Novos aspectos da terapia do câncer: fármacos multialvos

New aspects of cancer therapy: multi-target drugs

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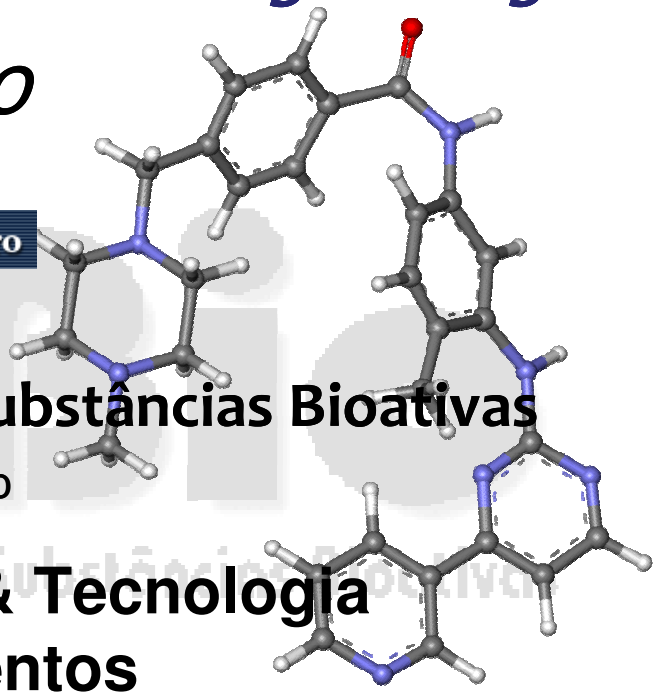
http://www.farmacia.ufrj.br/lassbio

Instituto Nacional de Ciência & Tecnologia
Fármacos & Medicamentos

INCT-INOFAR

http://www.inct-inofar.ccs.ufrj.br



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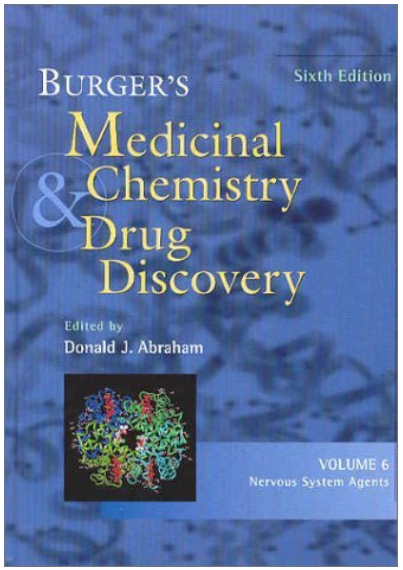
Summary

- A Medicinal Chemistry approach
- The Fischer-Ehrlich paradigm
- Drug innovation in the 20th century
- ***M***ultifactorial ***D***iseases – ***M***ulti-target ***D***rugs (MTD)
- FBDD & MTDD & Cancer
- TK's inhibitors: the change of paradigm
- INCT-INOFAR & anti-cancer new leads
- INCT-INOFAR in the incremental innovation
- Concluding remarks
- Acknowledgments

Approach

medicinal chemistry

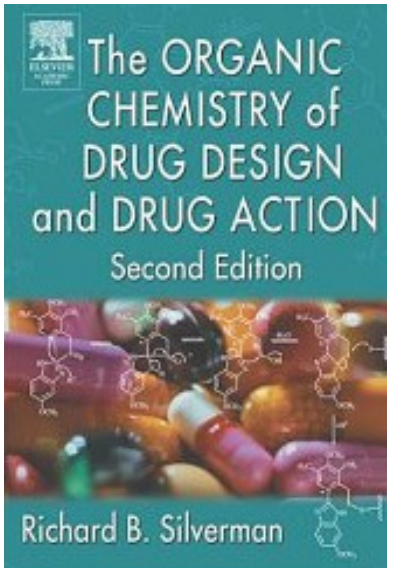


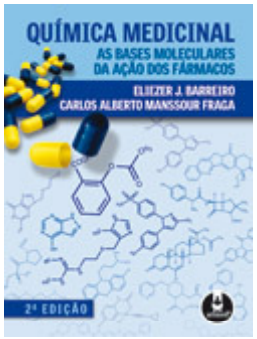
"Medicinal Chemistry tried to be based on the ever-increasing hope that biochemicals rationales for drug discovery "

Alfred Burger, 1980

Richard B. Silverman, 1992

"Medicinal Chemistry is the *science* that deals with the discovery or design of new therapeutic chemicals and their development into useful medicines..."





TheFischer-Ehrlich paradimg

Emil Fischer
1852-1919
1902

1908

Paul Ehrli
1854-1915

LOCK & KEY
CONCEPT

+

1900

postulated the existence of specific receptors,
ociated with cells or distributed in the blood

K Strebhardt & A Ullrich, Paul Ehrlich magic bullet concept: 100 years of progress, *Nature Rev. Cancer* **2008**, *8*, 473

Receptor
macromolecule
Structure-based DD

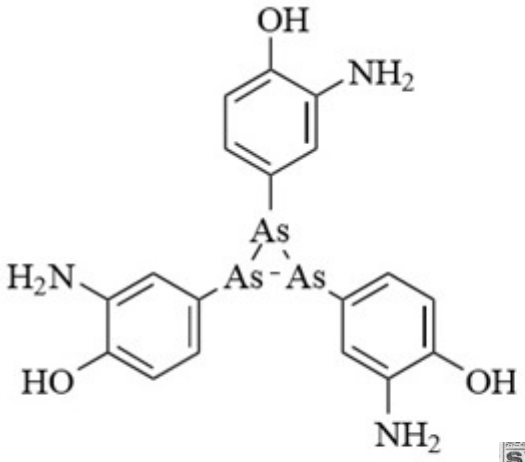
Rational Drug Design (20th century)

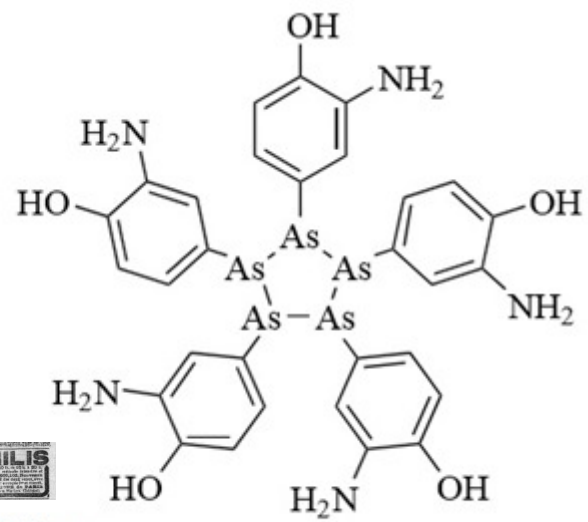
Drug
Small molecule
Ligand-based DD

One-molecule, one-target

20th Century

Drugs innovation in the 20th century





Mono-target

Salvarsan

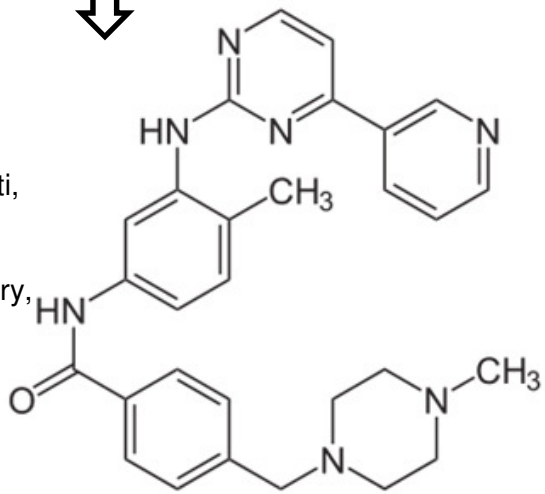
1909

Ehrlich & Hata

NC Lloydet al., *The composition of Ehrlich's salvarsan: resolution of a century-old debate, Angew. Chem. Int. Ed. Engl.* ***2005****, 44,* 941.

Multi-target

J. L. Medina-Franco, M. A. Giulianotti, G. S. Welmaker, R. A. Houghten, Shifting from the single to the multitarget paradigm in drug discovery, *Drug Discov. Today* **2013**, *18*, 495



Imatinib

1902

Innovation

1905 – Introduced

1912 – the leading drug

"Arsenic-containing drug"

~1.5 year

translational

~100y

translational

Authentic innovation

Novartis

<< 10 anos

Innovation

2001

C. S. Fishburn, Translational research The changing landscape of drug discovery, *Drug Discov Today* **2013**, *18*, 487.

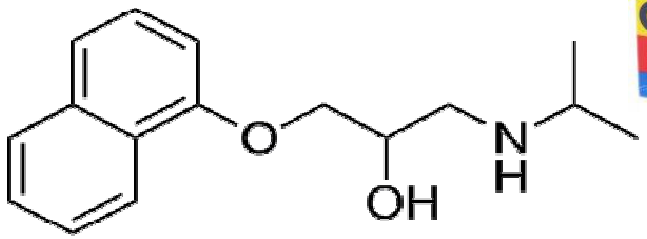
Drug Innovation during 20th Century

1964

propranolol
cimetidine
captopril
omeprazole

paclitaxel
lovastatin
penicillin

1942



Mono-target

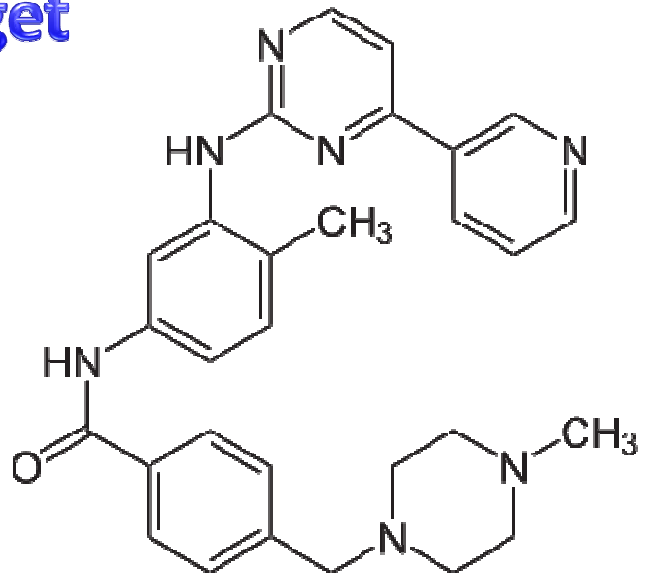
Multi-target drug design

2001

imatinib

Multi-target

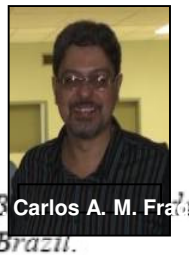
Therapeutic innovations



Current Drug Therapy, 2008, *3*, 1-13

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

Eliezer J. Barreiro and Carlos Alberto Manssour Fraga

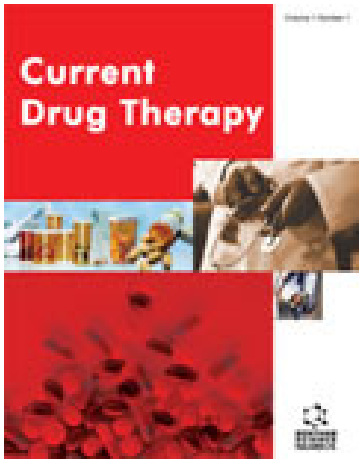


medicinal chemistry

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.



& "WHO has recently recognized that noncommunicable diseases such as cardiovascular, diabetes, cancer, respiratory and neurological disorders are now also a great emerging epidemic *among the poor*"

& AB Reitz, Future horizons in drug discovery research, *ACS Med. Chem. Lett.* **2012**, *3*, 80

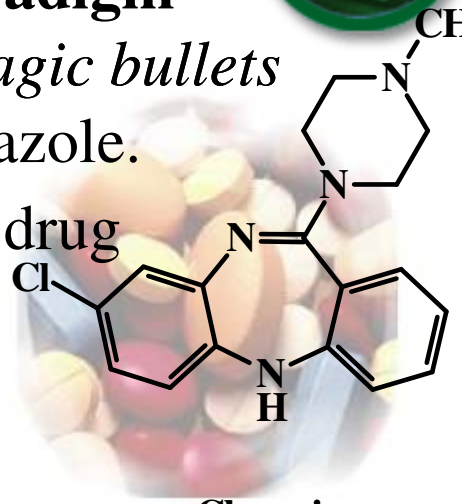
JL Medina-Franco, MA Giulianotti, GS Welmaker, RA Houghten, Shifting from the single to the multitarget paradigm in drug discovery, *Drug Discov Today* **2013**, *18,* 495; S Reardon, A world of chronic disease, *Science* **2011**, *333*, 558.

