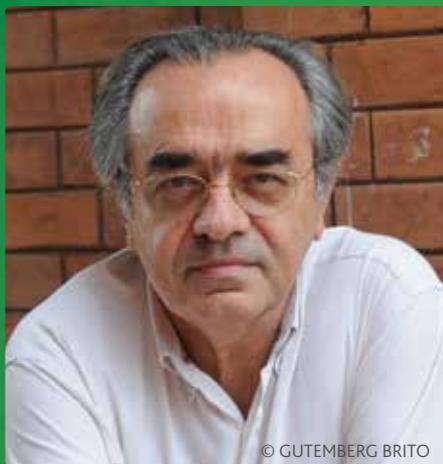


Bridging the gap

Dr Carlos Morel, former World Health Organization Director of the Special Program for Research and Training in Tropical Diseases, shares details of his work developing translational research in Brazil



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Who was Oswaldo Cruz, the founder of the Oswaldo Cruz Foundation (Fiocruz)?

Cruz was a Brazilian physician who was trained at the Pasteur Institute in Paris and specialised in bacteriology. In the late 1800s, public health in Brazil had deteriorated due to infectious diseases, which greatly affected international trade and tourism. In response, the Brazilian Government asked for help from the Pasteur Institute, and was informed that Cruz could lead the implementation of policies and healthcare initiatives to combat the situation.

He oversaw the construction of a building complex to manufacture vaccines, perform research and train young investigators. His efforts were immensely successful and he became a national hero. That complex formed the beginning of the Oswaldo Cruz Foundation, which was named in his honour for his contributions to improving public health in Brazil.

Have the aims and objectives of the organisation changed since its formation?

The goals of improving Brazilian public health through science and policy have remained the same at Fiocruz, but healthcare priorities are expanding from infectious diseases to include a broader agenda due to the modernisation of a large segment of the Brazilian population, which

has altered their lifestyles and increased their lifespan. This expansion covers the emergence of noncommunicable diseases such as diabetes, obesity, heart disease and cancer.

As Coordinator of the new Center for Technological Development in Health (CDTS) project, which aims to foster translational research, what does your role involve?

I lead a team of 20 permanent staff at Fiocruz, which includes researchers, planners, managers and a lawyer. This team is responsible for two main parts of the project: first, the managerial aspects of CDTS, which include shaping the business plan, interacting with scientific and industrial partners and working together with other Fiocruz sectors to finish construction of the CDTS building; second, the management of ongoing scientific projects, in particular those funded by the National Institute of Science and Technology for Innovation in Neglected Diseases (INCT-IDN), which are carried out in laboratories and organisations in several locations around the country.

Why were you, in particular, chosen for this task?

I was invited by the President of Fiocruz to head the CDTS programme, one of the top priorities of Fiocruz, due to my professional and academic background. I was the former President of Fiocruz (1993-97), and former World Health Organization (WHO) Director (1998-2004) of the Special Program for Research and Training in Tropical Diseases, co-sponsored by UNICEF, the United Nations Development Programme, World Bank and WHO in Geneva, Switzerland. My experience has included public health in Brazil and coordinating interactions between basic science and industry before it was termed translational science.

Since your 2003 article 'Neglected diseases: under-funded research and inadequate health interventions', has the situation changed?

Many changes have occurred, some positive and some negative. To my mind, the most important advances have included the inauguration of the

Bill & Melinda Gates Foundation, which is now a key player in this area; the founding and full implementation of several 'product development partnerships' such as the Medicines for Malaria Venture (MMV), Drugs for Neglected Diseases initiative (DNDi), Global Alliance for Tuberculosis Drug Development (TB Alliance), Foundation for Innovative New Diagnostics (FIND) and others that are contributing to the emergence of robust drug portfolios, vaccine development programmes and new product pipelines; and finally, the introduction of an international, peer-reviewed publication dedicated to neglected diseases – *PLoS Neglected Tropical Diseases*.

Equally, however, the intervening years have seen the emergence of the 'Valley of Death', a chasm between biomedical researchers and the patients who need their discoveries. Pharmaceutical companies continue to use drug development processes that are slow, inefficient, risky and expensive, despite advances in basic science and the recent move from pharmaceuticals to biopharmaceuticals.

Have there been significant contributions from CDTS and INCT-IDN researchers in this time?

CDTS and INCT-IDN were critical players leading to the establishment of the R&D on Neglected Diseases programme by the Brazilian Ministry of Health. I was invited to coordinate the planning and implementation of the first two national calls for applications that were funded at the level of R \$20 million and R \$17 million in 2006 and 2009, respectively (approximately US \$10 million each at the exchange rate in those years).

