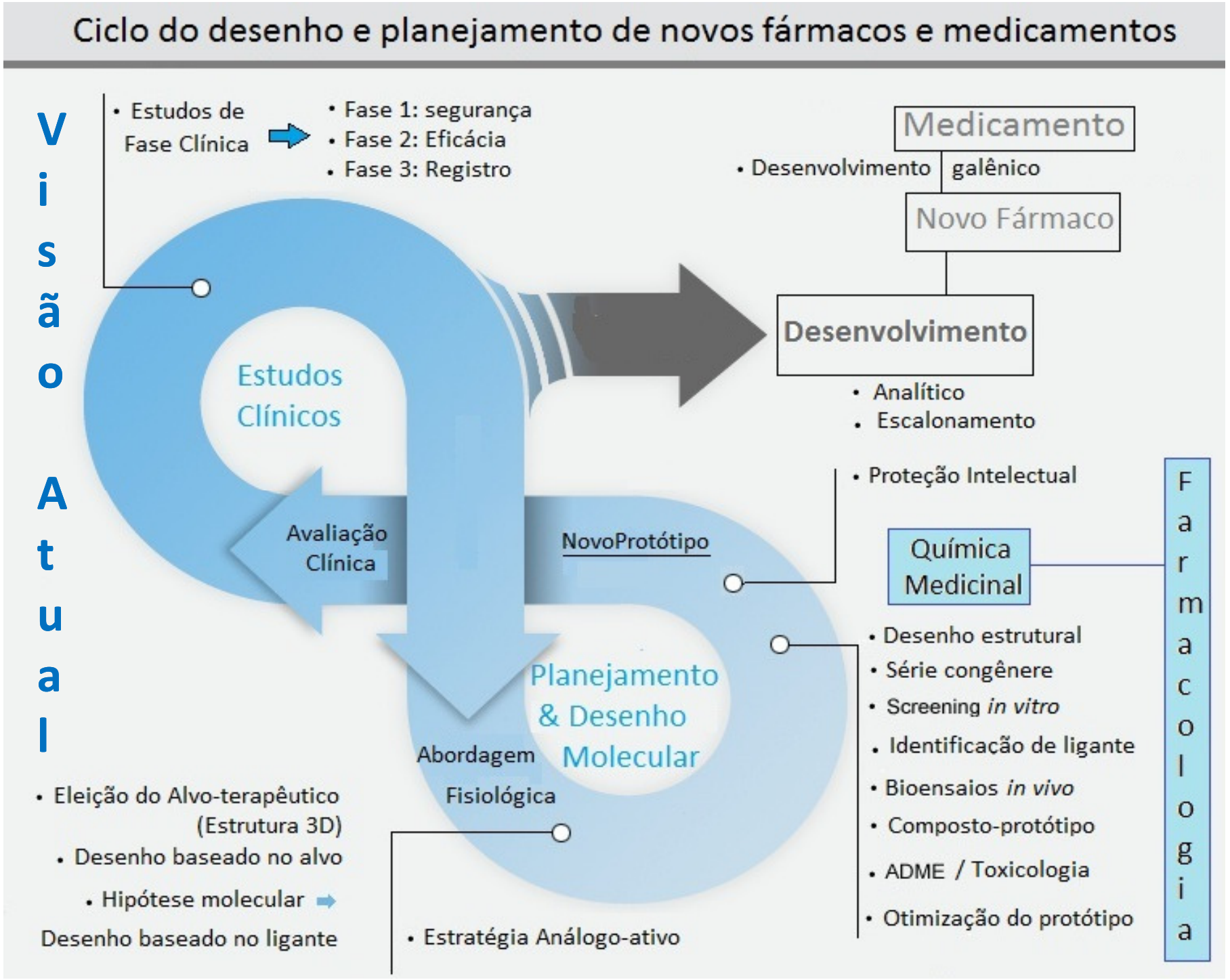
Química Medicinal

reiro, CAM Fraga, ALP Miranda, Estratégias em Química Medicinal para
lanejamento de Fármacos, *Braz. J. Pharm. Sc., 37*, 269-292 (2001).

O processo de desenvolvimento de fármacos

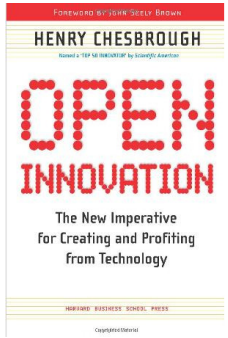


Ciclo do desenho e planejamento de novos fármacos e medicamentos



O *atual modelo de gestão da inovação em fármacos (na IF)*

Universidade Federal do Rio de Janeiro



Inovação = criatividade

Terceirização

Start-ups

Plataformas específicas

Identificação e validação de novos alvos

Serviços

Pessoal Qualificado

Parcerias

Externa

Novo Fármaco

Interna

gestão

Mercado

ICT's

Dossiê regulatório

Identificação e otimização de novos protótipos

Alianças

Fase Pré-clínica

Agências

Colaboração

Universidades

Novas empresas

Publicações

OCIP's

Outras empresas

Associações

Proteção intelectual

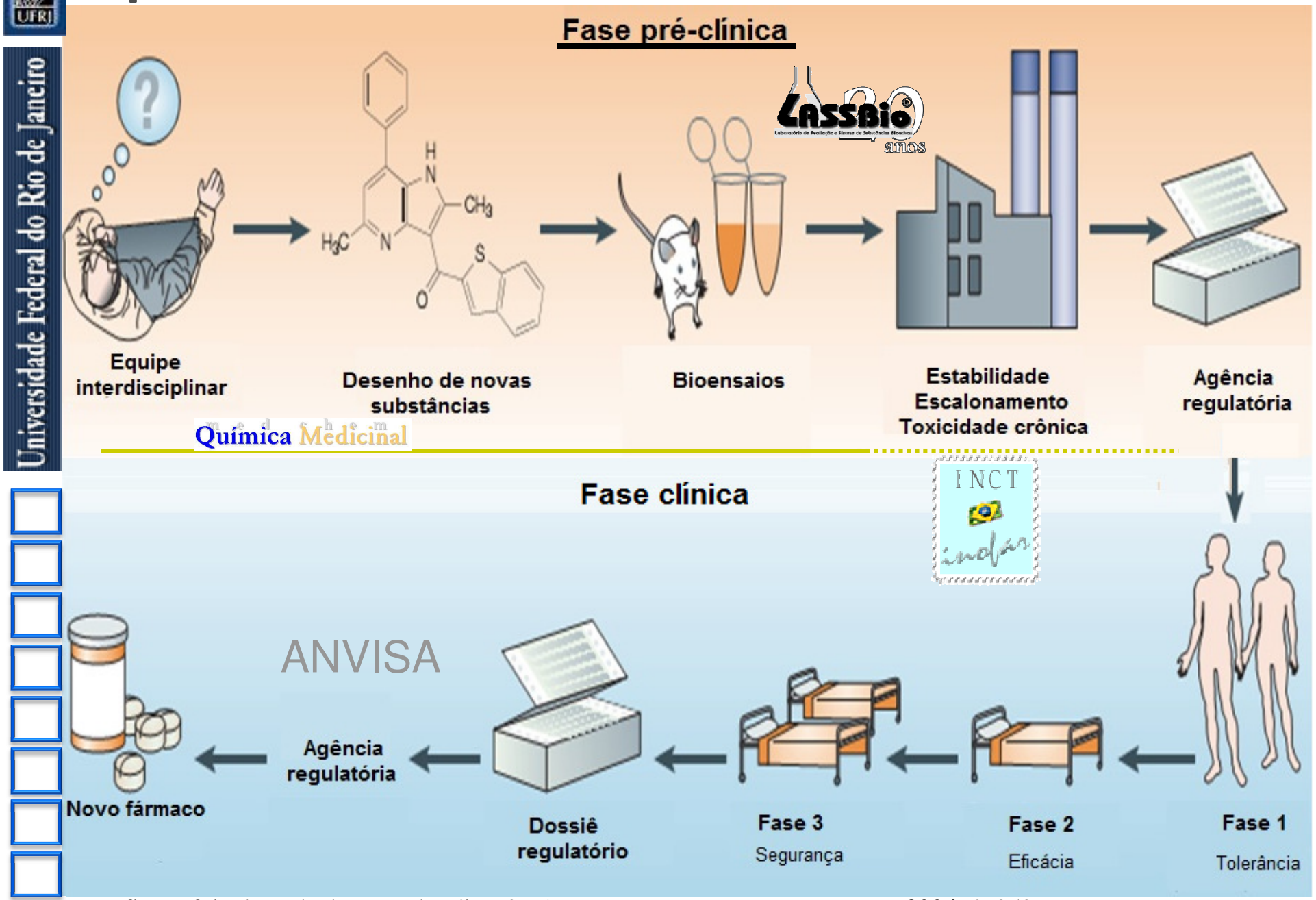
Contratos

Consórcios

Dinâmica organizacional

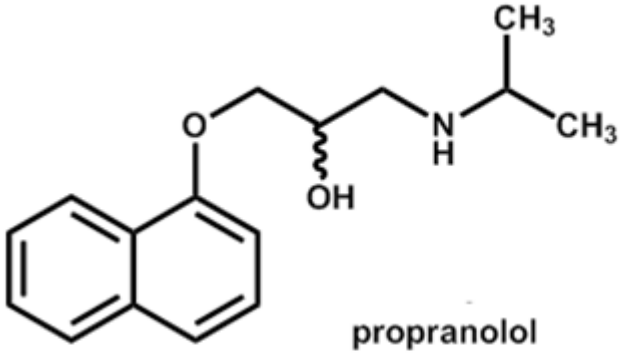
Novos modelos de gestão

O processo de desenvolvimento de novo fármaco

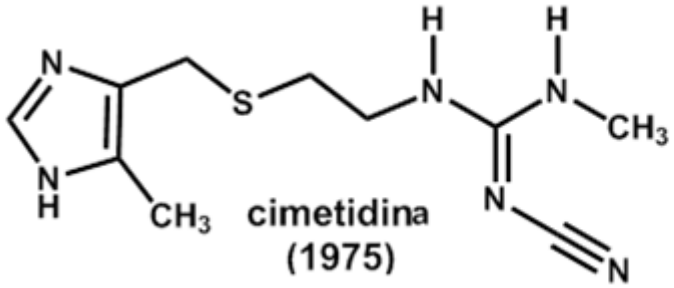


Esta figura foi adaptada de J Lombardino & JA Lowe III *Nature Rev. Drug Disc.* **2004**, *3*, 853.