- **One-target-one-ligand: the 20th century paradigm**

  One-ligand / one-disease – *Lock & Key & Magic bullets*

  e.g. propranolol, cimetidine, captopril, omeprazole.

  Clozapine (1971), an "*atypical*" neuroleptic drug has affinity for the D_4 central receptor & D_2, D_3, 5-HT_{2A}, 5-HT_3, α1 and α2, is an exception considered as "*promiscous*" drug.



Clozapine

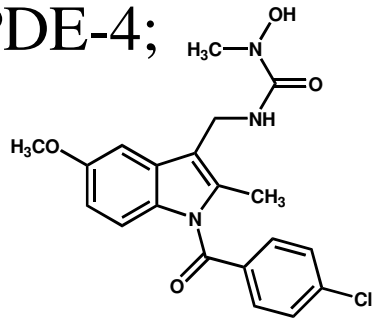
- **Ligands for <u>multi-target</u>: the 21th Century paradigm**

  Dual, binary, dimeric, bivalent, symbiotic = multiple ligands:

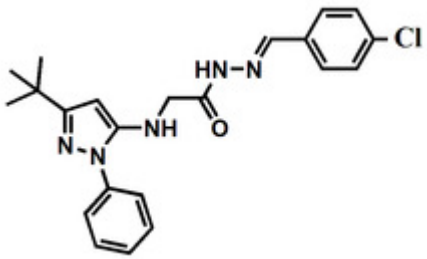
  5-LOX/COX-2 ; TXS/TP_{ant}; COX-1/LTA_4 hydrolase;

  5-$HT_{1A}R_{ant}$/SSRI; TP_{ant}/IP_{ag}; SSRI/PDE-4; PDE-3/PDE-4

  TNFα/PDE-4;

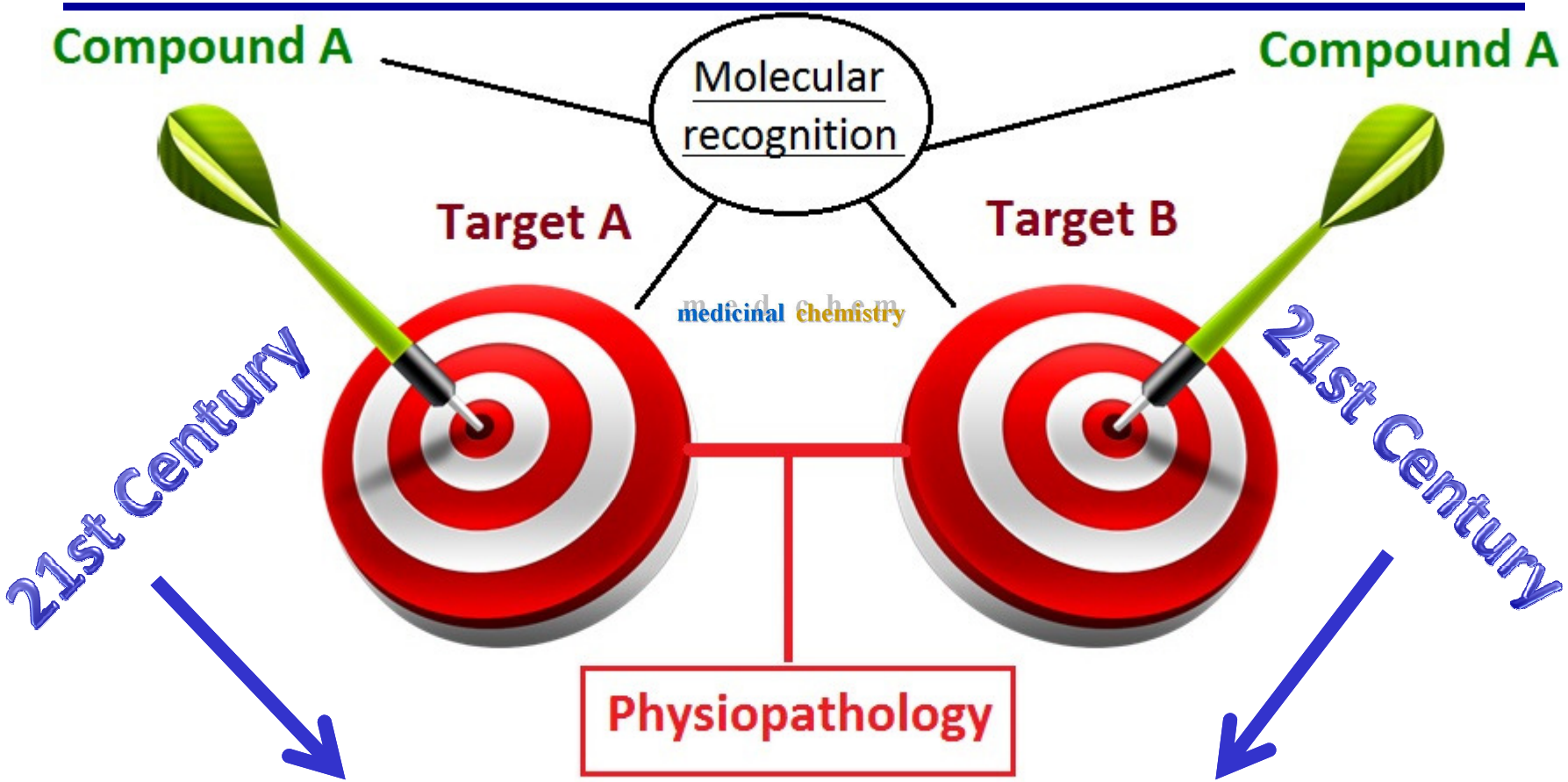


Leval, 2002



Lacerda, 2012

The multi-target lead-candidate design



The multi-target approach is related to a new lead-compound with a dual recognition pattern by receptors wdhich are involved with a disease pathology, in general multi-factorial. A multiple lead with this profile can be structurally designed by combining molecular pharmacophoric fragments for each target.

Simple drugs do not cure complex multifactorial diseases!

The rational-based design of multiple ligand

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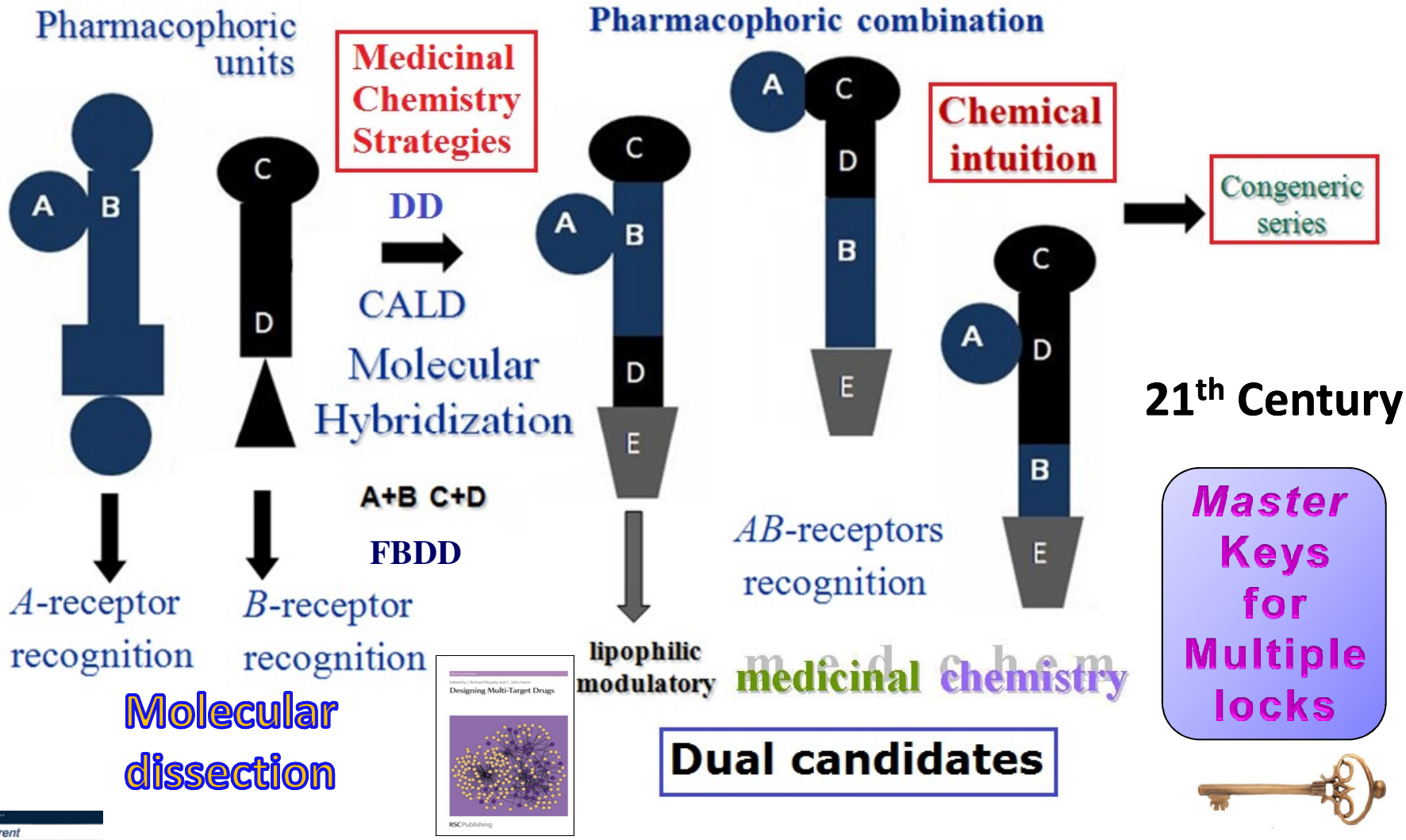


J R Morphy, C J Harris, Eds, Designing Multi-Target Drugs , RSC, 2012.

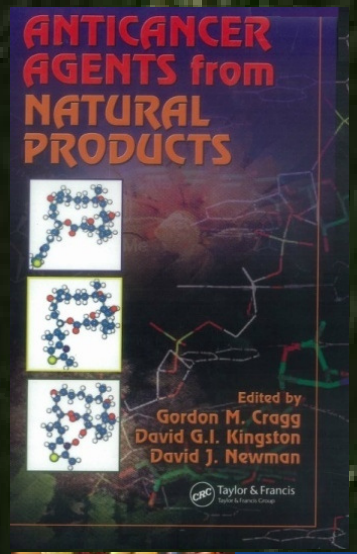
C Viegas-Jr, A Danuello, VS Bolzani, EJ Barreiro, CAM Fraga, Molecular Hybridization: A useful tool in the design of new drug prototypes, *Curr Med Chem* **2007**, *14*, 1829

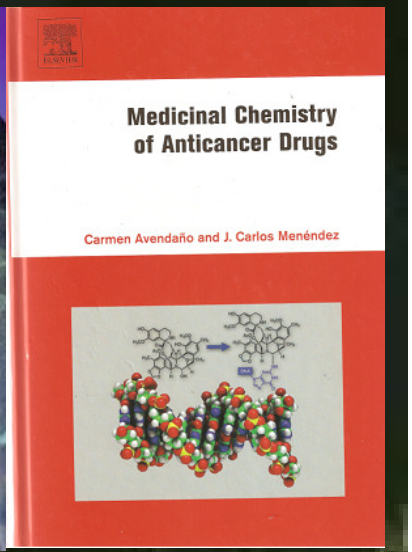
DA Erlanson, RS McDowell, T O'Brien, Fragment-Based Drug Discovery, *J Med Chem* **2004**, *47*, 3463;

Quimioterapia do Câncer

Produtos naturais

Alcalóides Vinca, colcichina
Derivados da podofilotoxina
Camptotecina & análogos
Taxóides (paclitaxel, docetaxel, ortataxel, cabazitaxel)
Epotilona-B (*e.g.* Ixabepilona)
Ecteinascidina (Yondelis^{R})





INCA INSTITUTO NACIONAL DE CÂNCER

GM Cragg, PG Grothaus, DJ Newman, Natural products in drug discovery: recent advances, em Plants Bioactives & Drug Discovery, V Cechinel Filho Ed., Wiley, 2012, p. 1- 42.

