

XXII Congresso Brasileiro de Parasitologia

24-27 de agosto de 2011

Centro de Convenções Rebouças, São Paulo, SP



Mesa-redonda 7

Desafios na pesquisa de fármacos para doenças negligenciadas

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INCT-INOFAR

Programa de Desenvolvimento de Fármacos ICB-UFRJ



Health topics

Data and statistics

Media centre

Publications

10 facts on neglected tropical diseases

Neglected Diseases: Onchocerciasis; Leprosy; Guinea worm disease; Lymphatic filariasis; Schistosomiasis; African trypanosomiasis; Chagas' disease; Dengue and Dengue haemorrhagic fever; Leishmaniasis, Tuberculosis; Malaria

This fact file provides an overview of the various factors that hamper the efforts to bring the NTDs out of the shadows as well as the progress made in preventing, eliminating and eradicating some of the diseases.

Schistosomiasis is endemic in 76 countries, although transmission appears to have been interrupted in several countries. Out of an estimated **200 million cases worldwide**. (WHO, 2011)

About 1 billion people are affected by one or more neglected tropical diseases

While such a large population (one out of six people) is affected by NTDs, less than 1% of the nearly 1400 drugs registered between 1975 and 1999 were for tropical diseases.

1975 – 2004 (30 anos) - 21 (1,3%) medicamentos foram registrados para o tratamento de doenças negligenciadas que compreendem *ca.* 11% das nossas doenças!

Novos medicamentos desenvolvidos entre 1975 e 2004: 1.556



1975 – 2004 - 1.535 outros novos medicamentos foram registrados



Fonte: Chirac P., Torreale E., *Lancet*, 2006, (May 12) 1560



Diseases of the developing world

More than one billion people – one-sixth of the world’s population – are affected by neglected diseases. There is an urgent need to develop better, more affordable vaccines and drugs for diseases that are devastating in developing countries.

Novartis is committed to researching treatments and vaccines for diseases of the developing world through two specialized institutes:

- 
The Novartis Institute for Tropical Diseases (NITD) in Singapore
- 
The Novartis Vaccines Institute for Global Health (NVGH) in Siena, Italy

Our efforts focus on major infectious diseases including **malaria, TB, dengue and infectious diarrhea.**



Novartis Institute for Tropical Diseases in Singapore

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Every day, everywhere,
we at sanofi-aventis
are working for what
really matters: **health**

Because health matters

Welcome to sanofi-aventis Singapore

We are pleased to provide you with an introduction to sanofi-aventis Singapore, an affiliate of the global healthcare company sanofi-aventis.

The ambition of sanofi-aventis is to become a diversified global healthcare leader, focused on patients' needs.

The largest pharmaceutical company in Europe and in emerging markets, sanofi-aventis is the fourth largest worldwide. The Group's vaccine division, sanofi pasteur, is the world leader for human vaccine production and commercialization.

With nearly 100,000 employees in over 100 countries, sanofi-aventis has core strengths in the field of healthcare: a worldwide presence, market leadership in vaccines, major biological products and a strong and long-established presence in emerging markets.

Company business activities also include consumer healthcare products, generics and animal health products.

For further information on any aspect of sanofi-aventis' operation in Singapore, please [contact us](#).



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Pfizer Singapore's nutritional plant, one of the largest in the world, supplies to key markets in Asia and globally

Delivering nutritious and safe food for our children

Working Together For a Healthier World

At Pfizer Singapore, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people. Our diversified global health care portfolio includes human biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments and local communities to support and expand access to reliable.