This led to collaborative work between our group researching social network analysis and the top political and managerial levels at the Ministry of Health, allowing us to shape an innovative approach for the strategic planning and implementation of this programme.

Boosting Brazil

The **Oswaldo Cruz Foundation** is one of Brazil's leading scientific institutions, and recently lived up to that title when it began groundbreaking work towards expanding and improving its infrastructure – acting as a model for other scientific organisations in the country and beyond

THE BIGGEST COUNTRY in South America, Brazil boasts a large and growing economy, as well as highly developed infrastructure. Less well known perhaps is that it is also a great contributor to the progression of science. In total, the country's researchers produced around 47,500 academic papers in 2012. Brazil leads Latin America in the quality of its research facilities; it is the only Latin American country with a particle accelerator and one of only two South American countries with an operational synchrotron laboratory. On top of this, it is also home to a number of leading scientific institutions.

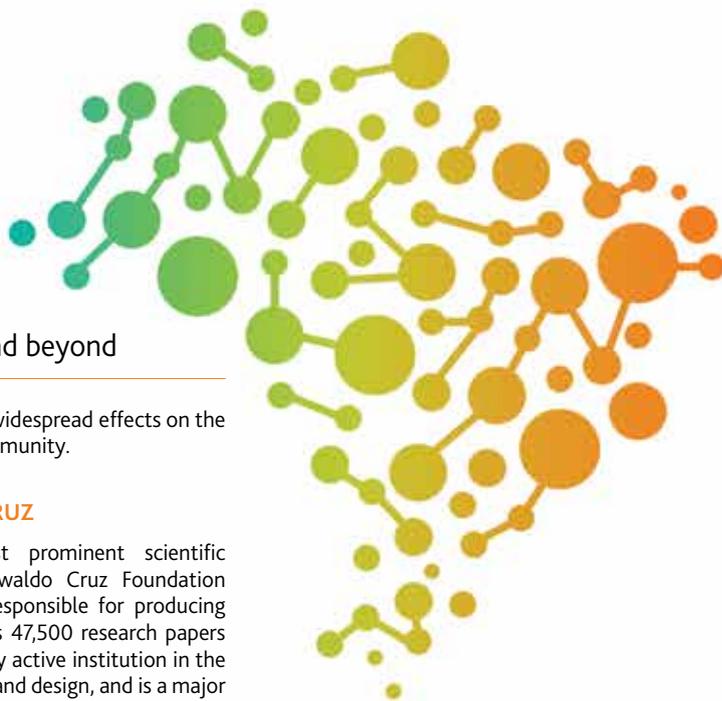
But like many other countries, Brazil has one great and fundamental problem: science, technology and production are each conducted in relative isolation. This phenomenon is prominent in developing countries, and in Brazil's case the problem has arisen because its main funding agencies – CNPq and CAPES – were created in 1951 at a time when basic sciences were considered fundamental, and a consideration for universities, whereas applied sciences were the responsibility of industry. Consequently, more than 60 years later, Brazil is an important contributor to basic science, but falls far behind other comparable countries in terms of industrial innovations. This is a state

of affairs that has had widespread effects on the country's scientific community.

FUNDING FOR FIOCRUZ

One of Brazil's most prominent scientific institutions is the Oswaldo Cruz Foundation (Fiocruz), which was responsible for producing around 1,300 of Brazil's 47,500 research papers in 2012. Fiocruz is a very active institution in the area of health research and design, and is a major manufacturer of vaccines, pharmaceuticals and biopharmaceuticals. However, at present research and industrial activities are not coordinated; little attention is devoted to translating scientific advances into new health products. Similarly, manufacturing activities are precipitated mostly through knowledge transfer from big pharmaceutical companies such as GlaxoSmithKline plc or partnerships with public, government and non-profit organisations.

In order to aggressively address this outdated research approach institutionally and nationwide, the Brazilian Government recently provided Fiocruz with US \$200 million in grants towards the implementation of two huge projects: the Center for Technological Development in Health (CDTS) and the Integrated Center for