AL Demain, P Vaishnav, Natural products for cancer chemotherapy, *Microbial Biotechnology* 2011, *6*, 687; D Shewach, Introduction to cancer chemotherapeutis, *Chem. Rev.* 2009, *109*, 2859 (*Special Issue*); A Conlin, M Fornier, C Hudis, S Kar, P. Kirkpatrick, *Nature Rev. Drug Discov.* 2007, *6*, 953;

Journal of Medicinal Chemistry

Perspective

pubs.acs.org/jmc

J. Med. Chem. 2012, 55, 8199–8208

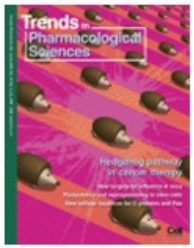
Potential Use of Selective and Nonselective Pim Kinase Inhibitors for Cancer Therapy

Miniperspective

Denis Drygin,[†] Mustapha Haddach,[‡] Fabrice Pierre,[§] and David M. Ryckman*[,†]

Review

Trends in Pharmacological Sciences March 2012, Vol. 33, No. 3



Targeting Src family kinases in anti-cancer therapies: turning promise into triumph

Siyuan Zhang and Dihua Yu

Department of Molecular and Cellular Oncology, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA

Sphingosine 1-phosphate and cancer

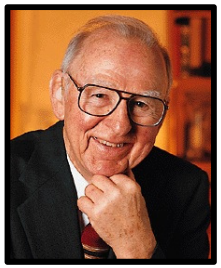
Nigel J. Pyne and Susan Pyne

Abstract | There is substantial evidence that sphingosine 1-phosphate (S1P) is involved in cancer. S1P regulates processes such as inflammation, which can drive tumorigenesis; neovascularization, which provides cancer cells with nutrients and oxygen; and cell growth and survival. This occurs at multiple levels and involves S1P receptors, sphingosine kinases, S1P phosphatases and S1P lyase. This Review summarizes current research findings and examines the potential for new therapeutics designed to alter S1P signalling and function in cancer.

NATURE REVIEWS | CANCER 2010, *10*, 489

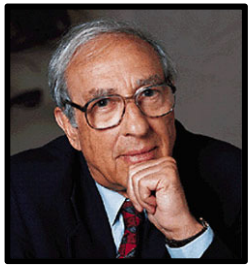
D-Y Lu, T-R Lu, H-Y Wu, S. Cao, Cancer Metastasis Treatments, *Current Drug Therapy*, **2013**, *8*, 24;
M. Rask-Andersen, M.S. Almén, H. B. Schiöth, Trends in the exploitation of novel drug targets, *Nature Rev. Drug Discov*. **2011**, *10*, 579.

Tinib´s: TK's inhibitors

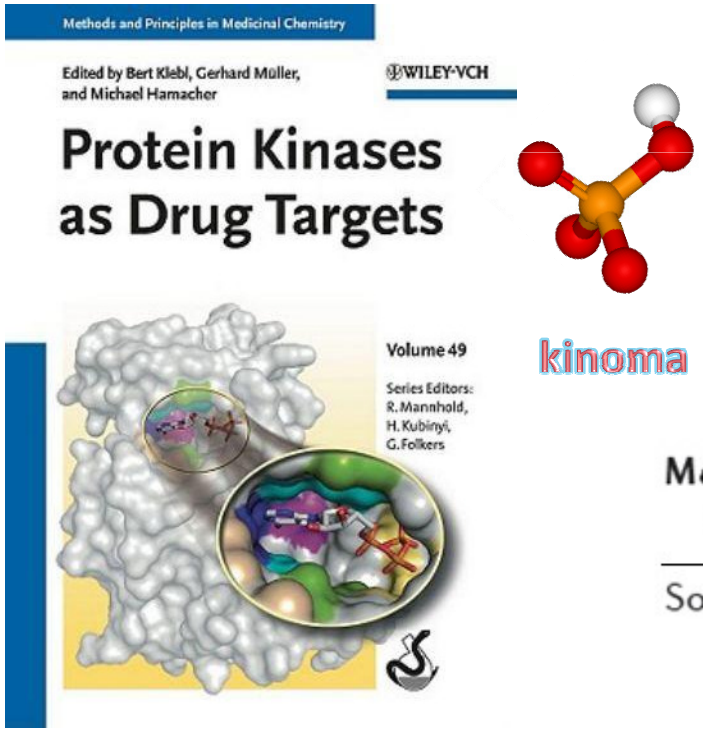


Edwin G Krebs
(1918 –2009)

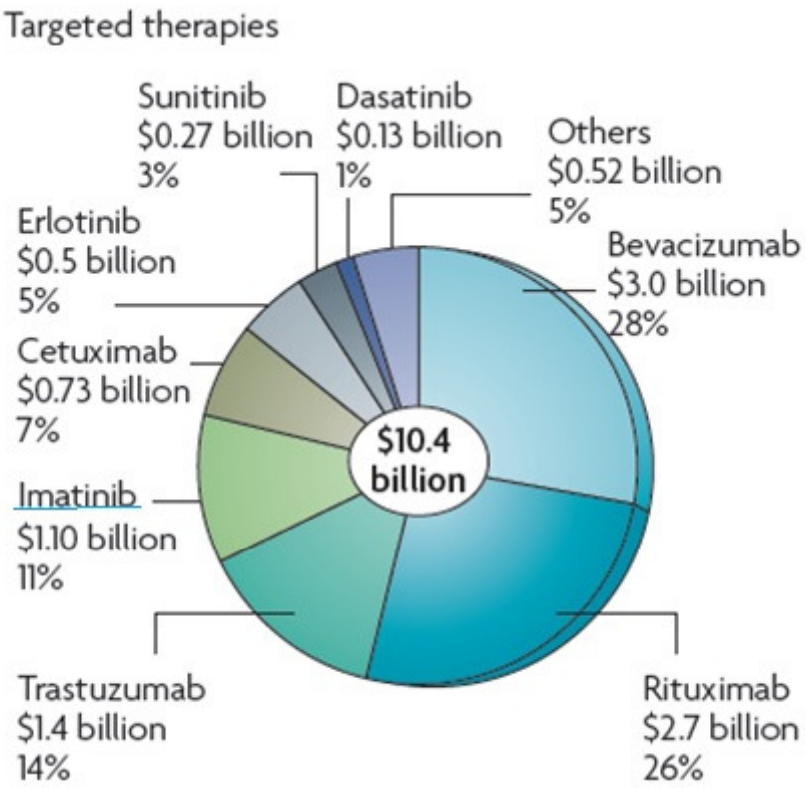
1992



Edmond H Fischer
(1920)



kinoma



Market for targeted cancer therapies. US sales of targeted therapies share of the US market based on 2009 sales.

Sources: company reports

World sales of imatinib in 2009: US$ 3,95 bi

S. Aggarwal, Targeted cancer therapies, *Nature Rev. Drug Discov.* **2010**, *9*, 427; P. Cohen, Timeline: Protein kinases — the major drug targets of the twenty-first century? *Nature Rev. Drug Discov.* **2002**, *1*, 309

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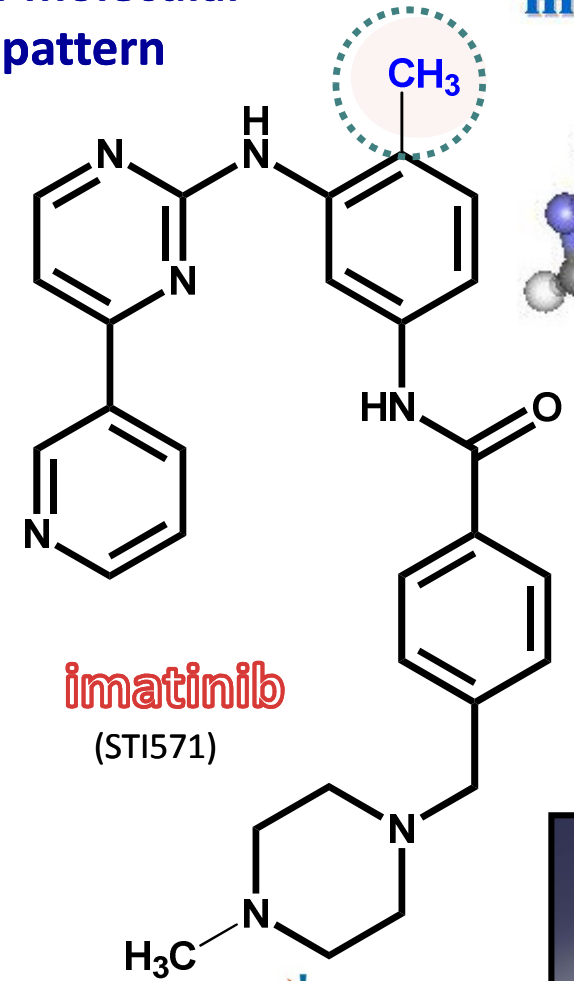
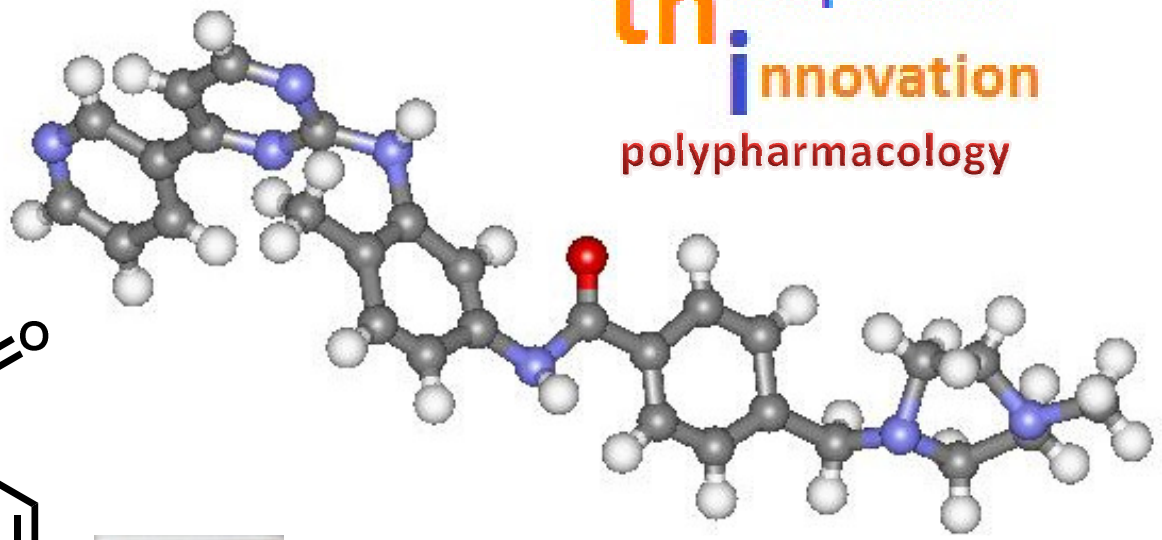
New molecular pattern

medicinal chemistry

therapeutic innovation

polypharmacology





imatinib

(STI571)

1988 – Nicholas Lydon, Brian J. Druker & Charles L Sawyers &
1995 - Compound STI571 ++
2001 – Imatinib (Gleevec^{R}, Novartis)[link]

chronic myelogenous leukemia (CML)

NOVARTIS

imatinibe

Nicholas B. Lydon
Blueprint Medicines Inc*

OREGON HEALTH & SCIENCE UNIVERSITY

Brian J. Druker*
Blueprint Medicines Inc

HHMI HOWARD HUGHES MEDICAL INSTITUTE

Charles L. Sawyers**
Blueprint Medicines Inc

& 2009 - Lasker Foundation Clinical Award (*J. Clin. Invest*. **2009**, *119*, 2863)

* B. J. Druker has been awarded with the 2012 Japan Prize in Healthcare and Medical Technology;