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Press Releases

Jul 26 2011

[New fixed dose combination therapy for high blood pressure approved in Singapore](#)

Jul 12 2011



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Domingo, 21 de Agosto de 2011



Projeto CNPq no 573.564/2008-6 « » FAPERJ no E-26/170.020/2008

Pagina Principal

O INCT-INO FAR

Equipe

Consultoria Cientfca

Grupos de Pesquisa

Pesquisadores

Inovaao Incremental
no INCT-INO FAR

Annual Activities
Report

Artigos

Publicaoes

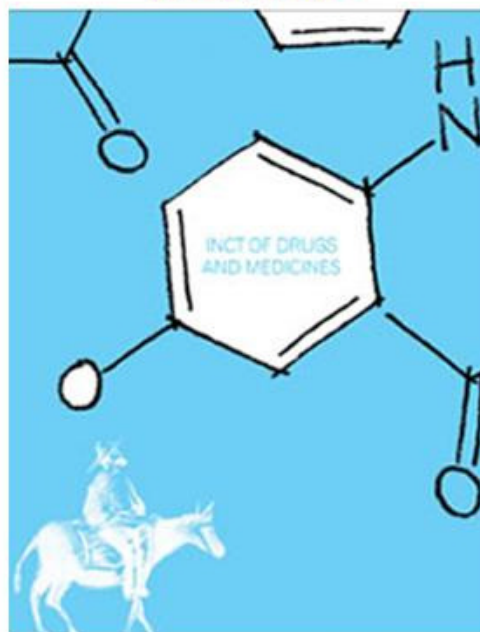
Reunioes

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ANNUAL ACTIVITIES REPORT 2010

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ATORVA STATINA

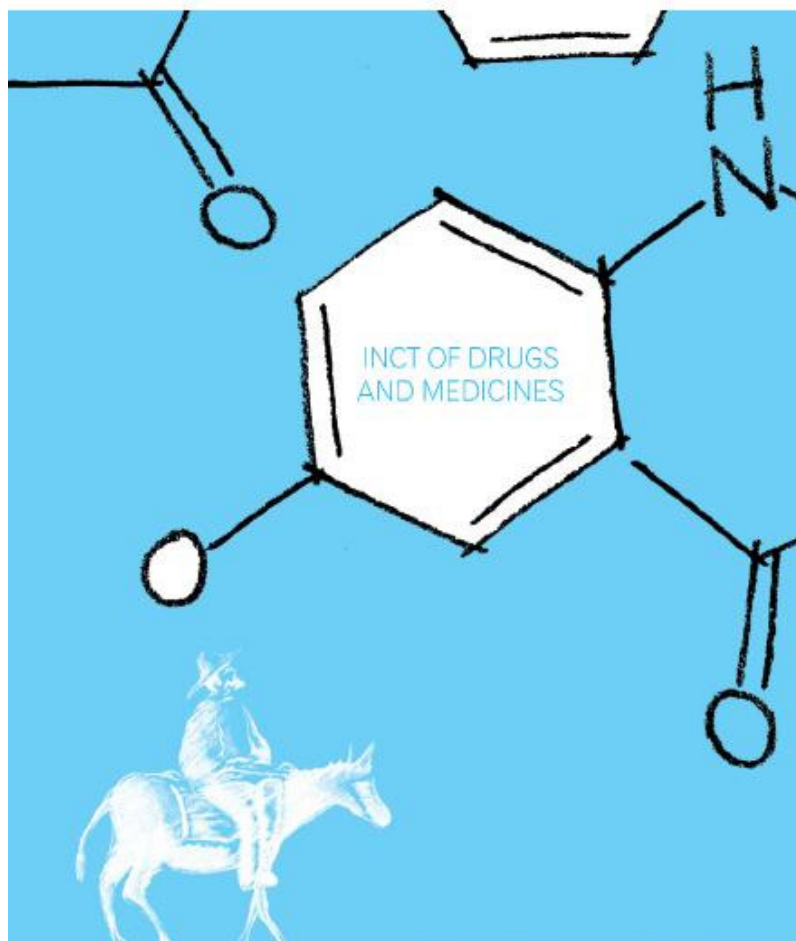
Brasil produz farmaco melhor contra
colesterol