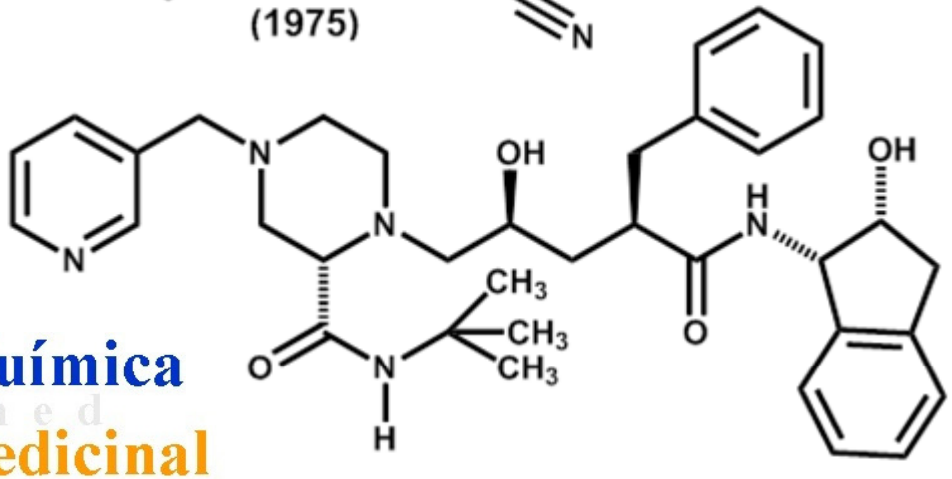
Fármacos ***inovadores*** *atuais*...



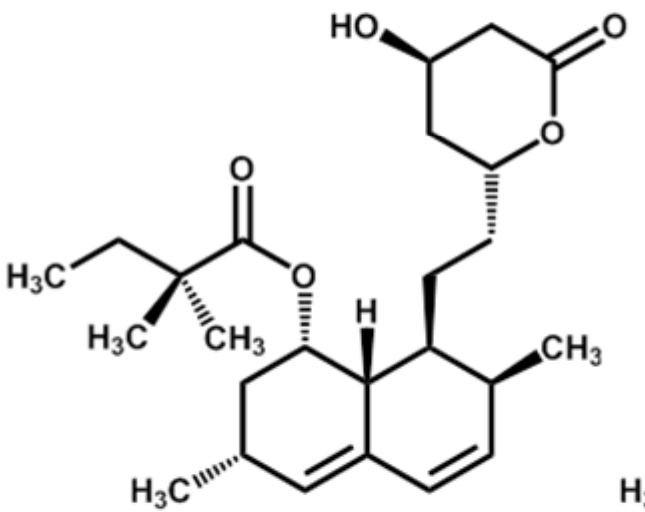
propranolol
(1964)



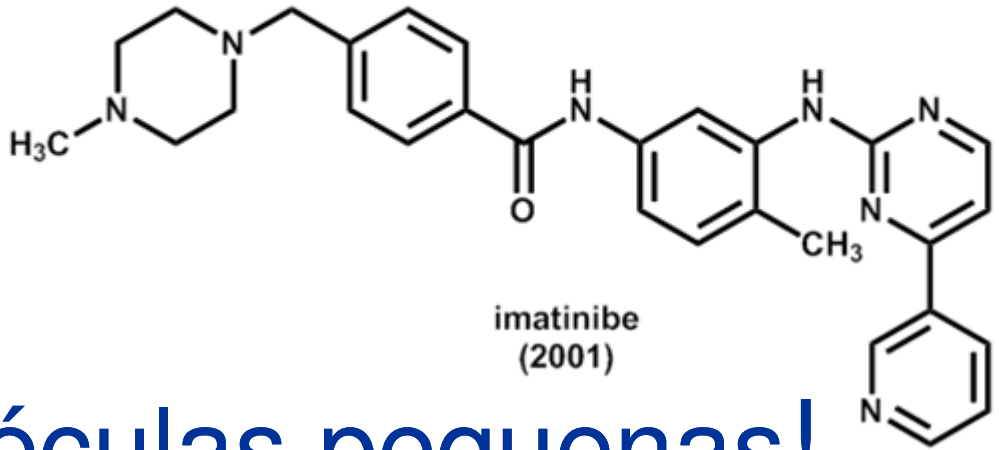
cimetidina
(1975)



indinavir
(1995)



sinvastatin
(1988)



imatinibe
(2001)

Química Medicinal

...são moléculas pequenas!

Universidade Federal do Rio de Janeiro

Estatinas

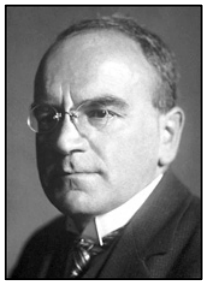
atorvastatina

rosuvastatina

sinvastatina

Moléculas inteligentes

Uma inovação bilionária: *as estatinas*



Heinrich Wieland
1877-1957

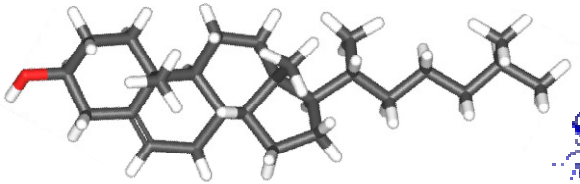
1927

1964

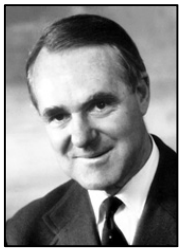
Konrad Bloch
1912-2000

Adolf Windaus
1876-1959

1928

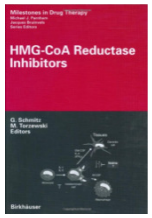


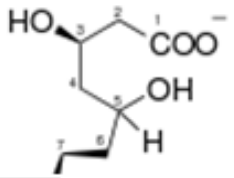
colesterol



John Cornforth

1975

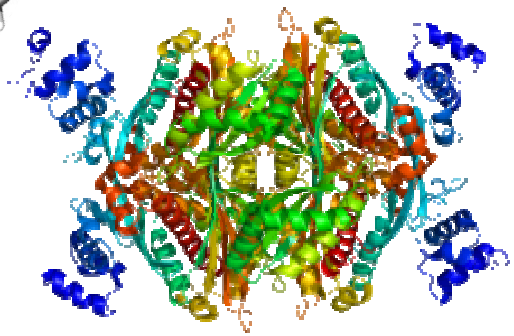




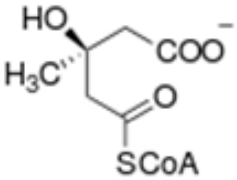
Ring

HMG CoA
Reductase inhibitor

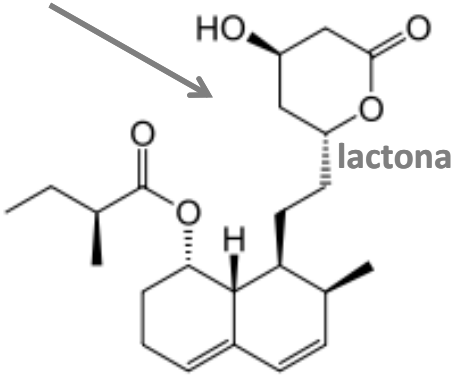
HMGCoAR



EC 1.1.1.34



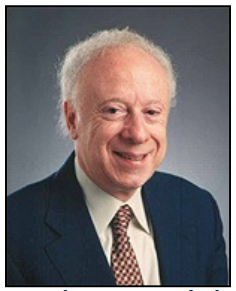
HMG CoA



Mevilonina
/compactina

1985

LDL



Joseph L Goldstein

Michael S Brown

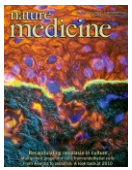
University of Texas, Dallas

Akira Endo

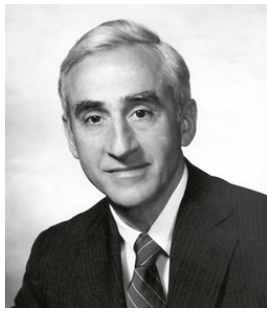
Albert Lasker Award
for Clinical
Medical Research, 2008*

J Med Chem
1985, *28*, 1

Daiichi-Sankyo



* A Endo, A gift from nature: the birth of the statins, *Nature Medicine* **2008**, *14*, 26



Dr P. Roy Vagelos

Vice-Presidente Pesquisa Farmacêutica da Merck (Presidente & CEO)

1975

1976 - confidentiality agreement

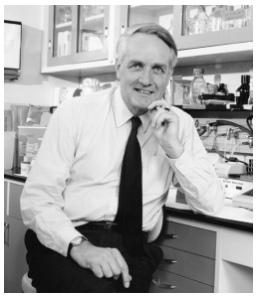
MERCK

Daiichi-Sankyo

Sankyo Laboratories Japan

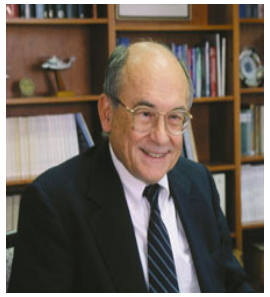
Alfred W. Alberts

1975



Georg Albers-Schönberg

1965

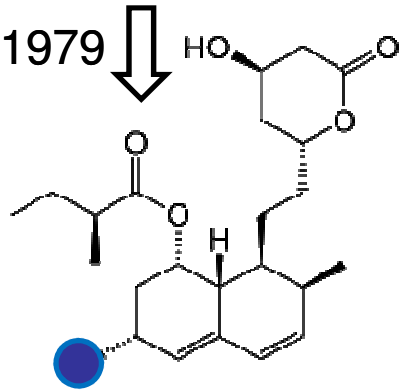


Arthur A. Patchett

Diretor do Departamento *New Lead Discovery*

Alfred Burger Award 2002

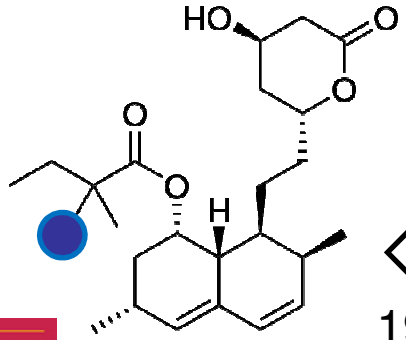
1979



Aspergillus terreus

lovastatina

1980



simvastatina

first-in-class

1982

ZOCOR® (SIMVASTATIN)

therapeutic innovation

Pfizer

1991

atorvastatina

fifth-in-class

"blockbuster mentality"