** C. L. Sawyers was named in 2011, Thomson Reuters Citation Laureate in Medicine;

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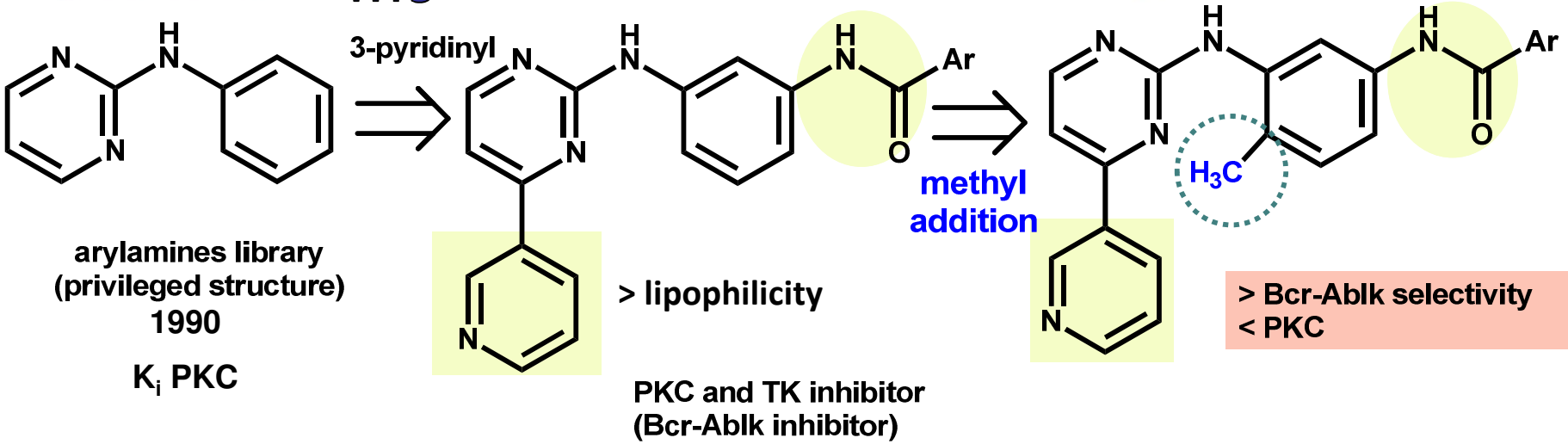
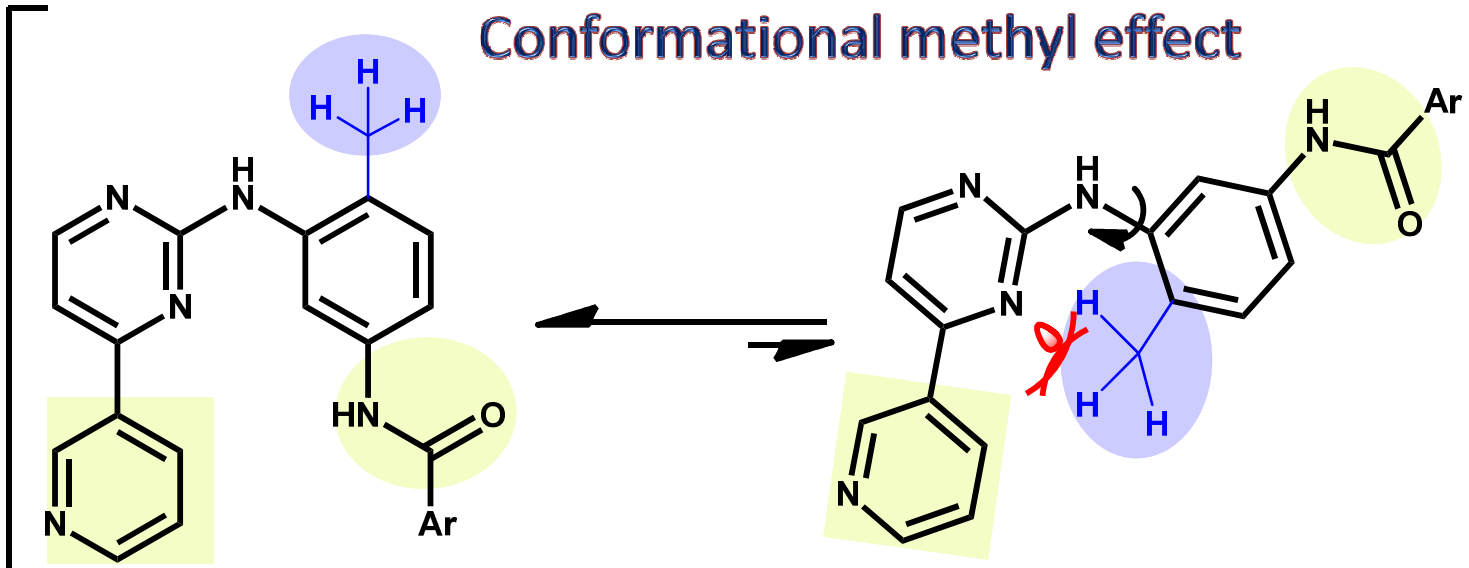
NOVARTIS

HTS

medicinal chemistry

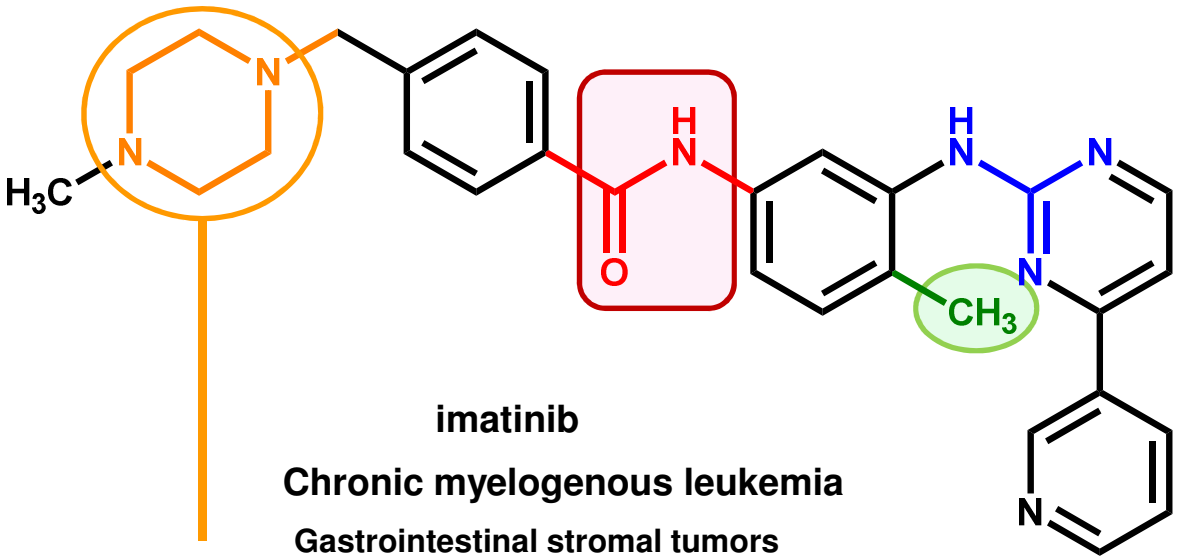


Conformational methyl effect



Steric hindrance leads to an arylamine bond rotation

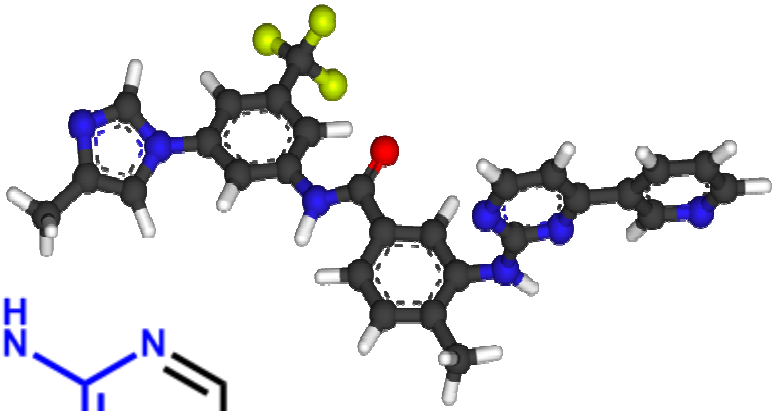
E.J.Barreiro, A.E.Kümmerle, C.A.M.Fraga, The methylation effect in medicinal, Chemistry, *Chem. Rev*. **2011**, *111*, 5215

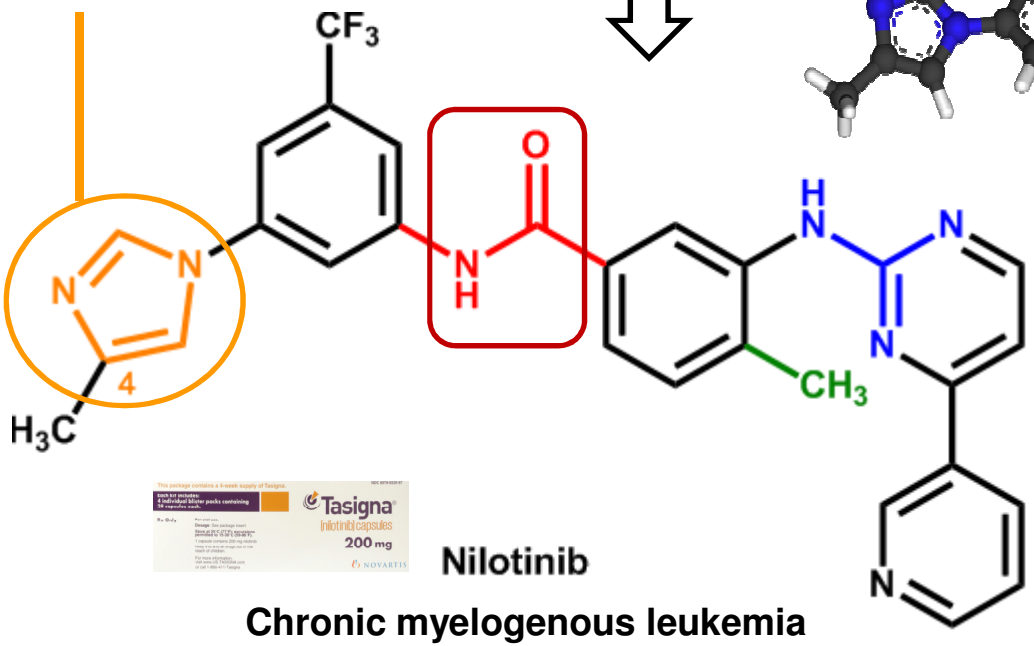


imatinib

Chronic myelogenous leukemia

Gastrointestinal stromal tumors





Nilotinib

Chronic myelogenous leukemia

Combination with other drugs (*e.g.* taxoids) is useful to CML imatinib-resistant cells (20 times more potent than imatinib)

PW Manley, J Zimmermann in Case Studies in Modern Drug Discovery and Development, X Huang & RG Aslanian, Eds.,Wiley, **2012**, p.88

GOVERNMENT & POLICY

INDIA'S PATENT POLICY RILES U.S.

U.S. government joins pharmaceutical firms in objections to INTELLECTUAL PROPERTY PRACTICES

GLENN HESS, C&EN WASHINGTON

MEDICINE Dr. Shyam Agrawal displays a pack of the Indian-made cancer drug named 'Veenat 400,' a generic form of Novartis' Gleevec.

CEN.ACS.ORG

SEPTEMBER 2, 2013

http://judis.nic.in/supremecourt/imgs1.aspx?filename=40212

C Harrison, Indian Supreme Court blocks Novartis' Glivec patent, *Nature Rev. Drug Discov.* **2013**, *12*, 336

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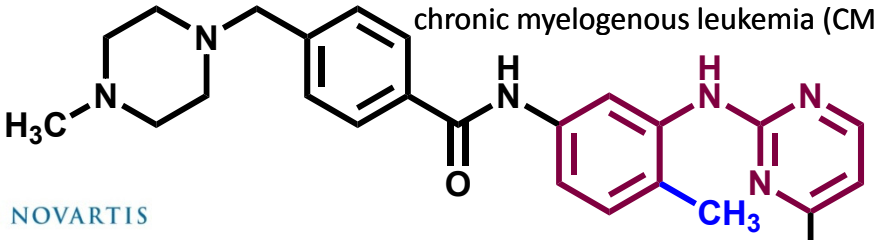
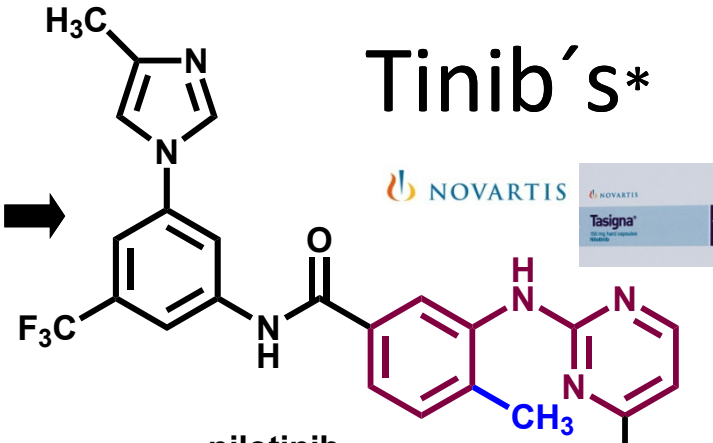
chronic myelogenous leukemia (CML) &