Inovaao incremental



Inovaao radical

Annual Activities Report



Interdisciplinary & multi-team research projects

- **Radical innovation**
pain, inflammation,
asthma, CNS,
neglected diseases,
cardiovascular system,
anticancer
- **Incremental innovation**
 SUS (BR healthcare)
 new generic drugs

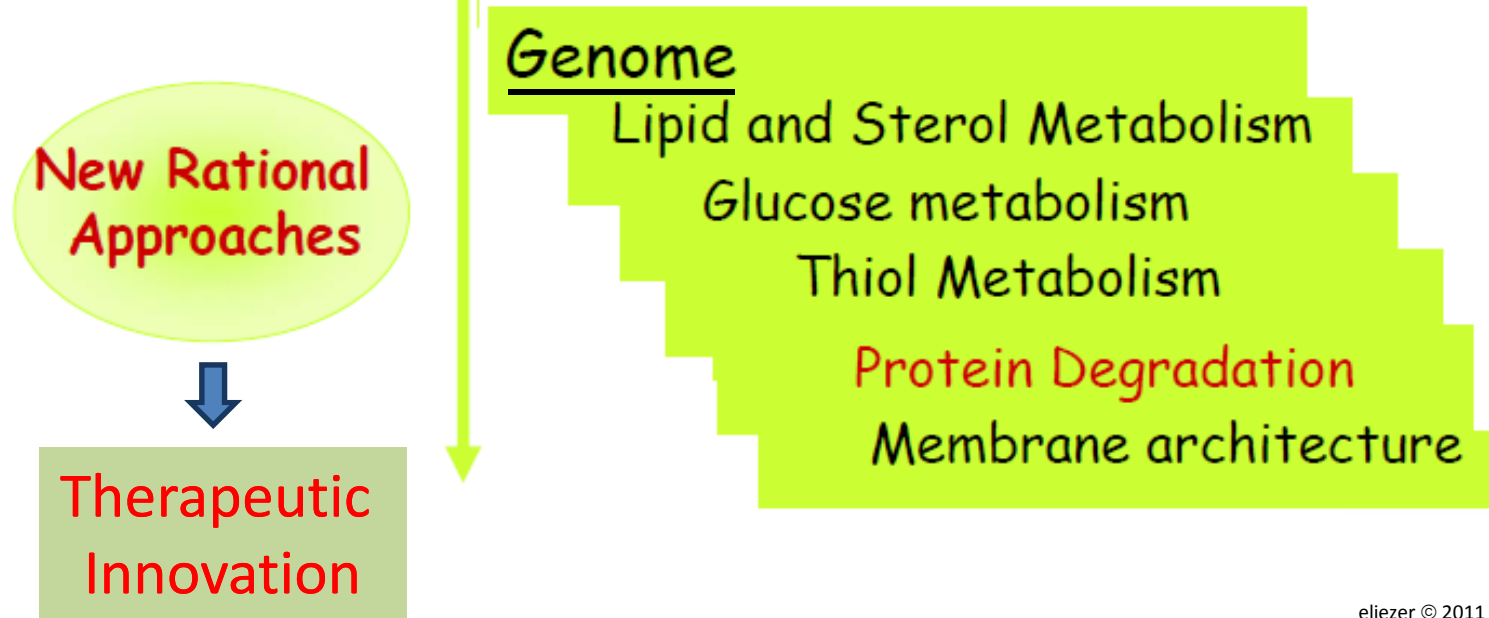
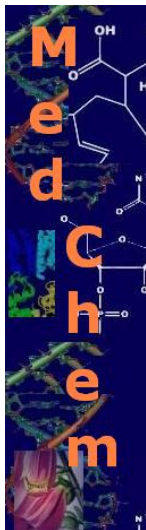
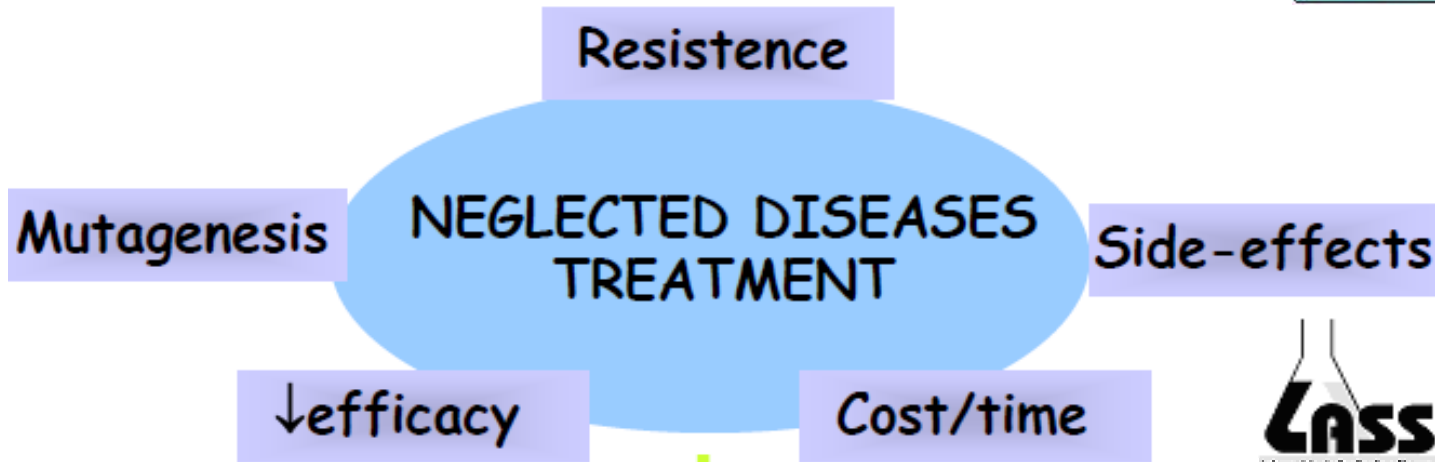