J. Med. Chem. **1986,** *29*, 849

Química Medicinal

[Descoberta da lovastatina]

> 45 milhões de pessoas usaram estatinas (2005)

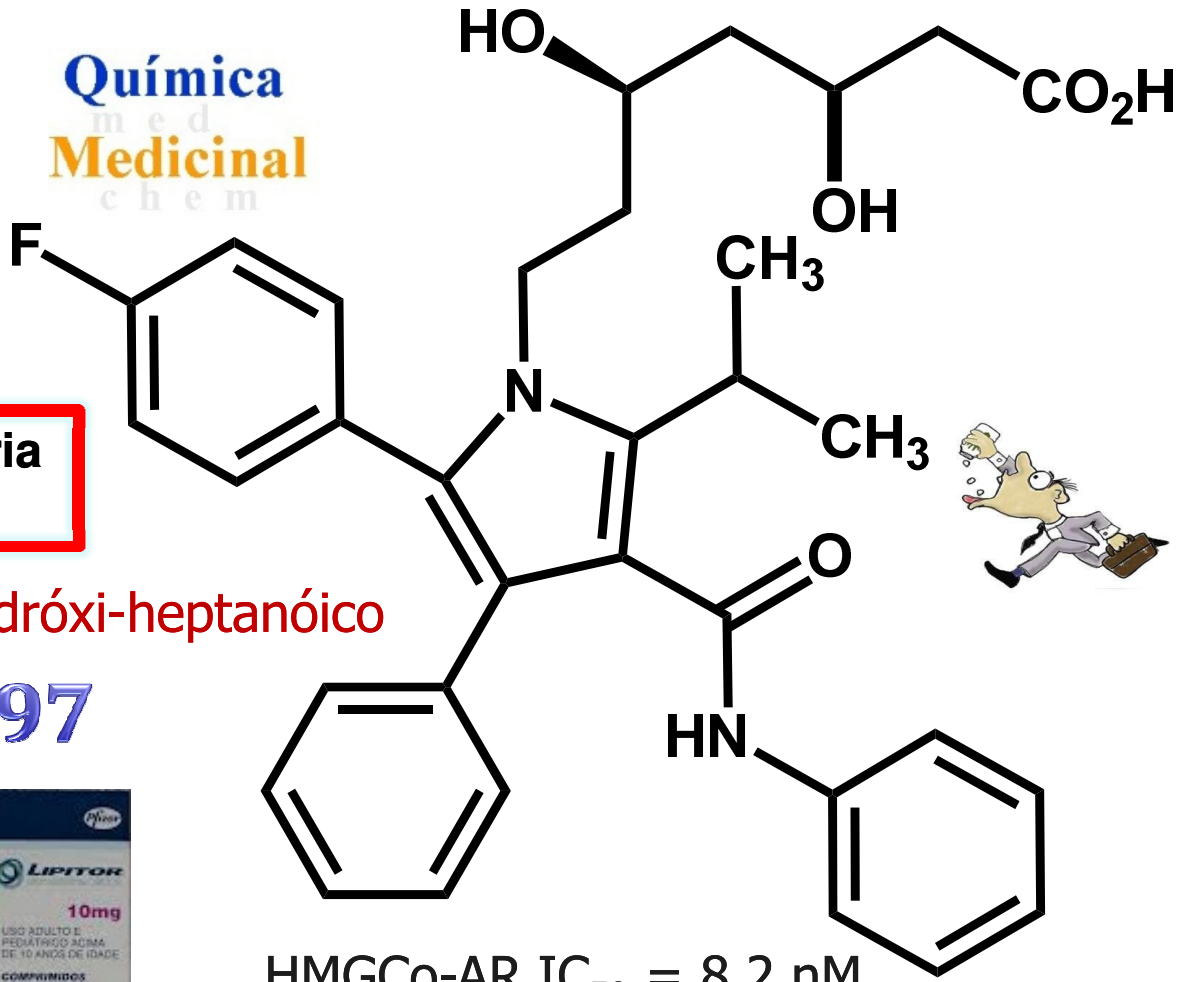
PS Anderson, Reflexions on medicinal chemistry at Merck, West Point, *Annu Rept Med Chem* **2012**, *47*, 3

Estatinas

Química Medicinal

atorvastatina

Maior *bestseller* da história dos fármacos



ácido (*N*-pirrol)-3,5-di-hidróxi-heptanóico

1991 → 1997

Bruce D Roth

2013 SCI Perkin Medal

Warner-Lambert → Pfizer

HMGCo-AR IC_{50} = 8,2 nM

Biodisponibilidade=12%

B. D. Roth, *Progr. Med. Chem.* **2002**, *40*, 1-22

B. D. Roth, et al., *J. Med. Chem.* **1990**, *33*, 21-31

2005 – US$ 13 bi; 2011 – US$ 13,3 bi;

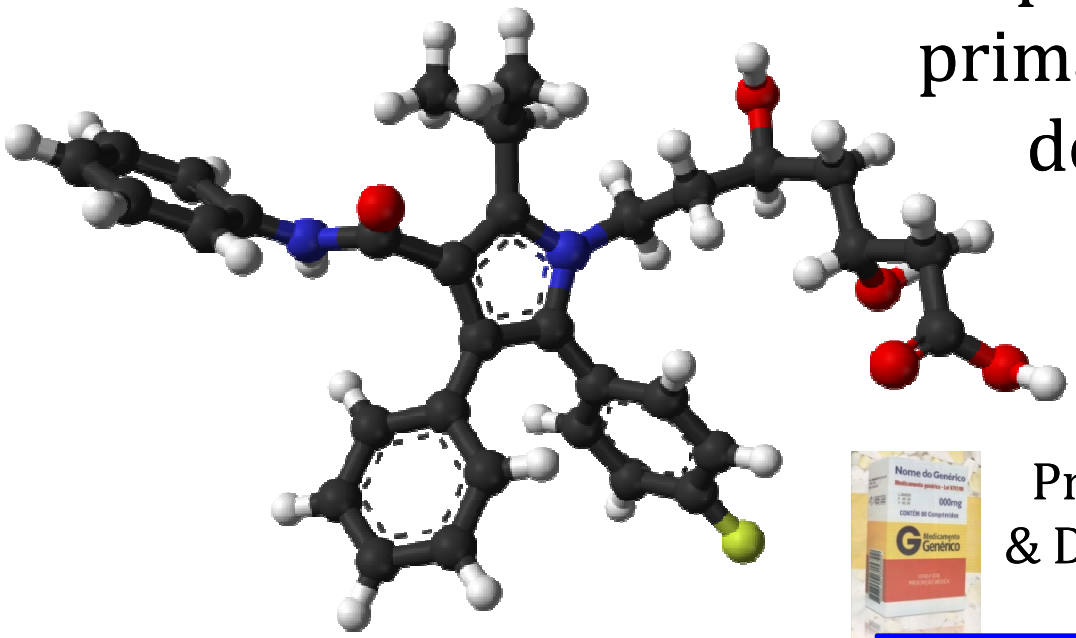
Síntese: *ca.* 220 toneladas/ano

ca. >> 45 milhões de pesoas (2005)

Total de Vendas = *ca.* US$ 145 bilhões (1991-2011)

Atorvastatina

sintetizada em 1985, por Bruce D. Roth,
na Parke-Davis Warner-Lambert Co.
Patent US 5273995 Pfizer (1991)
19 etapas; 5% rendimento



O maior *bestseller* da história da indústria farmacêutica mundial

Estudo de rotas de síntese, a partir de intemediários primários de menor custo, de fármacos genéricos:

Professor Luiz Carlos Dias
& Dr Adriano Siqueira Vieira
IQ, UNICAMP

18 etapas; 19% rendimento; 5g escala

- **INPI Patente 018110015039, 2001 (BR)**
  Nova rota de síntese da atorvastatina cálcica usando novos intermediários.