NOVARTIS

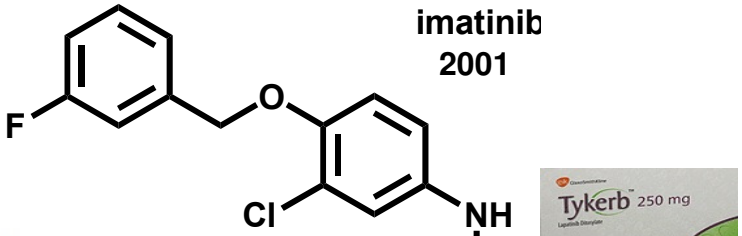
imatinib
2001

Tinib´s*

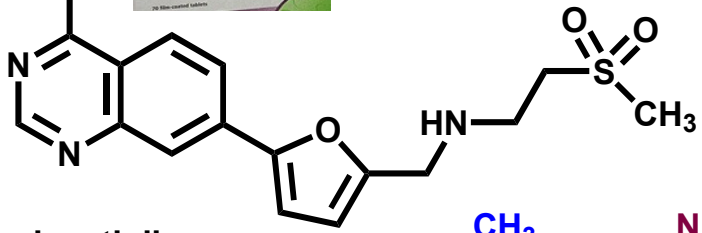


NOVARTIS

nilotinib
2006

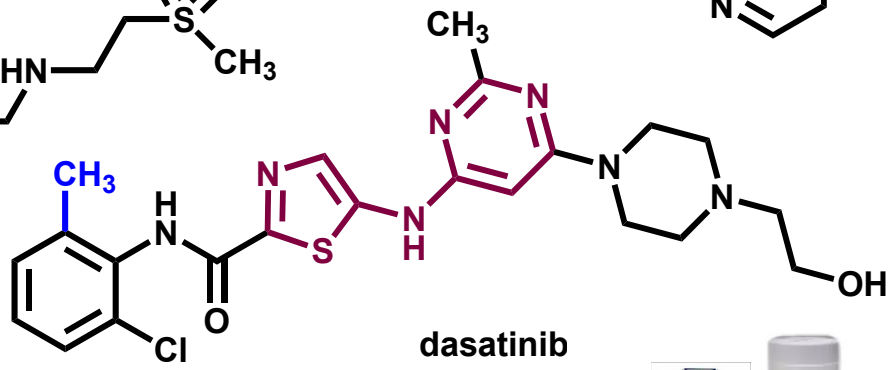


therapeutic innovation

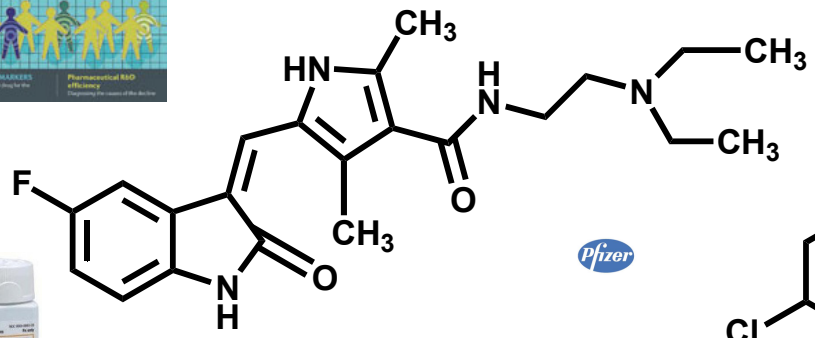


gsk

lapatinib
2007

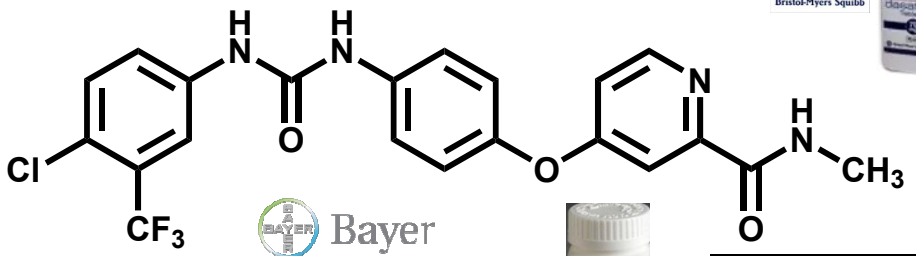


dasatinib
2007



Pfizer

sunitinib
2006



Bayer

sorafenib
2007

2011- crizotinib
2012- bosutinib

Pfizer

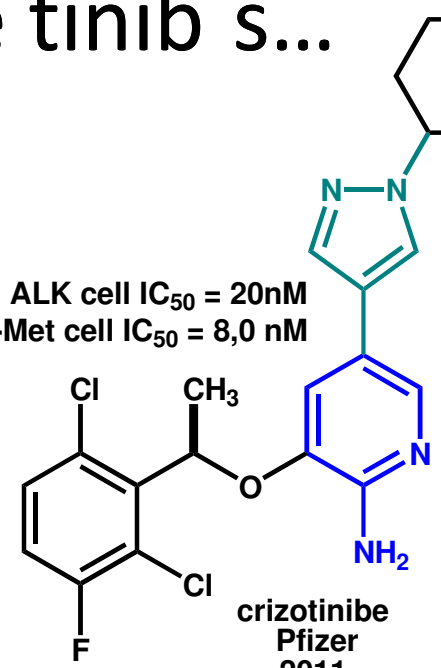
- **US market in 2009: US$ 18,5 bi ***
- **Imatinib world sales in 2009: US$ 4,0 bi***

- S Aggarwal, *Nature Rev Drug Discov* **2010**, *9*, 427

& R Ren, *Nature Rev Cancer* **2005**, *5*, 172

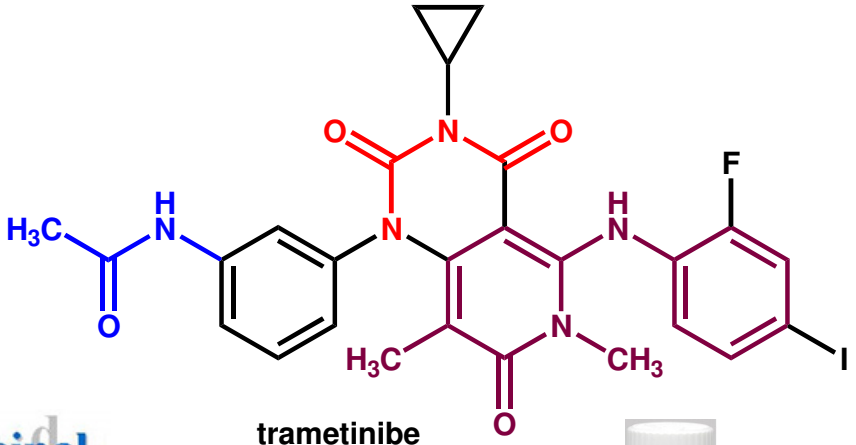
More tinib´s...

ALK cell IC_{50} = 20nM
C-Met cell IC_{50} = 8,0 nM

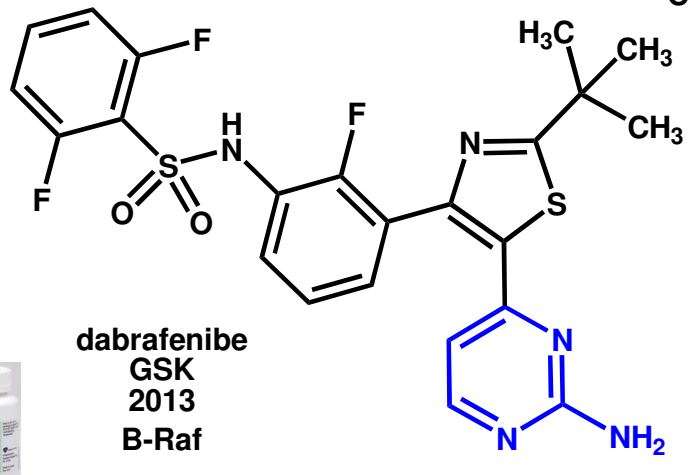


crizotinibe
Pfizer
2011

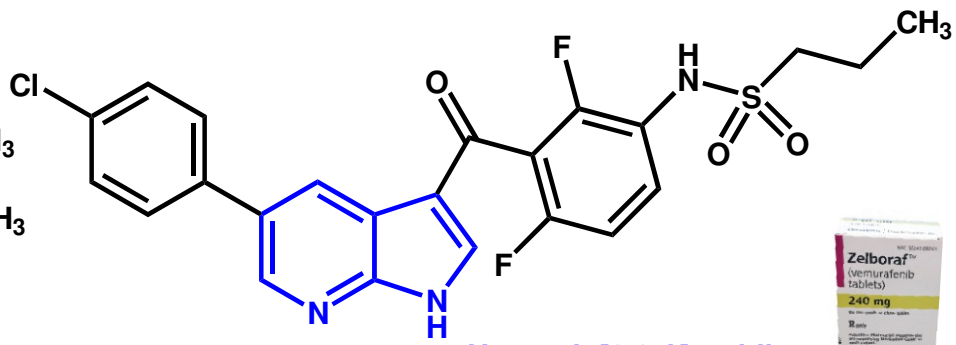
medicinal chemistry



trametinibe
GSK
2013
MEK1, MEK2 (MAPK/ERK)



dabrafenibe
GSK
2013
B-Raf



1*H*-pyrrolo[2,3-*b*]pyridine

vemurafenibe
Daiichi Co
2011
B-Raf/MEK/ERK

HER2; HSP90; mTOR; PARP1

fragment-based drug discovery (FBDD)

J.J. Cui et al., Structure Based Drug Design of Crizotinib (PF-02341066), a Potent and Selective Dual Inhibitor of MesenchymalEpithelial Transition Factor (c-MET) Kinase and Anaplastic Lymphoma Kinase (ALK), *J Med Chem* **2011**, *54*, 6342; A. Opar, New class of kinase inhibitors poised to join the anticancer arsenal, *Nature Rev. Drug Discov*. **2012**, *11*, 819; K Nguyen, Market watch: Upcoming market catalysts in Q2 2013, *Nature Rev.Drug Discov*. **2013**, *12*, 254; D.A. Erlanson, Introduction to Fragment-Based Drug Discovery, *Top. Curr. Chem.* **2012**, *317*, 1.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UFRJ
Instituto Nacional de Ciência e Tecnologia
em Fármacos & Medicamentos
(INCT-INOFAR)
INCT
inofar
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.

Articular competências...

... INCT-INOFAR.

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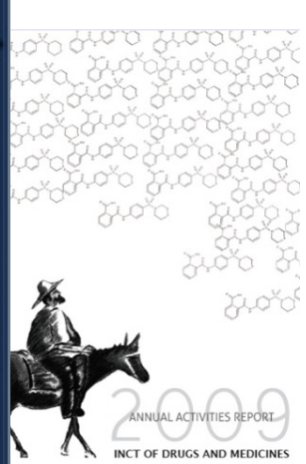
inct inofar

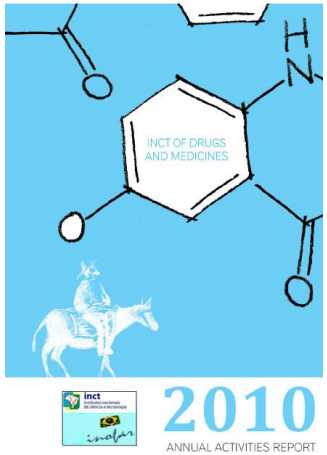
UNIVERSIDAD DE LA REPÚBLICA URUGUAY

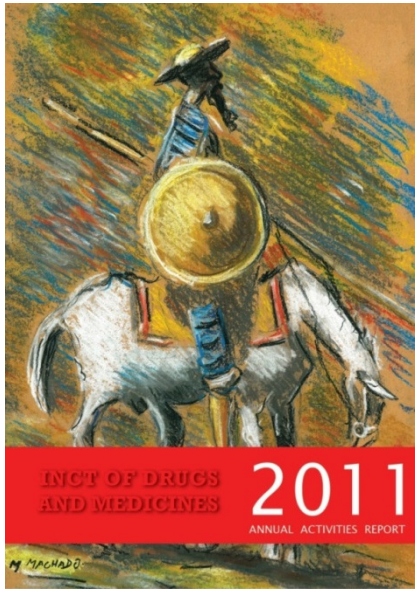
UNIVERSITÄT TÜBINGEN

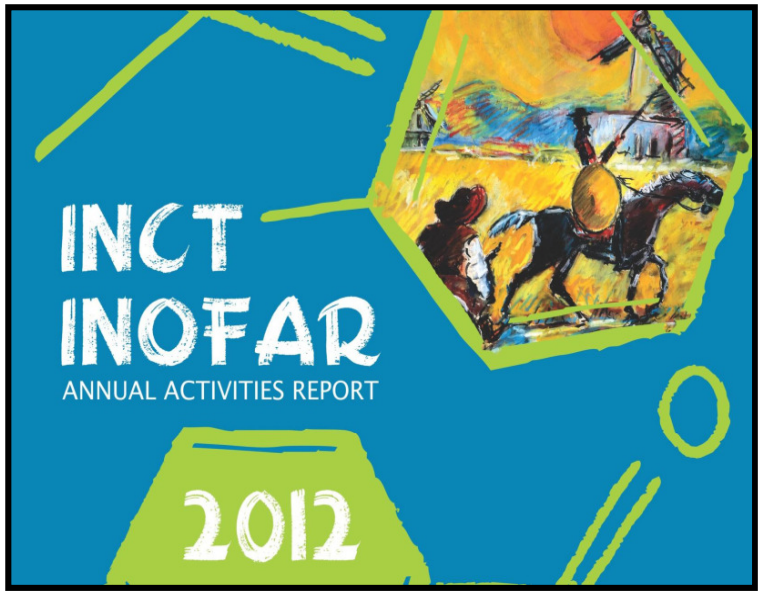
Annual Activities Report

(Public reports)