2010

ANNUAL ACTIVITIES REPORT

www.inct-inofar.ccs.ufrj.br/download/aar/2010.pdf

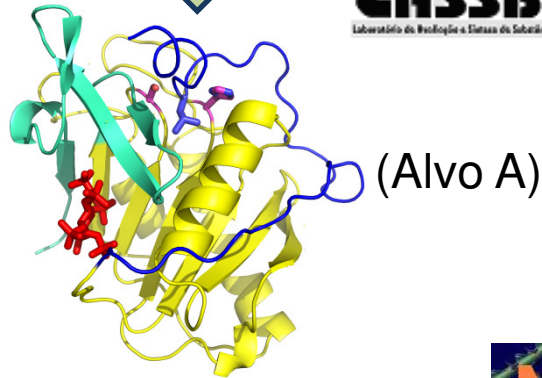
New rational approaches



Cisteíno proteases



Malária

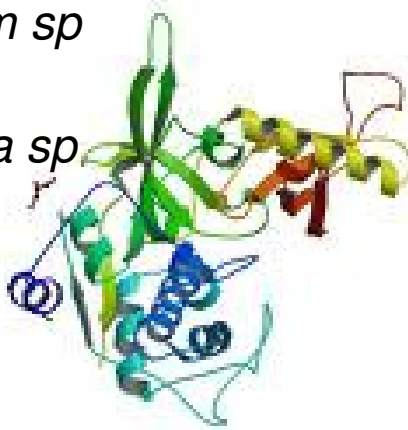


falcipaina

Plasmodium sp

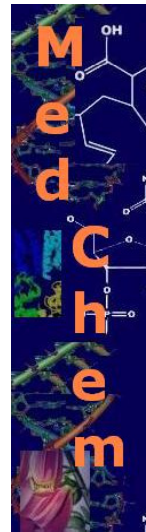
Trypanosoma sp

(Alvo A')