INCT-INOFAR: *www.inct-inofar.ccs.ufrj.br*

Escalonamento

Conexão Xérem

Universidade Federal do Rio de Janeiro

UFRJ

40 ANOS

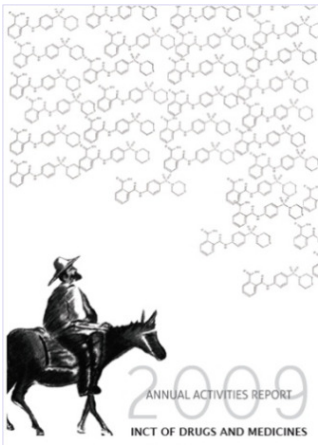
INMETRO

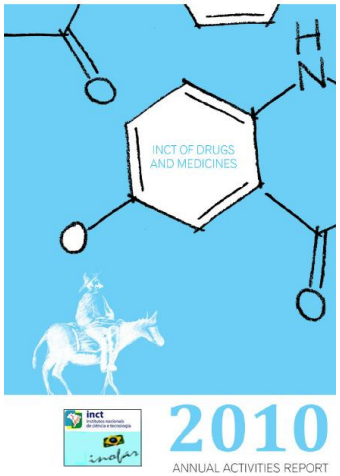
INCT

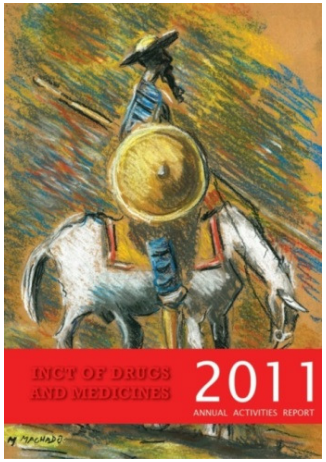
NORTEC QUÍMICA

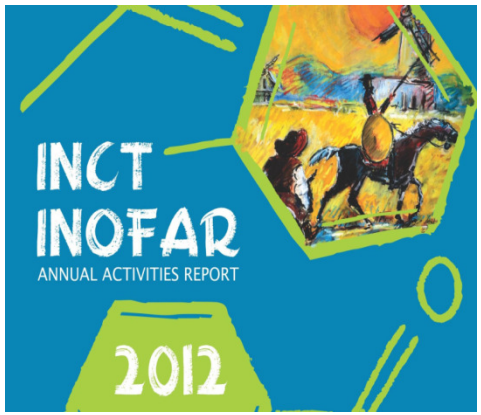
Annual Activities Report

Universidade Federal do Rio de Janeiro









Coordinator:
Eliezer J. Barreiro

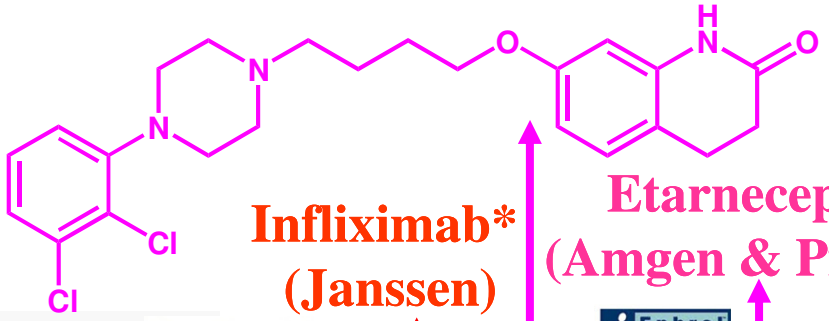
www.inct-inofar.ccs.ufrj.br

Os medicamentos *bestseller* em 2013

Universidade Federal do Rio de Janeiro

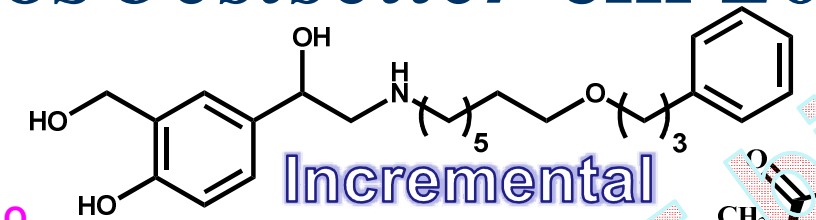
Radical

Aripiprazola (BMS)



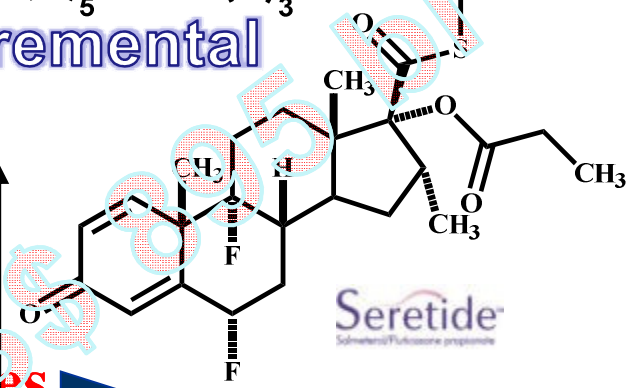
Infliximab* (Janssen)

Etarnecept* (Amgen & Pfizer)



Incremental

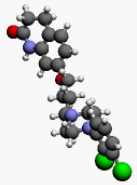
fluticazona salmeterol (GSK)



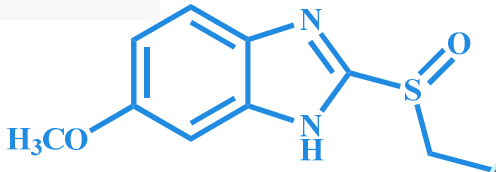
Seretide

em US$ bilhões

1	2,0	7,7	7,8	7,8	7,9	7,9	8,2	9,2	9,8	66,3



Remicade INFLIXIMAB



Incremental

Esomeprazola (AZ)

Insulina (Lantus, Sanofi)

Adalimumab* (Abbott)

HUMIRA

Incremental

Rosuvastatina (AZ)

*** Biofármacos: anti-TNFα**

Fórmula molecular geral: $C_{109}H_{134}F_4Cl_2N_9O_{19}S_3$

Fonte:http://www.statista.com/statistics

Os fármacos no século 21

Universidade Federal do Rio de Janeiro

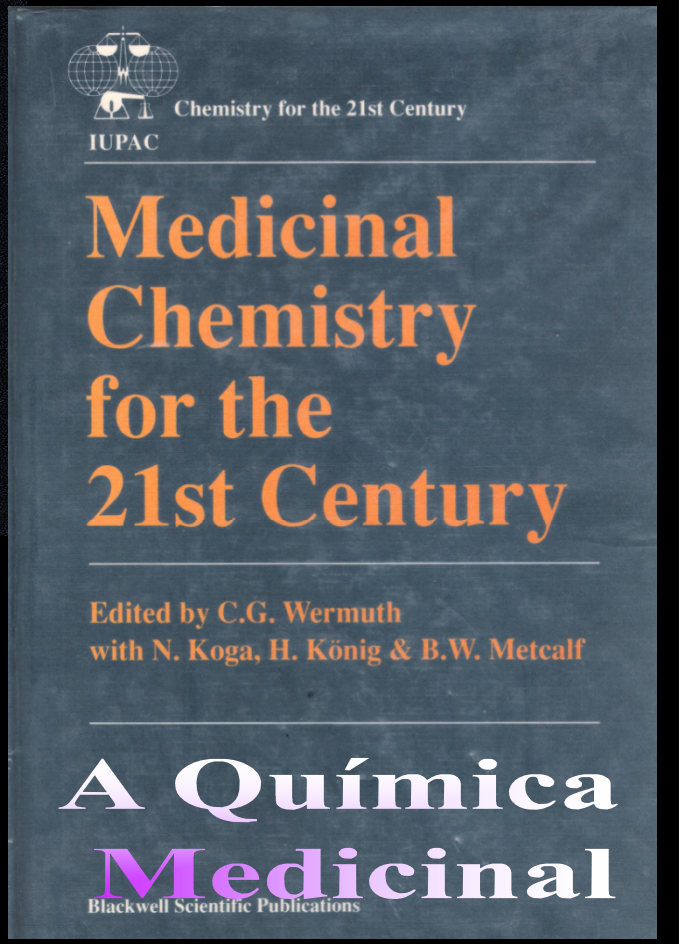
UFRJ

Século 21

Química
med
Medicinal
chem

Siglo 21

21st Century



Segundo paradigma da *QuimMed*

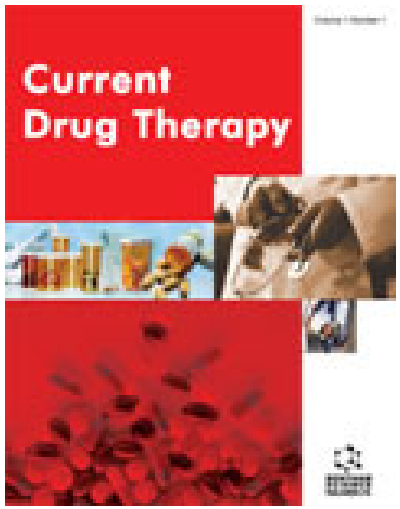
New Insights for Multifactorial Disease Therapy: The Challenge of the Symbiotic Drugs

Eliezer J. Barreiro and Carlos Alberto Manssour Fraga

Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio), Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, P.O. Box 68023, 21944-971, Rio de Janeiro, RJ, Brazil.

Abstract: Some physiopathological processes involved in the genesis of diseases could suggest the necessity of designing bioligands or prototypes that aggregate, in only one molecule, dual pharmacodynamical properties, becoming able to be recognized by two elected bioreceptors. This approach can have distinct aspects and, when a novel ligand or a prototype acts in two elected targets belonging to the same biochemical pathway, *e.g.* arachidonic acid cascade, it receives the denomination of dual or mix agent. On the other hand, if these two targets belong to distinct biochemical routes and both are related to the same disease, we can characterize the agents able to modulate it as symbiotic ligands or prototypes. In the present work, we provide some examples and applications of the molecular hybridization concept for the structural design of new symbiotic ligands and prototypes, especially those applied in the treatment of chronic-degenerative disorders.

Key Words: Symbiotic drugs; molecular hybridization; multifactorial diseases; therapeutic innovation; drug design; dual compounds.



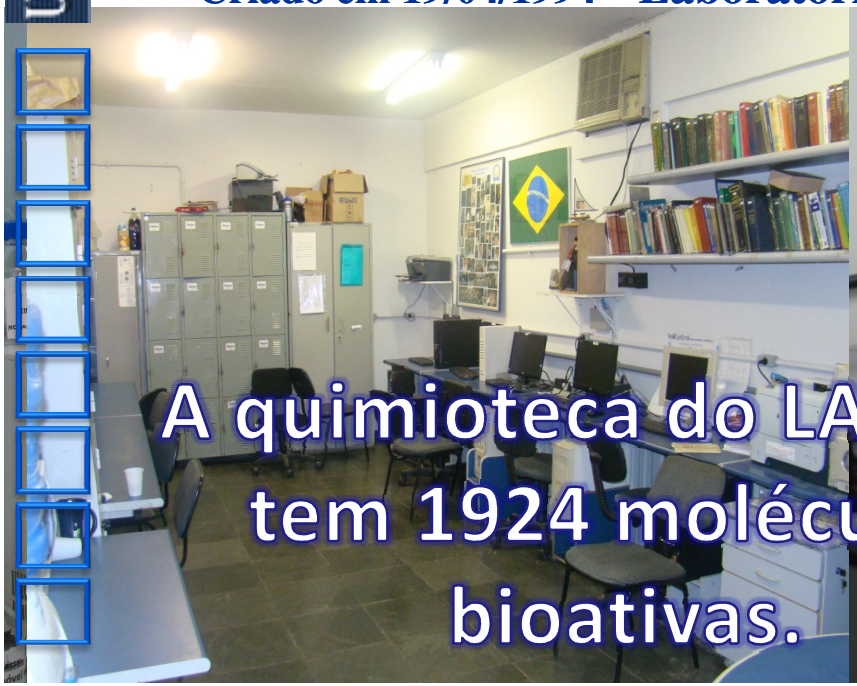
Fármacos simples, não curam doenças complexas!