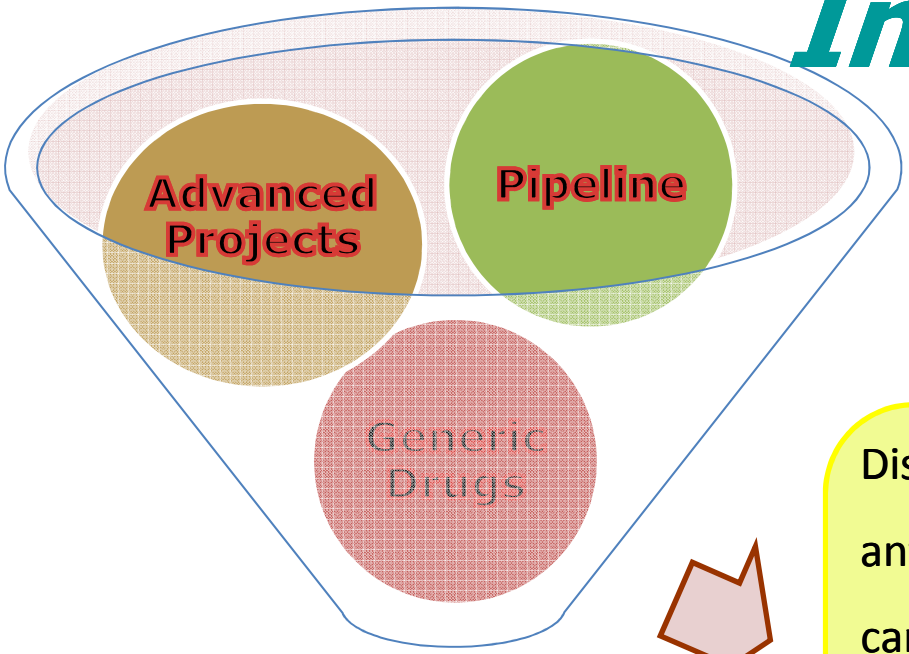


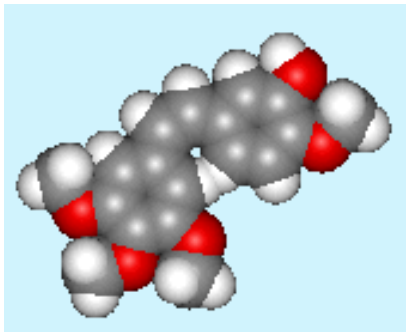


www.inct-inofar.ccs.ufrj.br/download/aar/2012.pdf

Interest areas: cancer;neuropathic pain; chronical inflammatory diseases: silicosis, asthma, COPD; CNS disorders as schizophrenia & neglected diseases as Leishmaniasis;

Inovação Radical





Biaryl

Discovery of novel anticancer drug candidates designed as novel combretastatin A4 analogues

LASSBio-UFRJ / FM-UFC

BR 10 2012 007619 5

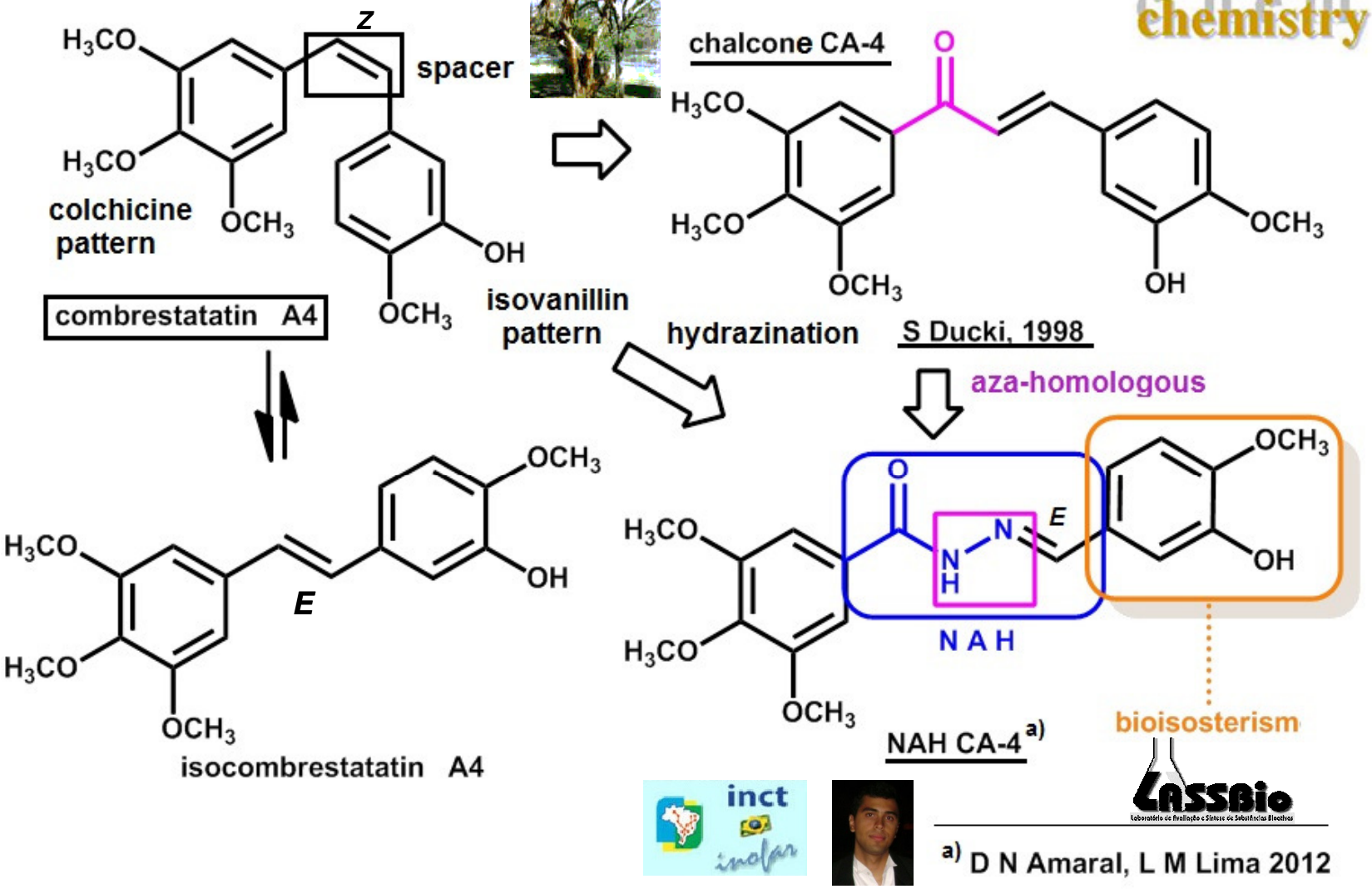
PCT BR 2013 000095

M. Abou-Gharbia, W. E. Childers, Discovery of Innovative Therapeutics: Today's Realities and Tomorrow's Vision. 1. Criticisms Faced by the Pharmaceutical Industry , *J. Med. Chem.* **2013**, *56*, 5659.

Universidade Federal do Rio de Janeiro

Combretum caffrum

medicinal chemistry

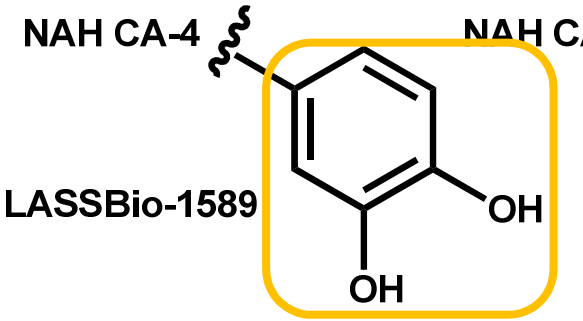


a) D N Amaral, L M Lima 2012

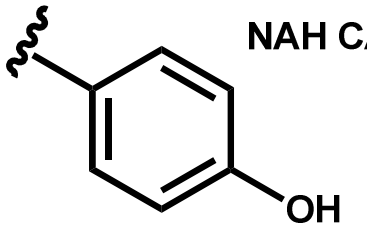
GM Tozer, C Kanthou, CS Parkins, SA Hill, The biology of the combretastatins as tumour vascular targeting agents, *Int. J. Exp. Pathol*. **2002**, *83*, 21; S. Ducki et.al., Potent Antimitotic and cell growth inhibitory properties of substituted chalcones, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1051; S Combes et al., Synthesis and Biological Evaluation of 4-Arylcoumarin Analogues of Combretastatins. Part 2, *J. Med. Chem*. **2011**, *54*, 3153; H Chen et al., Design and Synthesis of Cyclopropylamide Analogues of Combretastatin-A4 as Novel Microtubule-Stabilizing Agents, *J. Med. Chem.* **2013**, *56,* 685

NAH CA-4

LASSBio-1589

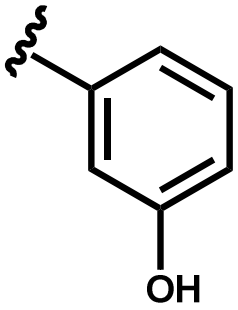


NAH CA-4



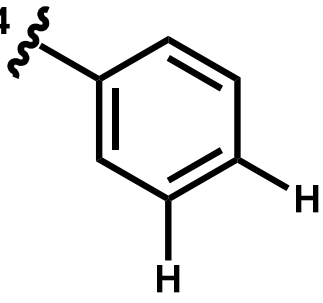
LASSBio-1588

NAH CA-4



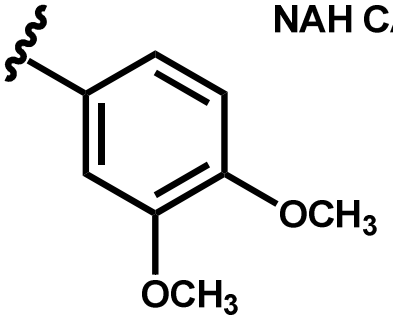
LASSBio-1587

NAH CA-4



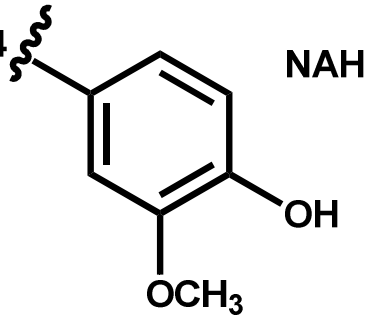
LASSBio-1586

NAH CA-4



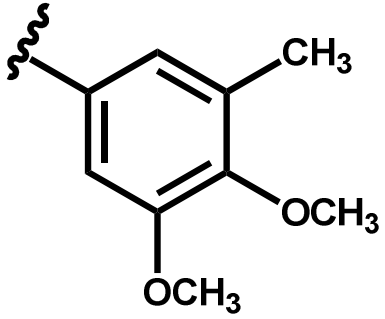
LASSBio-1590

NAH CA-4



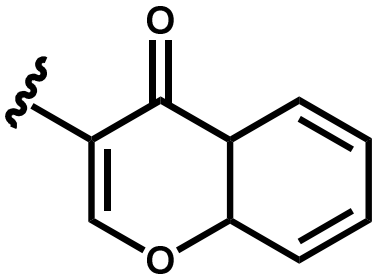
LASSBio-1593

NAH CA-4



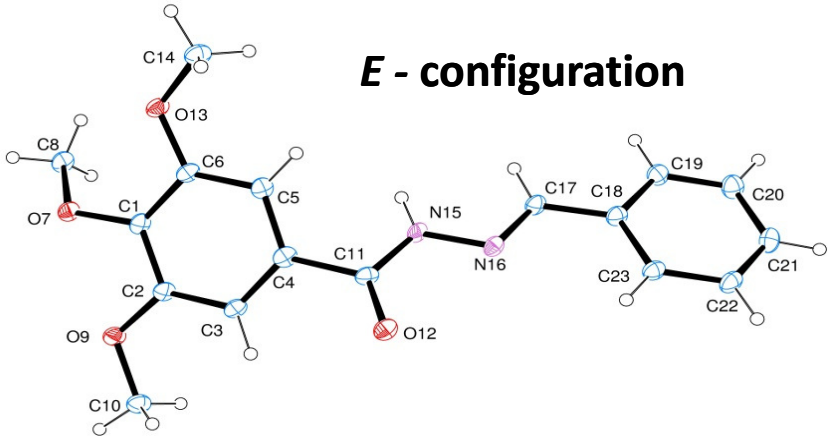
LASSBio-1594

NAH CA-4



LASSBio-1595

NAH



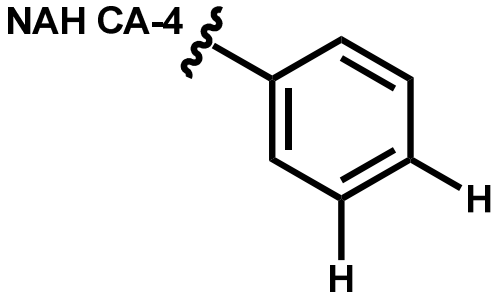
***E* - configuration**

DN Amaral, Dissertação de Mestrado, Instituto de Química, UFRJ, 2012.