Chagas

cruzaína



Nova abordagem

Desenho molecular de novos candidatos a fármacos inovadores para o tratamento de doenças negligenciadas:

Alvo terapêutico **A** & alvo terapêutico **A'** = mesmo mecanismo bioquímico (adequado grau de homologia);

- *Biorreceptor quimérico*

Bioquímica comparada

New dual drug lead-candidates for neglected diseases.

therapeutic target



high homology index

disease B

essential biochemical pathway



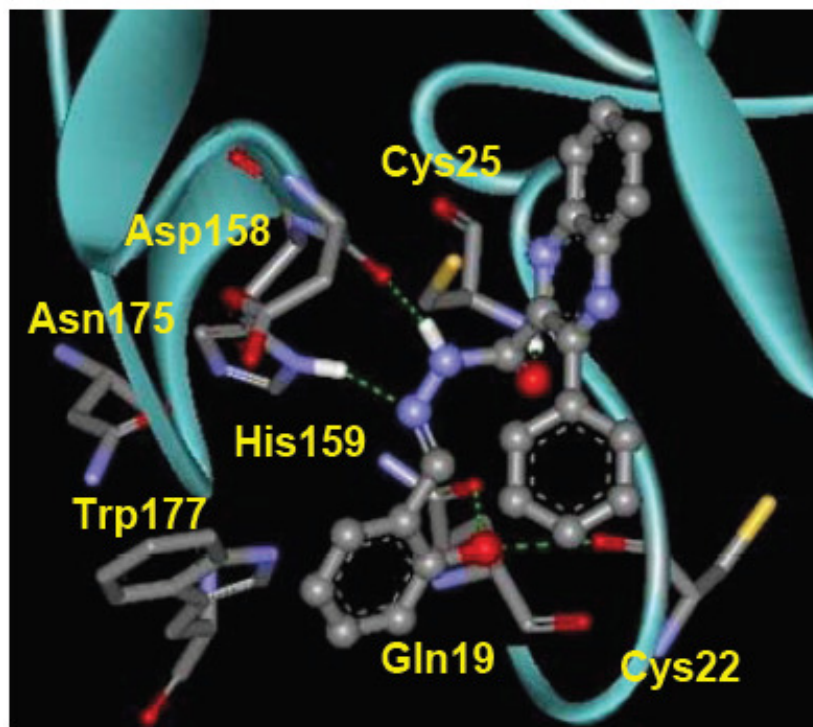
drug

disease A

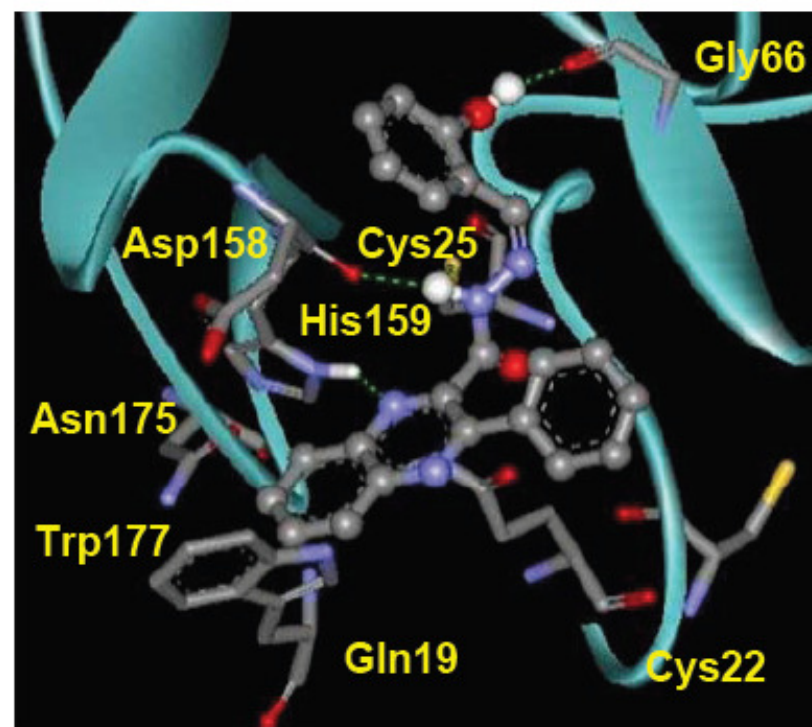
essential biochemical pathway



Docking Studies (FLE_xE)