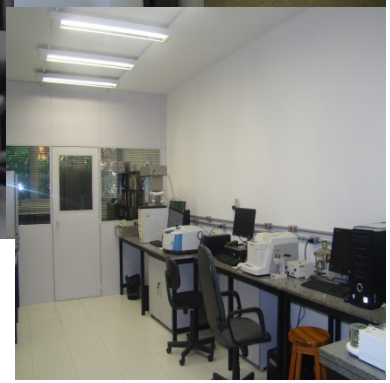
Fármacos do século 21

O desenho racional de fármacos *multi-alvos* depende da capacidade de se combinarem fragmentos moleculares farmacofóricos, capazes de assegurarem reconhecimento molecular pelos receptores envolvidos na patologia multifatorial

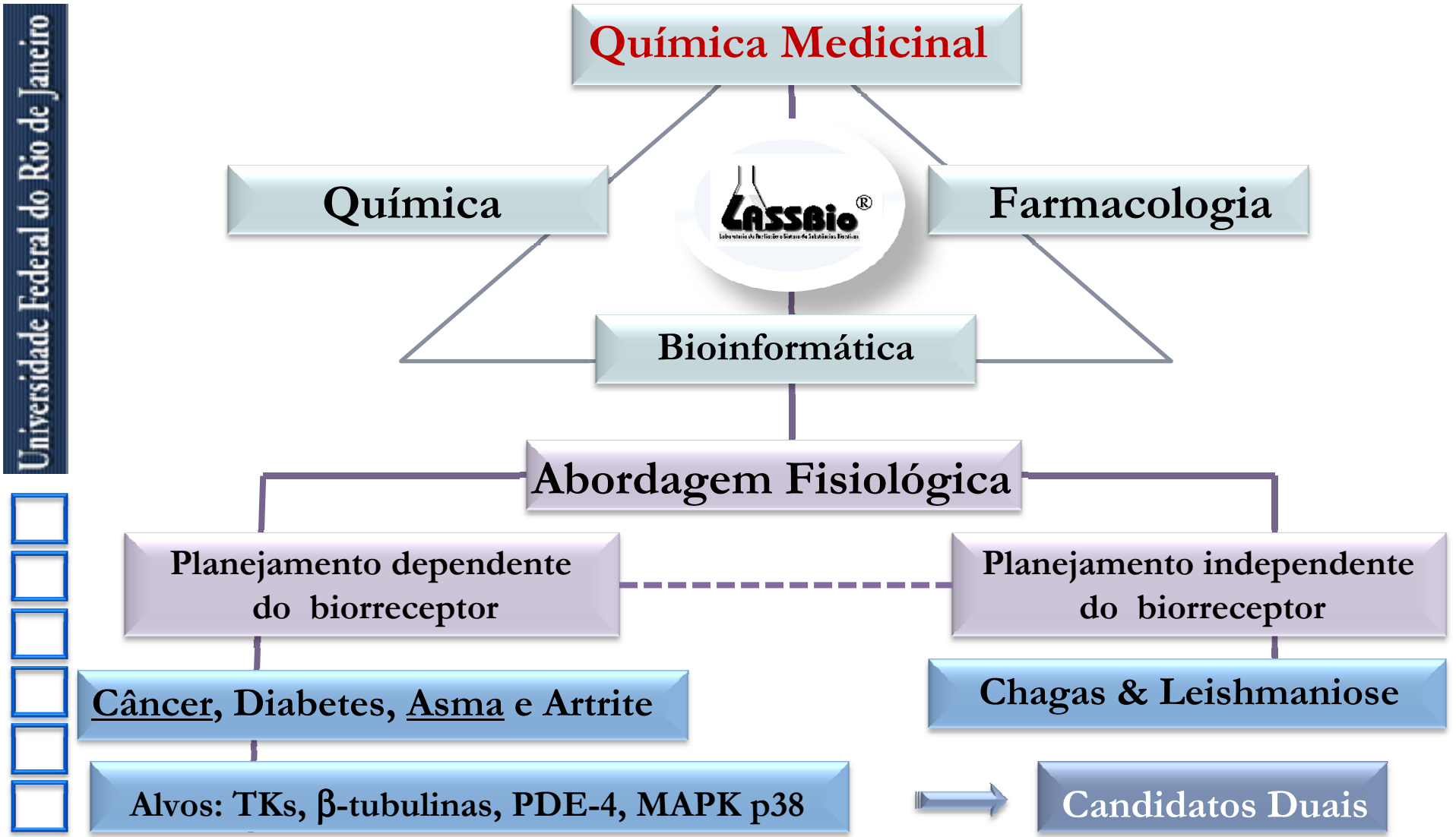
JL Medina-Franco et al. Shifting from the single to the **multitarget paradigm** in drug discovery, *Drug Discov. Today* **2013**, *18,* 495; C Hiller, J Kühhorn, P Gmeiner, Class A G-Protein-Coupled Receptor (GPCR) Dimers and Bivalent Ligands, *J. Med. Chem.* **2013**, *56*, 6542; G Phillips, M Salmon, **Bifunctional compounds** for the treatment of COPD, *Annu. Rev. Med. Chem*. **2012**, *47*, 209; S Reardon, A world of chronic disease, *Science* **2011**, *333*, 558.

Criado em 19/04/1994 Laboratório de Avaliação e Síntese de Substâncias Bioativas

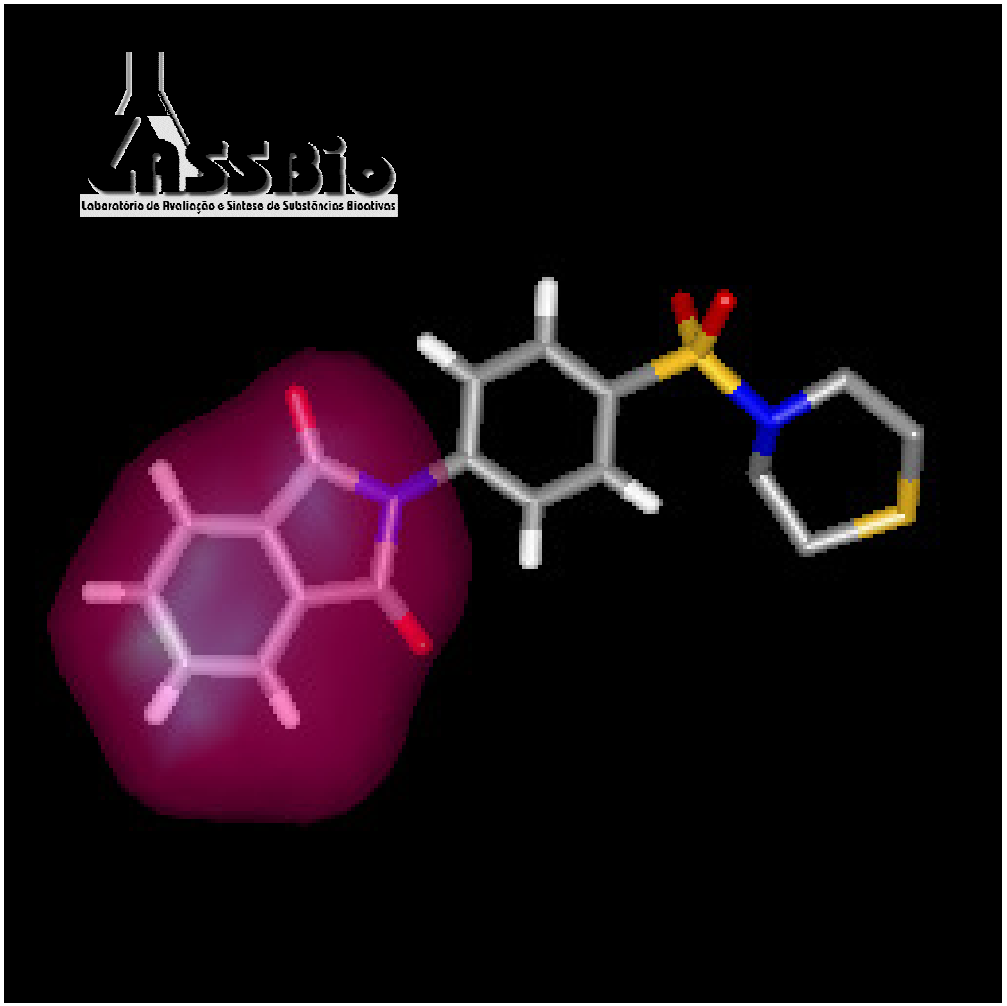




Universidade Federal do Rio de Janeiro



Novos candidatos a fármacos duais



LASSBio-468

Desenhado por hibridação molecular

TNF-α PDE-4

TNF-α ED_{50} 2,5 mg/Kg

PDE-4 IC_{50} = 13,6 μM

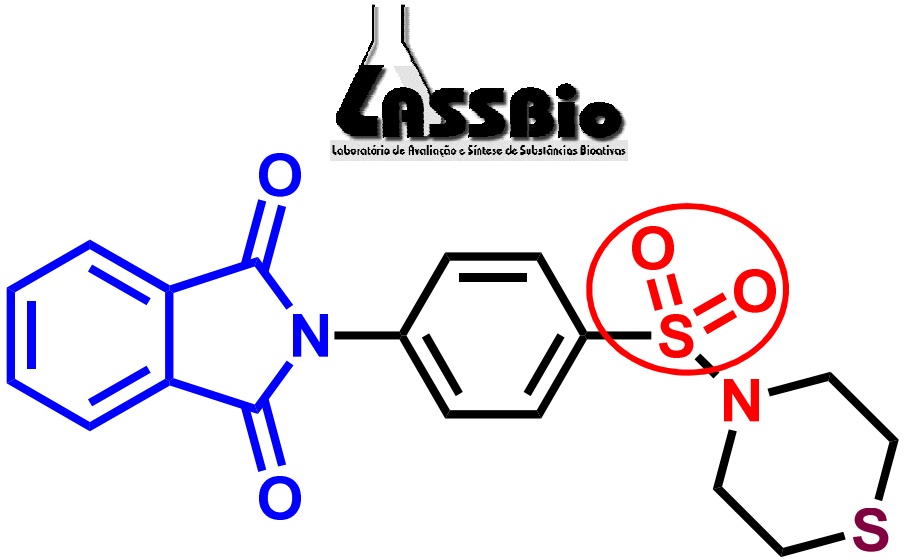
LASSBio-596

L. M. Lima, P. Castro, A. L. Machado, C. A. M. Fraga, C. Lugnier, V. L. G. Moraes, E. J. Barreiro, *Bioorg. Med. Chem.* **2002**, *10*, 3067.