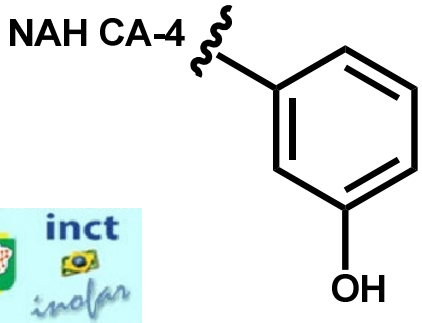
Antiproliferative activity of the NAH CA-4 compounds in selected cancer cell lines

Compounds	HL-60 (IC_{50}-µM)	SF295 (IC_{50}-µM)	HCT-8 (IC_{50}-µM)	MDA-MB435 (IC_{50}-µM)	Lymphocytes (IC_{50}-µM)
CA-4	0,0021 (0,0009-0038)	0,0062 (0,0037-0,0085)	0,0053 (0,0013-0,0071)	0,0079 (0,0046-0,0092)	0,0032 (0,0001-0,0036)
Colchicine	0,038 (0,026-0,055)	0,054 (0,023-0,072)	0,077 (0,056-0,090)	0,061 (0,012-0,085)	0,064 (0,042-0,085)
LASSBio-1586	**0,29 (0,29 – 0,32)**	**0,26 (0,13 – 0,54)**	**0,45 (0,35 -0,57)**	**0,064 (0,02 – 0,16)**	1,34 (1,05 – 1,66)
LASSBio-1587	1,63 (1,48 – 1,78)	13,05 (6,33 – 26,91)	4,3 (2,88 – 6,35)	0,12 (0,02 – 0,79)	4,48 (3,63 – 5,54)
LASSBio-1591	3,07 (0,28 - 0,33)	0,86 (0,47 – 1,59)	55,81 (0,42 – 0,7)	**0,11 (0,06 – 0,22)**	1,31 (0,84 – 2,01)

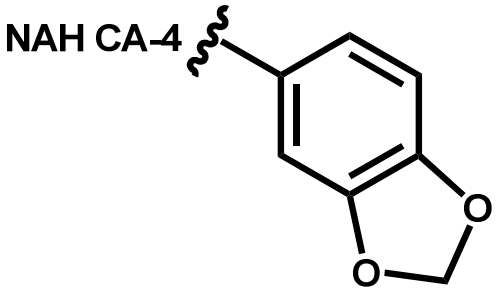
Tumor cell lines: HL-60: human leukemia; SF295: human glioblastome ; HCT-8: ileocecal colorectal adenocarcinoma e MDA-MB435: melanoma.



LASSBio-1586



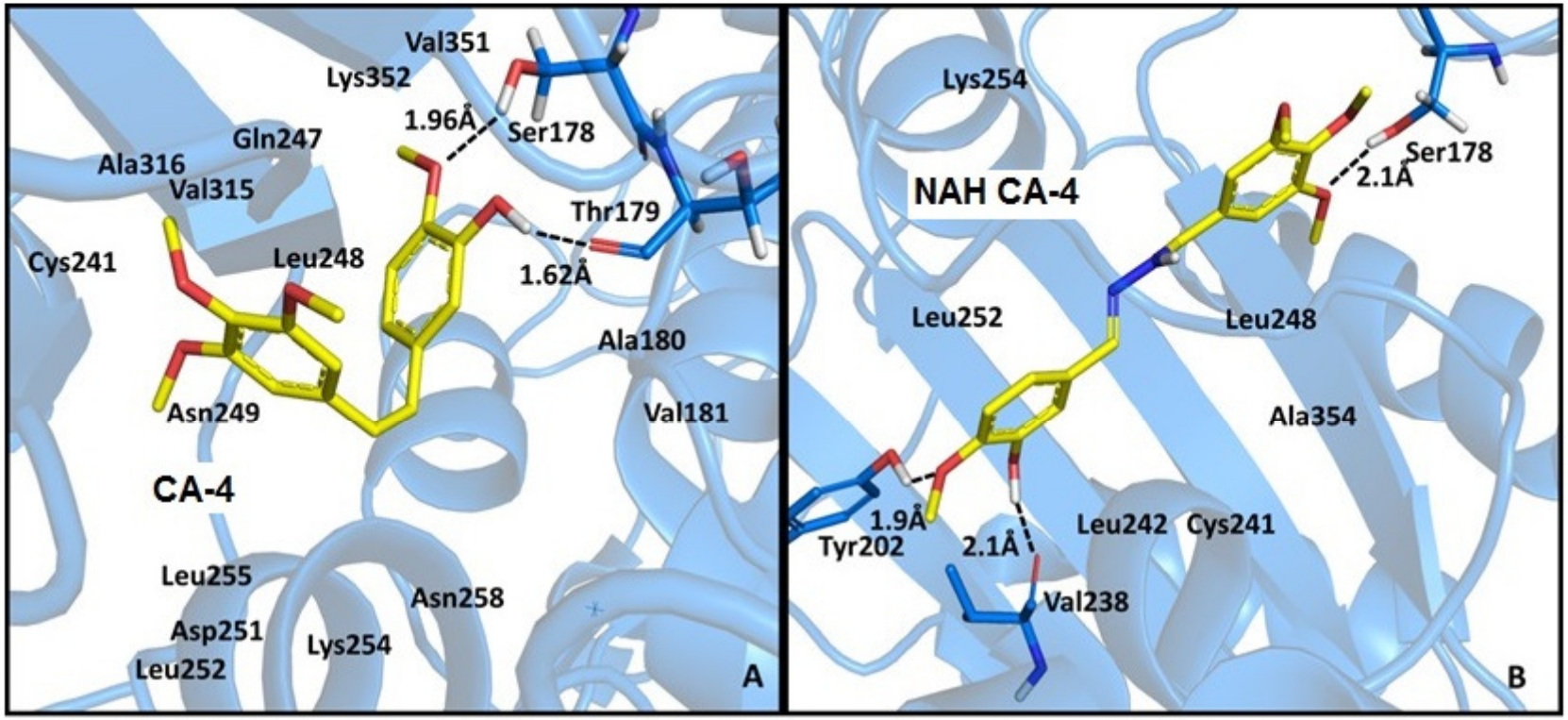
LASSBio-1587



LASSBio-1591

DN Amaral, LM Lima, EJ Barreiro, unpublished results

Docking studies to optimization of NAH CA-4 compounds



A) Molecular docking of CA-4 at the colchicine active site of tubulin to identify the principal pharmacophores points (5A limit: Ser178; Thr179;)
B) Molecular docking of NAH CA-4 at the same active site of the receptor (Ser178; Tyr202;Val238)

DN Amaral, LM Lima, EJ Barreiro, unpublished results

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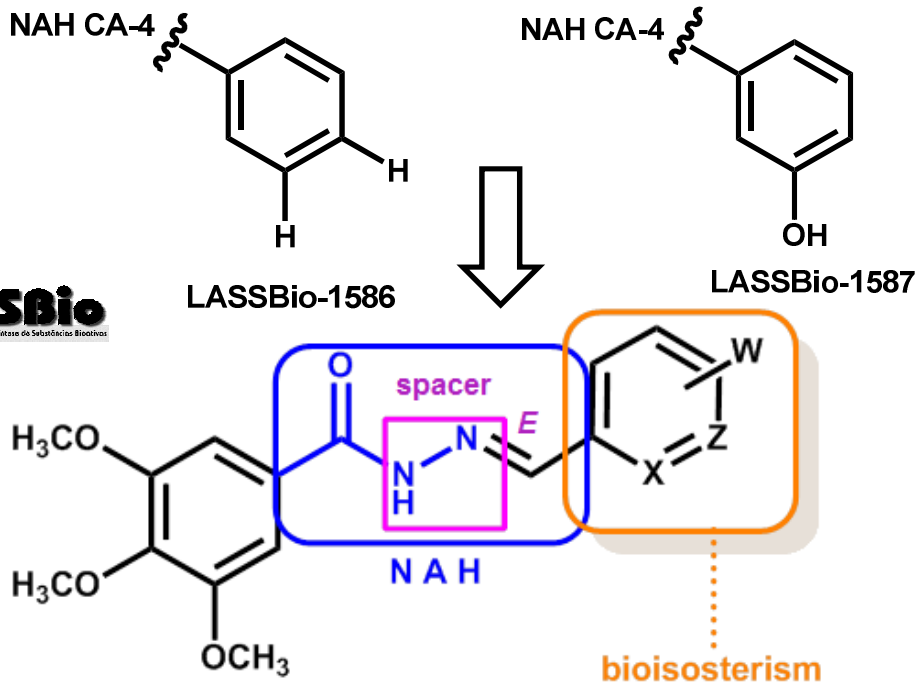
Percentage of inhibition of tubulin polymerization of **LASSBio-1586** and **LASSBio-1587** at $3x10^{-5}M$ (vinblastine as control)

Compounds	% inhibition of control values*
LASSBio-1586	91
LASSBio-1587	81

* Assays done by CEREP® (www.cerep.com)



NAH CA-4 optimized derivatives

⇩

Antiproliferative activity on tumor cell lines

Colchicine
a) 54 nM; b) 7 nM

LASSBio-1738
IC_{50} 4,0 nM
MDA-MB435[a)]
IC_{50} 5,4 nM
OVCAR-8[b)]