LASSBio-1016(E)



LASSBio-1016(Z)

HYDROGEN BONDING INTERACTIONS:

cruzaína

LASSBio-1016(E)

$\Delta G_{\text{binding}}$ (kJ/mol) = -27,796

LASSBio-1016(Z)

$\Delta G_{\text{binding}}$ (kJ/mol) = -25,838

Gln19, Cys22, Cys25, Asp158, His159

Cys25, Gly66, Asp158, His159

Pharmacological Assay

Table 1: In vitro anti-trypanosomatid activity. As a first screening the ability of derivatives to inhibit the growth of the epimastigote form of *T. cruzi* (Tulahuen 2 strain)¹ was evaluated at 25 μ M and the IC₅₀ was determined for the most active compounds

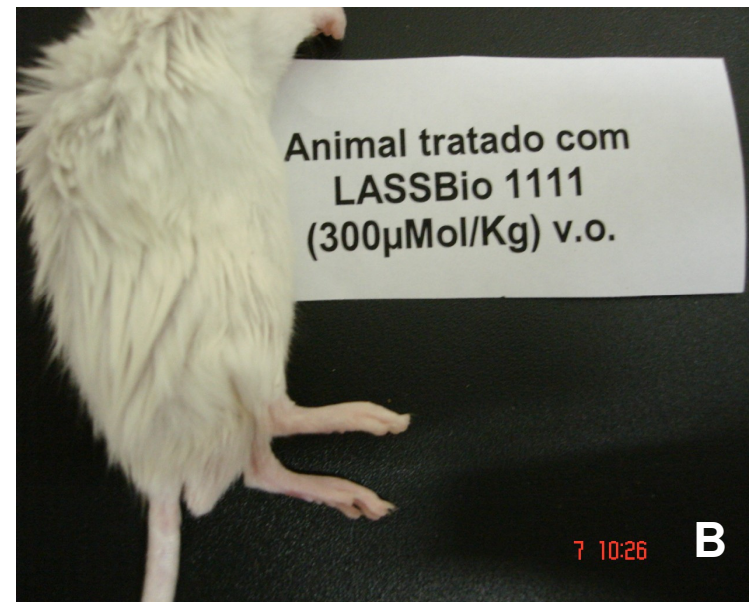
Compounds (25 μ M)	% inhibition of epimastigote forms of <i>T. cruzi</i>	IC ₅₀ (μ M)
Nifurtimox®	100	10
LASSBio-1008	3	n.d.
LASSBio-1009	22	n.d.
LASSBio-1010	40	n.d.
LASSBio-1011	53	n.d.
LASSBio-1012	47	n.d.
LASSBio-1013	35	n.d.
LASSBio-1014	29	n.d.
LASSBio-1015	19	n.d.
LASSBio-1016	96	15,9

Compounds (25 μ M)	% inhibition of epimastigote forms of <i>T. cruzi</i>	IC ₅₀ (μ M)
LASSBio-1017	27	n.d.
LASSBio-1018	36	n.d.
LASSBio-1019	0	n.d.
LASSBio-1020	0	n.d.
LASSBio-1021	0	n.d.
LASSBio-1022	81	20,0
LASSBio-1023	0	n.d.
LASSBio-1024	4	n.d.
LASSBio-1025	0	n.d.