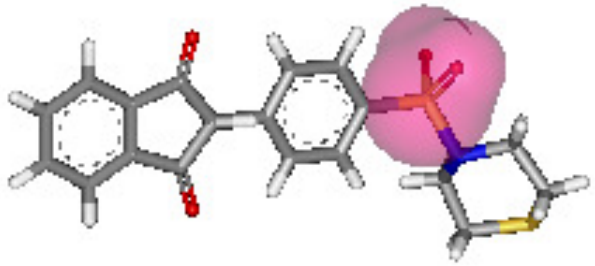
Universidade Federal do Rio de Janeiro

LEAD COMPOUND

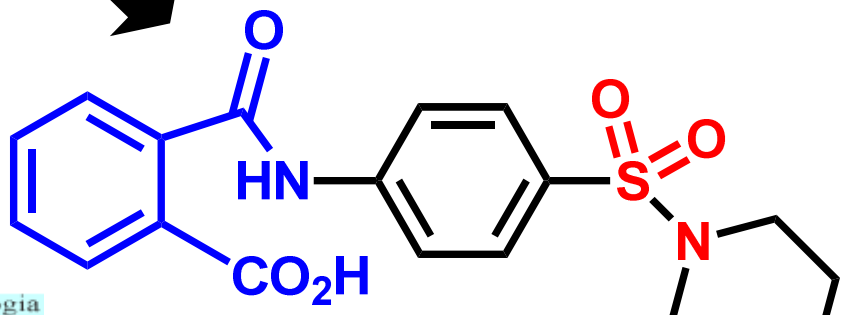
Lead-optimization



LASSBio-468



Metabolism studies



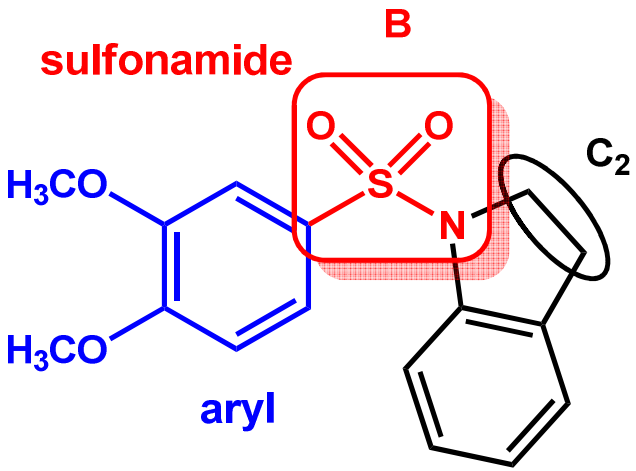
LASSBio-596

Instituto Nacional de Ciência e Tecnologia de Fármacos e Medicamentos

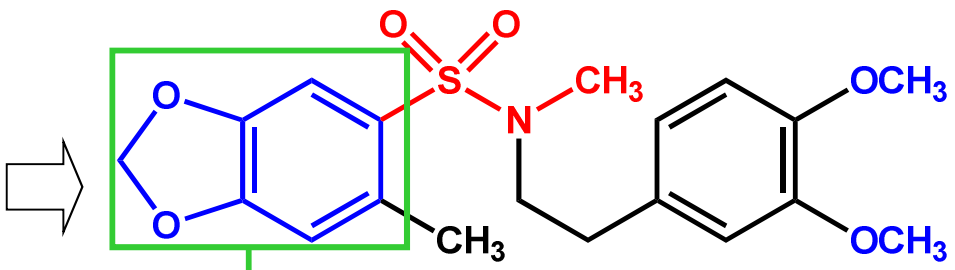
www.inct-inofar.ccs.ufrj.br

P.R. M. Rocco et al., *European Respiratory Journal*, **2003**, *22*, 20; NV Casquilhoet al., *Toxicon* **2011,** 58, 195; JCML Ribeiroet al. , *Ophthalmic Research* **2012***, 48*, 177; PR Rocco et al, *Rev. Virtual Quim*., **2010,** *2*, 10; AL Araújo et al., *Food Chemical Toxicology* **2014**, 000.

Mais do mesmo…



Montana *et al*., 1998



2nd generation

LASSBio-959

Biophore from natural safrole

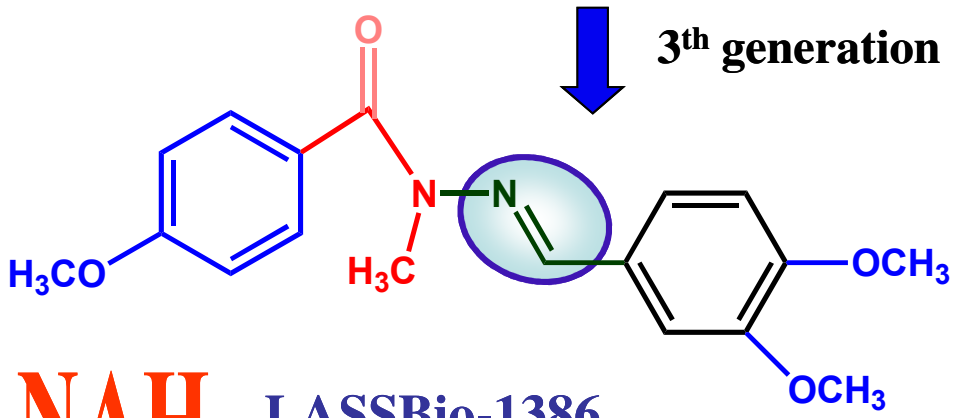
IC_{50} = **6,7** µM PDE-4

Lead -optimization

IC_{50} = **105 nM** PDE-4

LASSBio
Laboratório de Avaliação e Síntese de Substâncias Bioativas

3th generation



NAH **LASSBio-1386**

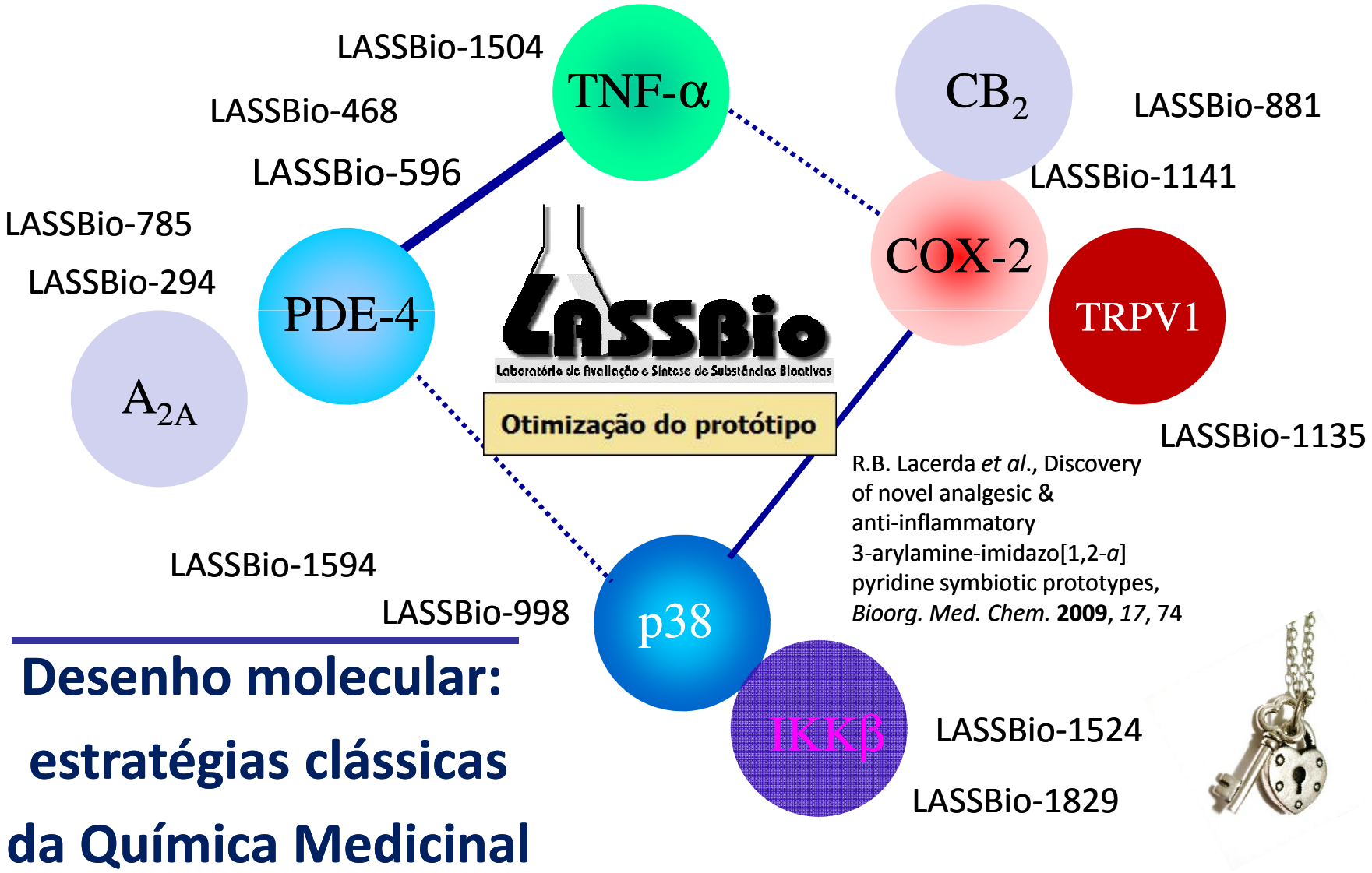
AE Kümmerle, et al., Design, synthesis, and pharmacological evaluation of *N*-acylhydrazones and novel conformationally constrained compounds as selective and potent orally active phosphodiesterase-4 inhibitors , *J. Med.Chem*. **2012**, *55*, 7525