LEAD COMPOUND
Lead-optimization

bioisosterism

⇩

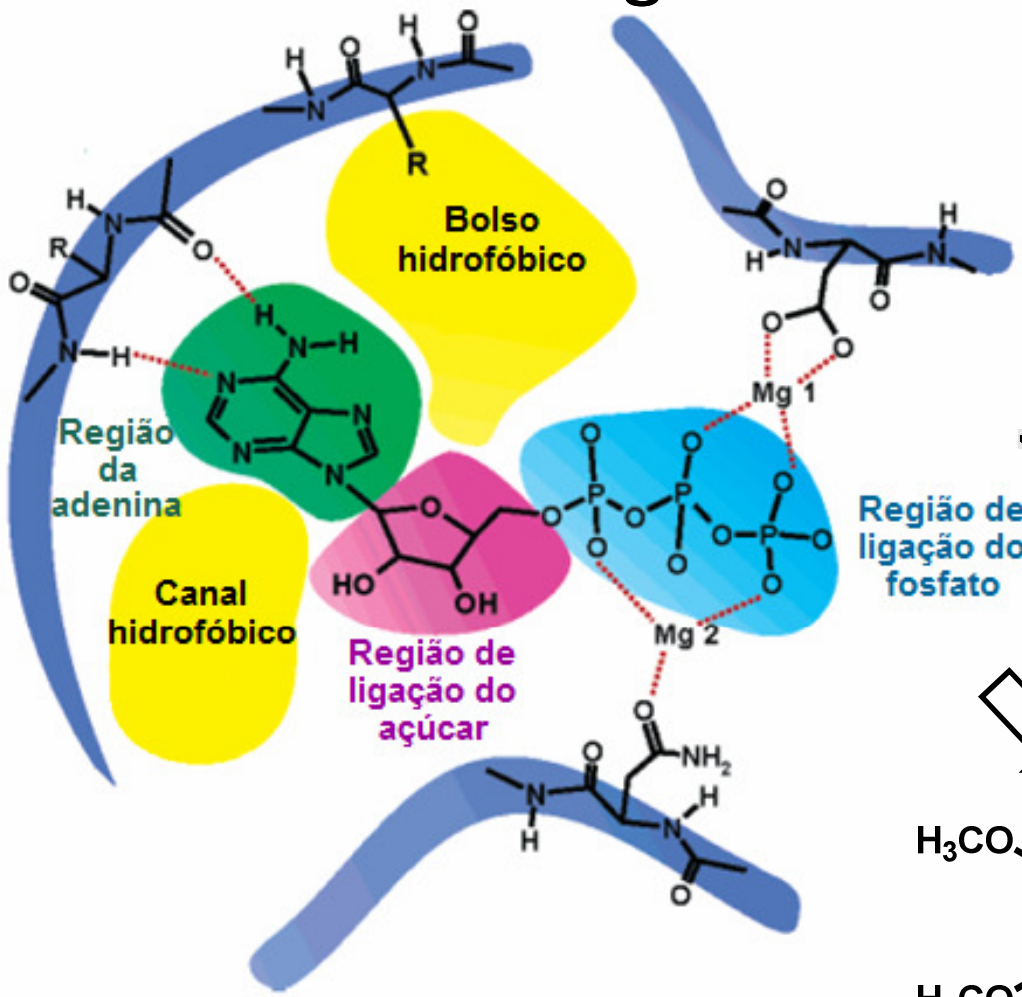
congeneric series ⇨

DN Amaral, LM Lima, EJ Barreiro, unpublished results

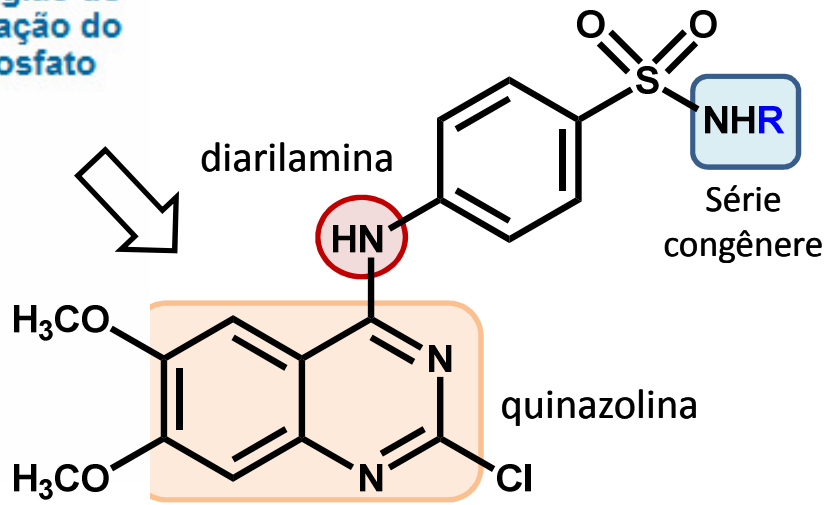
* D. Bonne et.al., 4'-6-Diamidino-2-phenylindole, a Fluorescent Probe for Tubulin and Microtubules, *J.Biol. Chem.* **1985**, *260*, 2819

New analogues of tinib

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



S Laufer et al., *J. Med. Chem.* **2005**, *48*, 710.



MLC Barbosa, Tese de Doutorado, Instituto de Química, UFRJ, 2013.

EGFR IC_{50} = 1,63 μM

VEGFR IC_{50} = 0,85 μM

dual

P. Agarwal et al., Novelty in the target landscape of the pharmaceutical industry, *Nature Rev. Drug Discov.* **2013**, *12*, 575.

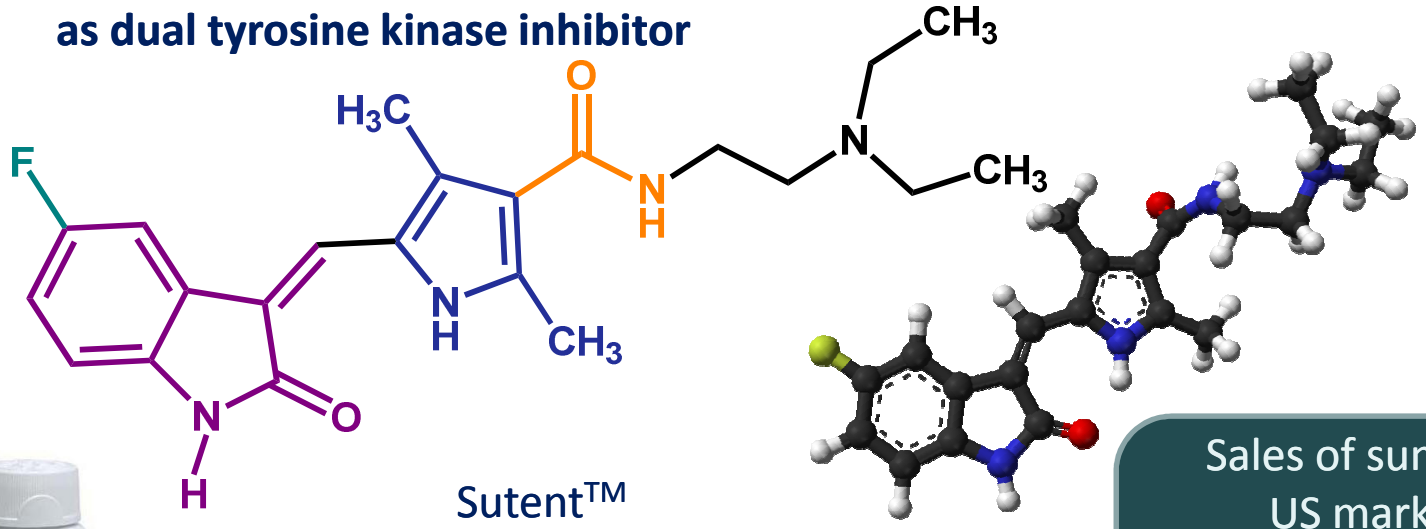
*In*ovação *In*cremental

- Sunitinib

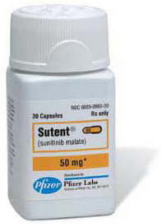
2006

- Total synthesis by Professor **Angelo da Cunha Pinto** & Dr **Bárbara Vasconcellos da Silva,** IQ-UFRJ, BR (**2011**)

2-oxo-1*H*-indol -1*H*-pyrrole-3-carboxamide as dual tyrosine kinase inhibitor



Sutent™

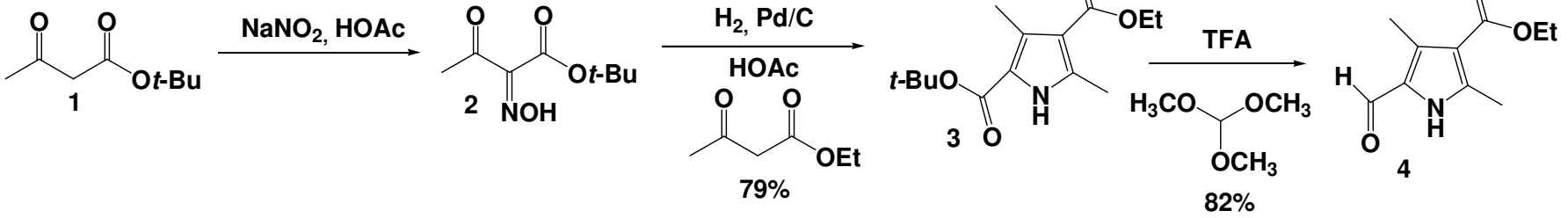


*Patent US 7211600 (2001)

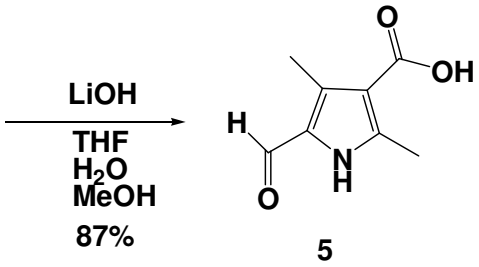
Sales of sunitib in US market:
ca.US$ 1,2 bi (2010/2011)
http://www.evaluategroup.com

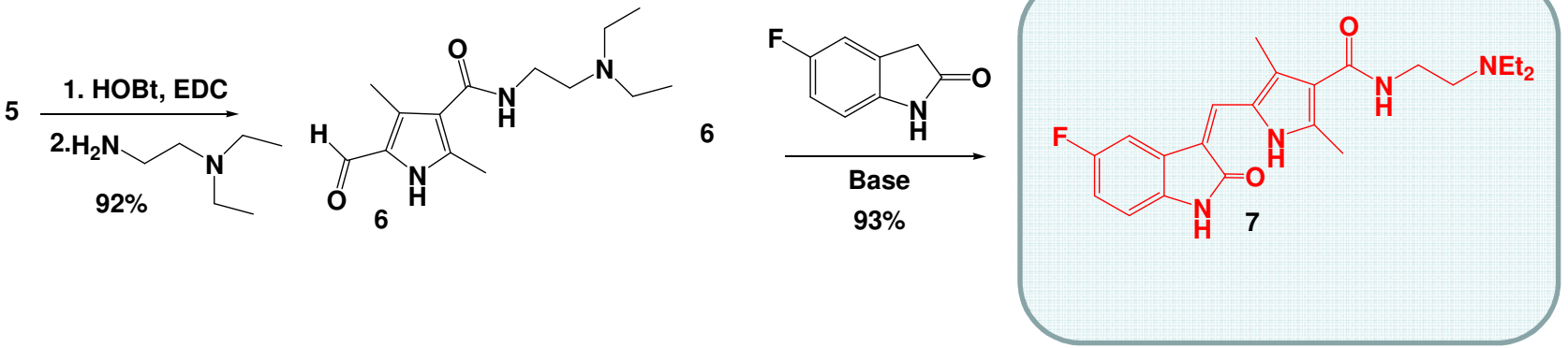
- Platelet-derived growth factor receptor (PDGF-Rs) IC_{50} < 50nM
- Vascular endothelial growth factor receptor (VEGFRs) IC_{50} = 40 nM

Pesquisadores do INCT-INOFAR da UFRJ desenvolvem síntese fármaco anti-câncer



Síntese do Sunitinibe





Sunitinibe
(~2,0g)

A. C. Pinto & B. V da Silva, Instituto de Química, UFRJ

Final remarks

THE ROLE OF THE MEDICINAL CHEMIST IN DRUG DISCOVERY — THEN AND NOW

Joseph G. Lombardino and John A. Lowe III‡*

medicinal chemistry

2011- ACS Award in Industrial Chemistry (ziprazidone)

Pfizer

" ...medicinal chemists today live in exciting times... their work can have a beneficial effect on millions of suffering patients – surely an important motivating factor for any scientist..."

The Role of the Medicinal Chemist in Drug Discovery – Then and Now, *Nature Rev. Drug Disc.* **2004**, *3*, 853.

Concluding remarks

ACS Medicinal Chemistry Letters

medicinal chemistry

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

Universidade Federal do Rio de Janeiro

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"

ACS Med. Chem. Lett. **2013**, *4*, 313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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.
Seja Bem-Vinda e Bem-Vindo
Total de visualizações de página
31,037
Convite
quinta-feira, 8 de agosto de 2013
Mais inovação terapêutica recente: novos fármacos aprovados pela agência regulatória norte-americana (FDA) entre janeiro e julho de 2013
Volto, conforme prometido no início da última postagem sobre o desenho das estruturas químicas através dos tempos, à temática da inovação terapêutica recente. Entretanto, desta vez serei mais sucinto que de hábito, pois vou apenas descrever as recentes inovações terapêuticas aprovadas pelo FDA norte-americano durante o primeiro semestre do corrente ano.
Ao ler o último número da revista Nature Reviews of Drug Discovery no Portal de Periódicos da CAPES, me deparei com a matéria sobre este assunto.
Foram aprovados 13 novas entidades moleculares (NEM) no período. São considerados como entidades moleculares os fármacos e biofármacos, além de novas associações (01: fluticasone com vilanterol para doença pulmonar obstrutiva crônica) e na tabela abaixo incluí apenas as sete novas entidades químicas (NEC) que representam pequenas moléculas ou novos fármacos. Descartei os biofármacos (02; mipomersen e ado-trastuzumabe) e outros como contrastes (02) para diagnósticos e sais inorgânicos coordenados (01).
www.ejb-eliezer.blogspot.com

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