Otimização do protótipo

Camundongo BALB/c: Injeção de 2×10^6 *L. amazonensis* na pata esquerda → tratamento diário (via oral) com os compostos testes → Medida das patas esquerda e direita com o paquímetro 2 vezes por semana por 30 dias.

“Leishpaína” ?



Tamanho das lesões.

(A) animal sem tratamento.

(B) animal tratado com LASSBio 1111 (300 µmol/kg/ via oral) após o período de 30 dias.

LASSBio-1491

FQ Cunha, LM Lima, H Cerecetto, M Gonzalez, MS Alexandre-Moreira, MV Martins, MP Nunes, EJ Barreiro, resultados não publicados.

R. E. Silva-López, Leishmania proteases: new targets for rational drug development, *Quim Nova* **2010**, *33*, 1541.

An illustration of a brown, rocky cliff on the left side. From the top edge of the cliff, several colorful pills (red and green capsules, and white tablets with a score line) are falling. The pills are scattered in the air and on the ground to the right of the cliff. The background is a light, textured yellowish-green.

The Big-Pharma productivity crisis

The productivity crisis in pharmaceutical R&D

Abstract | Advances in the understanding of the molecular basis of diseases have expanded the number of plausible therapeutic targets for the development of innovative agents in recent decades. However, although investment in pharmaceutical research and development (R&D) has increased substantially in this time, the lack of a corresponding increase in the output in terms of new drugs being approved indicates that therapeutic innovation has become more challenging... we examine the decline of R&D productivity in the past two decades...



F. Pammolli, L. Magazzini, M. Riccaboni, *Nature Rev Drug Discov* 2011, 10, 428.



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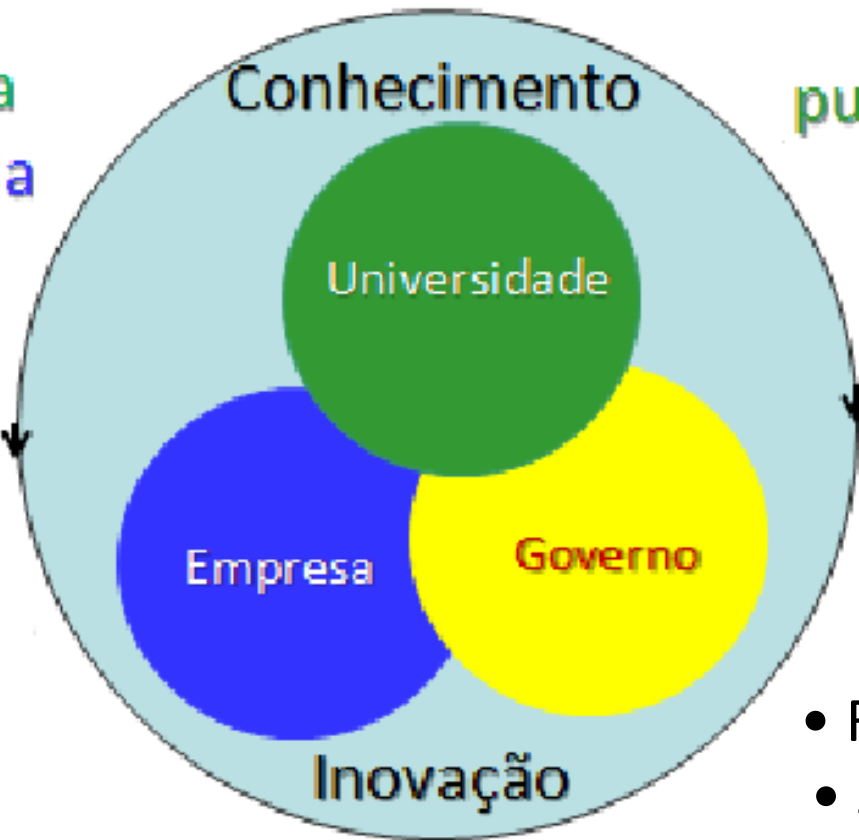
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