Novos protótipos de fármacos multialvos

Universidade Federal do Rio de Janeiro

Química Medicinal

Doenças crônico-degenerativas



R.B. Lacerda *et al.*, Discovery of novel analgesic & anti-inflammatory 3-arylamine-imidazo[1,2-*a*] pyridine symbiotic prototypes, *Bioorg. Med. Chem.* **2009**, *17*, 74

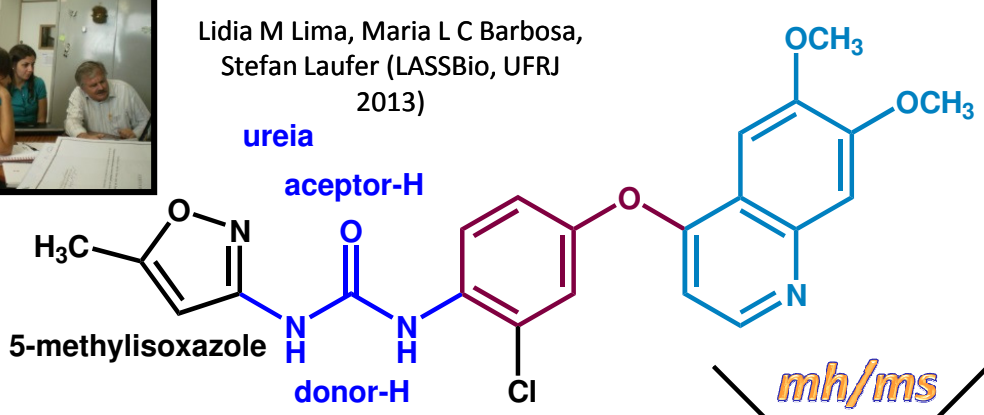
Desenho molecular: estratégias clássicas da Química Medicinal

Um novo *tinibe* dual: LASSBio-1630

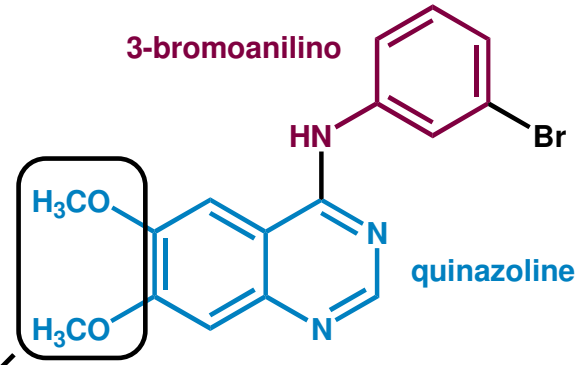
Lidia M Lima, Maria L C Barbosa, Stefan Laufer (LASSBio, UFRJ 2013)

Universidade Federal do Rio de Janeiro

Química Medicinal



mh/ms



oral VEGF receptor tyrosine kinase inhibitor

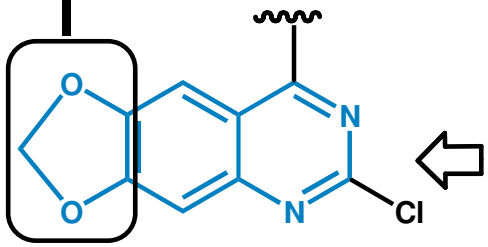
inhibits tyrosine kinase activity of the EGFR

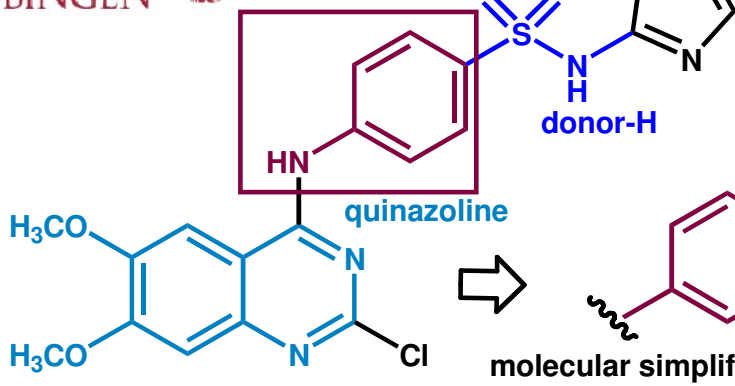
safrole

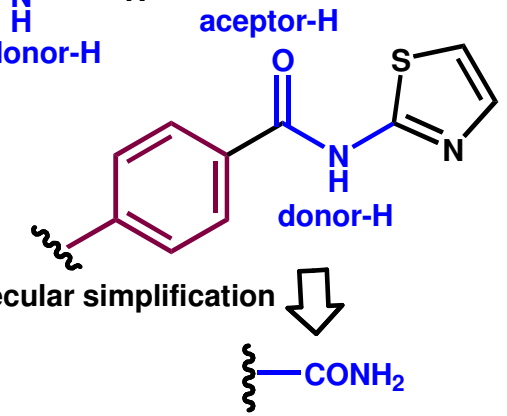
LASSBio

Laboratório de Avaliação e Síntese de Substâncias Bioativas

UNIVERSITÄT TÜBINGEN







VEGF & EGFR inhibitor

M L C Barbosa, L M Lima, R Tesch, C M R Sant'Anna, F Totzke, M HG Kubbutat, C Schächtele, S A Laufer, E J Barreiro, Novel 2-chloro-4-anilino-quinazoline derivatives as EGFR and VEGFR-2 dual inhibitors, *Eur J Med Chem* **2014**, *71*, 1-14.

Universidade Federal do Rio de Janeiro

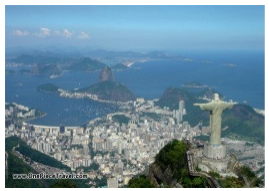
Novel 2-chloro-4-anilino-quinazoline derivatives as EGFR and VEGFR-2 dual inhibitors

Maria Letícia de Castro Barbosa [a,b], Lídia Moreira Lima [a,b], Roberta Tesch [a], Carlos Mauricio R. Sant'Anna [c], Frank Totzke [d], Michael H.G. Kubbutat [d], Christoph Schächtele [d], Stefan A. Laufer [e], Eliezer J. Barreiro [a,b,*]

[a] Laboratory of Evaluation and Synthesis of Bioactive Substances (LASSBio), Federal University of Rio de Janeiro, P.O. Box 68024, 21944-971 Rio de Janeiro, RJ, Brazil
[b] Graduate Program of Chemistry (PGQu), Chemistry Institute, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[c] Department of Chemistry, Federal Rural University of Rio de Janeiro (UFRRJ), Seropédica, RJ, Brazil
[d] ProQinase GmbH, Freiburg, Germany
[e] Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, Eberhard-Karls-University Tübingen, Tübingen, Germany

European Journal of Medicinal Chemistry 71 (2014) 1–14

Dual Inhibitors Dual



Química Medicinal

LASSBio Laboratório de Avaliação e Síntese de Substâncias Bioativas

UNIVERSITÄT TÜBINGEN

LASSBio-1630

Novel molecular pattern with EGFR/VEGFR dual activity!

Atividade dual

IC_{50} (EGFR) = 0,90 µM

IC_{50} (VEGFR) = 1,17 µM

Impact Innovation Ideas Inspiration Initiative

BR 10 2013 001809-0 A2

MLC Barbosa, Novos derivados quinazolínicos funcionalizados inibidores duais das tirosina cinases receptoras EGFR & VEGFR-2, Tese de Doutorado, Instituto de Química, UFRJ, 2013.

2014

OPEN ACCESS Freely available online

PLOS ONE

LASSBio-1135: A Dual TRPV1 Antagonist and Anti-TNF-Alpha Compound Orally Effective in Models of Inflammatory and Neuropathic Pain

Cleverton K. F. Lima[1], Rafael M. Silva[2], Renata B. Lacerda[3], Bruna L. R. Santos[1], Rafaela V. Silva[1], Luciana S. Amaral[2], Luís E. M. Quintas[2], Carlos A. M. Fraga[2,3], Eliezer J. Barreiro[3], Marília Z. P. Guimaraes[2],

Bioorganic & Medicinal Chemistry 17 (2009) 74–84

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

journal homepage: www.elsevier.com/locate/bmc

Discovery of novel analgesic and anti-inflammatory 3-arylamine-imidazo[1,2-*a*]pyridine symbiotic prototypes

Renata B. Lacerda [a,b], Cleverton K. F. de Lima [a,c], Leandro L. da Silva [a,c], Ana Luisa P. Miranda [a,c], Eliezer J. Barreiro [a,b,c], Carlos A. M. Fraga [a,b,c,*]

[a] Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio), Faculty of Pharmacy, Federal University of Rio de
[b] Programa de Pós-Graduação em Química, Chemistry Institute, Federal University of Rio de Janeiro, Rio de Janeiro, RJ,
[c] Programa de Pós-Graduação em Farmacologia e Química Medicinal, Institute of Biomedical Sciences, Federal Universit

doi: 10.1111/j.1472-8206.2012.01076.x

Radiation Physics and Chemistry 95 (2014) 292–295

Contents lists available at ScienceDirect

Radiation Physics and Chemistry

journal homepage: www.elsevier.com/locate/radphyschem

Synchrotron X-ray powder diffraction data of LASSBio-1515: A new *N*-acylhydrazone derivative compound

F.N. Costa [a,*], D. Braz [a], F.F. Ferreira [b], T.F. da Silva [c,d], E.J. Barreiro [c,d], L.M. Lima [c,d], M.V. Colaço [e], L. Kuplich [e], R.C. Barroso [e]

International Journal of Cardiology 173 (2014) 154–162

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Vasodilator and antihypertensive effects of a novel *N*-acylhydrazone derivative mediated by the inhibition of L-type Ca^{2+} channels

Sharlene Lopes Pereira[a], Arthur Eugen Kummerle[b], Carlos Alberto Manssour Fraga[a,c], Eliezer Jesus Barreiro[a,c], Roberto Takashi Sudo[a,c], Gisele Zapata-Sudo[a,c,*]

OPEN ACCESS Freely available online

PLOS ONE

N-acylhydrazone derivative ameliorates monocrotaline-induced pulmonary hypertension through the modulation of adenosine AA2R activity

Allan K.N. Alencar [a,1], Sharlene L. Pereira [a,1], Flavia E. da Silva [a,1], Luiza V.P. Mendes [b,1], Valéria do M.N. Cunha [b,1], Lidia M. Lima [a,1], Tadeu L. Montagnoli [a,1], Celso Caruso-Neves [d,1], Emanuelle B. Ferraz [d,1], Roberta Tesch [a,1], arlos M.R. Sant'Anna [c,1], Carlos A.M. Fraga [a,1], Eliezer J. Barreiro [a,1], apata-Sudo [a,*,1]

Novel Potent Imidazo[1,2-*a*]pyridine-*N*-Glycinyl-Hydrazone Inhibitors of TNF-α Production: *In Vitro* and *In Vivo* Studies

Renata B. Lacerda[1,2], Natália M. Sales[3,5], Leandro L. da Silva[3,4], Roberta Tesch[1,3], Ana Luisa P. Miranda[3,4], Eliezer J. Barreiro[1,2,3], Patricia D. Fernandes[3,5], Carlos A. M. Fraga[1,2,3]*

LASSBio
Laboratório de Avaliação e Síntese de Substâncias Bioativas

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Universidade Federal do Rio de Janeiro

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Subject Area

- Biochemistry, Genetics and Molecular Biology (1)
- Immunology and Microbiology (1)
- Neuroscience (1)
- Pharmacology, Toxicology and Pharmaceutical Science (1)

Year

- 2014 (1)
- 2013 (2)
- 2012 (2)
- 2008 (1)
- 2007 (2)

Keywords

- amnesia
- cholinergic
- escape latency
- nicotinic
- nicotinic receptors

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Piperidinic derivatives, pharmaceutic compositions containing the same and preparation processes
UNITED STATES PATENT AND TRADEMARK OFFICE GRANTED PATENT, September 2012
(+) Viegas, Cláudio ; Bolzani, Vanderlan da Silva ; Barreiro, Eliezer Jesus De Lacerda ; Castro, Newton G. ; Young, Maria Cláudia Marx ; Rocha, Mônica Santos (VIEGAS JR CLAUDIO ; BOLZANI
Full text available at patent office. For more in-depth searching go to LexisNexis

HETEROCYCLIC N-GLYCINYL-N-ACYL HYDRAZONE COMPOUNDS, SYNTHESIS METHOD, PHARMACEUTICAL COMPOSITIONS AND TREATMENT METHOD
PATENT COOPERATION TREATY APPLICATION, June 2013
(+) MANSSOUR FRAGA CARLOS ALBERTO ; DE LACERDA BARREIRO ELIEZER DE JESUS ; BARBOSA LACERDA RENATA ; PALHARES DE MIRANDA ANA LUISA ;
Full text available at patent office. For more in-depth searching go to LexisNexis

UREIDIC COMPOUNDS, PHARMACEUTICAL COMPOSITIONS CONTAINING THE SAME AND THEIR USE ON THE TREATMENT OF INFLAMMATORY DISEASES
PATENT COOPERATION TREATY APPLICATION, December 2006
(+) LACERDA BARREIRO, Eliezer Jesus de ; MANSSOUR FRAGA, Carlos Alberto ; SPERÄNDIO DA SILVA, Gilberto Marcelo ; MOREIRA LIMA, Lidia ; MEDEIROS DE CARVALHO, Fátima ;
Full text available at patent office. For more in-depth searching go to LexisNexis

PIPERIDINIC DERIVATIVES, PHARMACEUTIC COMPOSITIONS CONTAINING THE SAME AND PREPARATION PROCESSES
PATENT COOPERATION TREATY APPLICATION, April 2006
(+) VIEGAS, Claudio ; BOLZANI, Vanderlan da Silva ; DE LACERDA BARREIRO, Eliezer, Jesus ; CASTRO, Newton G. ; YOUNG, Maria, Cláudia, Marx ; ROCHA, Mônica, Santos
Full text available at patent office. For more in-depth searching go to LexisNexis

HYDRAZIDE-N-ACYLHYDRAZONE COMPOUNDS, METHOD FOR PRODUCING HYDRAZIDE-N-ACYLHYDRAZONE COMPOUNDS, USE OF INTERMEDIATE COMPOUNDS FOR PRODUCING HYDRAZIDE-N-ACYLHYDRAZONES FOF THE TREATMENT OF LEISHMANIASIS AND CHAGAS DISEASE, AND THUS OBTAINED PHARMACEUTICAL COMPOSITIONS
PATENT COOPERATION TREATY APPLICATION, February 2014
LIDIA MOREIRA LIMA ; ELIEZER JESUS DE LACERDA BARREIRO ; MARINA AMARAL ALVES (UNIV RIO DE JANEIRO ; UNIV FED DE ALAGOAS)
Full text available at patent office. For more in-depth searching go to LexisNexis

Processes for the preparation of piperidinic derivatives and pharmaceutic compositions containing the same
UNITED STATES PATENT AND TRADEMARK OFFICE GRANTED PATENT, May 2013
(+) Viegas, Claudio ; Bolzani, Vanderlan da Silva ; Barreiro, Eliezer Jesus de Lacerda ; Castro, Newton G. ; Young, Maria Claudia M
Full text available at patent office. For more in-depth searching go to LexisNexis

Piperidinic derivatives, pharmaceutic compositions containing the same and preparation processes
UNITED STATES PATENT AND TRADEMARK OFFICE GRANTED PATENT, September 2012
(+) Viegas, Claudio ; da Silva Bolzani, Vanderlan ; De Lacerda Barreiro, Eliezer Jesus ; Castro, Newton G. ; Marx, Maria Claudio ; F
Full text available at patent office. For more in-depth searching go to LexisNexis

PHARMACEUTICAL COMPOSITIONS CONTAINING 1-METHYL-3,6,7,8- TETRAHYDROPIRAZOLO[3,4-b]PIRROLO[4,3-d PROCESS FOR PREPARING THEM
PATENT COOPERATION TREATY APPLICATION, September 2006
(+) DE LACERDA BARREIRO, Eliezer de Jesus ; MANSSOUR FRAGA, Carlos Alberto ; ZAPATA SUDO, Gisele ; TAKASHI SUDO, Roberto ; MENEGATTI, Ricardo (UNIVERSIDADE FEDERAL
Full text available at patent office. For more in-depth searching go to LexisNexis

Área de Trabalho | Bibliotecas | Eliezer J Barreiro | PT | 10:31

Consideração final:

ACS Medicinal Chemistry Letters

medicinal chemistry

Drug Discovery in an Academic Setting: Playing to the Strengths

Donna M. Huryn*

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Inter-alia: S Laufer, U Holzgrabe, D Steinhilber, Drug Discovery: A modern decathlon, *Angew. Chem. Int. Ed*. **2013**, *52*, 4072; A S Kesselheim, J Avorn, The most transformative drugs of the past 25 years: a survey of physicians, *Nature Rev. Drug Discov*. **2013**, *12*, 425; H Wild, C Huwe, M Lessl, Collaborative Innovation — Regaining the Edge in Drug Discovery, *Angew. Chem. Int. Ed*. **2013**, *52*, 2684; W L Jorgensen, Challenges for Academic Drug Discovery, *Angew. Chem. Int.Ed.* **2012**, *51*,11680; S Frye et al., US Academic Drug Discovery, *Nature Rev. Drug Discov.* **2011**, *10*, 409; C J Tralau-Stewart et al., Drug Discovery: New models for Industry-Academic partnerships, *Drug Discov. Today* **2009**, *14*, 95; PG Wyatt, The emerging academic drug discovery sector, *Future Med. Chem*. **2009**, *1*, 1013.

" 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"

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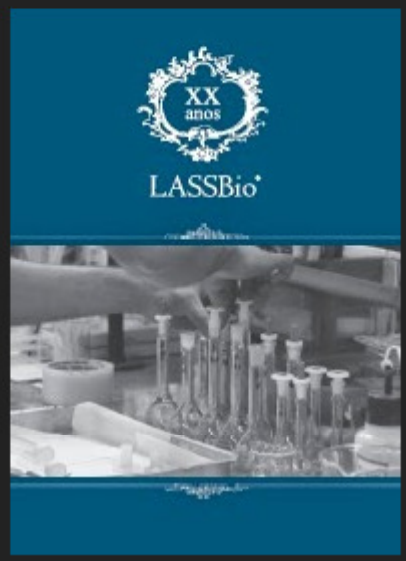

O registro da história é sempre necessário para garantirmos a construção de uma memória fiel. Na verdade, estas palavras, além de rimarem, referem-se ao passado, ao que já vivemos, ao que já foi vivido. Entretanto, se sob esta ótica podem sugerir apenas lembranças, documenta-las representa o cumprimento e o exercício de cidadania, sobretudo quando dizem respeito a realizações coletivas, assegurando a

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