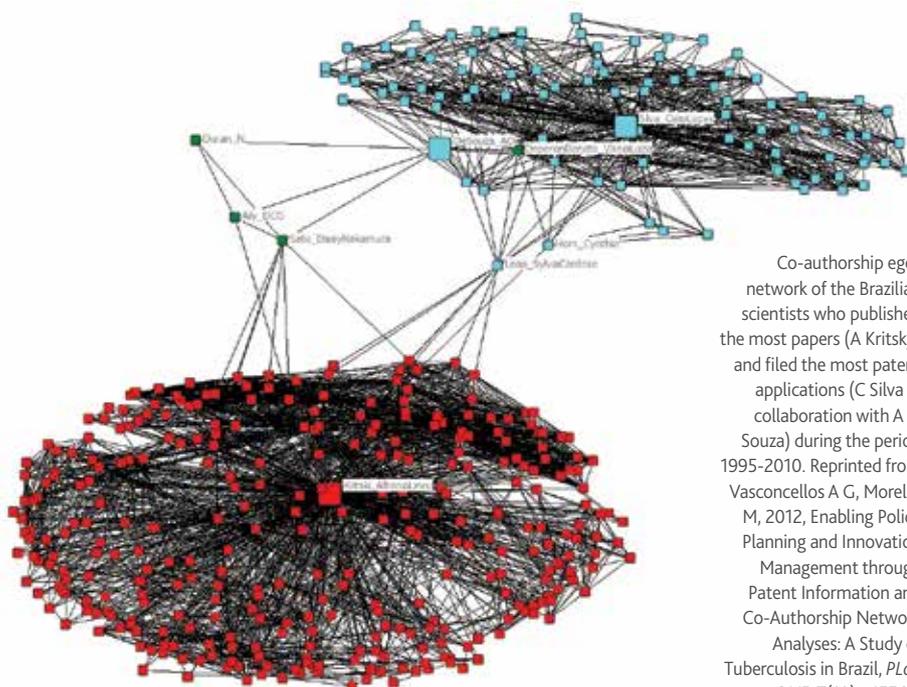
Prototypes, Biopharmaceuticals and Reagents for Diagnoses (CIPBR), which will be operational in 2015 and 2014, respectively. CDTS will focus on the preclinical development of new health products, whereas CIPBR will work on late development, clinical stages and regulatory aspects of development and manufacture on the same products. The two facilities will be located side by side in order to facilitate collaboration. Their division of responsibilities will allow the two facilities to refocus Brazilian research for the benefit of citizens.

DRAMATIC CHANGES

Dr Carlos Morel, former President of Fiocruz, is leading the CDTS project team. The group is responsible for overseeing the construction of the 20,000 m² facility, which will include ample space for 'flexible labs' – areas that will be reserved for collaborative projects originating from partnerships between Fiocruz and industrial or non-profit entities; the first time that a Brazilian public institution will set aside space on its campus for such partnerships.

The establishment of the physical facility, however, is only one-third of the group's responsibilities. CDTS is also home to the National Institute of Science and Technology for Innovation in Neglected Diseases (INCT-IDN). This Institute, which was formed as part of a highly competitive programme developed by four of Brazil's most eminent funding agencies, was approved in 2009 and consolidated a group of 49 national and international scholars, researchers and technologists.

Another CDTS activity is the foundation of the CAPES-Fiocruz/CDTS Fellowship Programme, a partnership between CDTS and Ministry of Education agency CAPES, which will aim to recruit young postdoctoral scientists and visiting professors and researchers to work in CDTS programmes and projects. The first of two five-



Co-authorship ego-network of the Brazilian scientists who published the most papers (A Kritsky) and filed the most patent applications (C Silva in collaboration with A O Souza) during the period 1995-2010. Reprinted from Vasconcellos A G, Morel C M, 2012, Enabling Policy Planning and Innovation Management through Patent Information and Co-Authorship Network Analyses: A Study of Tuberculosis in Brazil, *PLoS ONE*, 7(10):e45569.

Group photo of participants at the international conference 'Translational science at Fiocruz: Building international collaborations', held in Rio de Janeiro, 2-6 December 2013.



year phases began in 2006, when two calls for applications were published in the international, high impact journals *Nature* and *Science*. 40 applications were received, 16 approved and today three of these collaborators have gone on to become a permanent part of the Fiocruz team.

The establishment of INCT-IDN and the fellowship programme are important achievements in terms of progressing scientific study in Brazil, ensuring that research serves neglected populations, and augmenting collaborative links with other countries.

A REPUTATION FOR RESEARCH

The laboratories within INCT-IDN focus on neglected diseases including HIV, tuberculosis and malaria – particularly the *Plasmodium vivax* species of malarial protozoan, which is especially prevalent in the Amazon basin area. In an ongoing collaboration with GlaxoSmithKline plc, for example, an INCT-IDN team led by Dr Marcus Lacerda has provided access to its world-class malarial clinical research centre in Manaus in order to perform a clinical trial of the new drug tafenoquine. Morel is also in the process of working with the Brazilian Ministry of Health and the Global Alliance for Tuberculosis Drug Development (TB Alliance) in order to involve Lacerda's lab and another INCT-IDN lab based in Rio de Janeiro in the clinical testing of a number of new drugs and therapeutic regimens to combat tuberculosis.

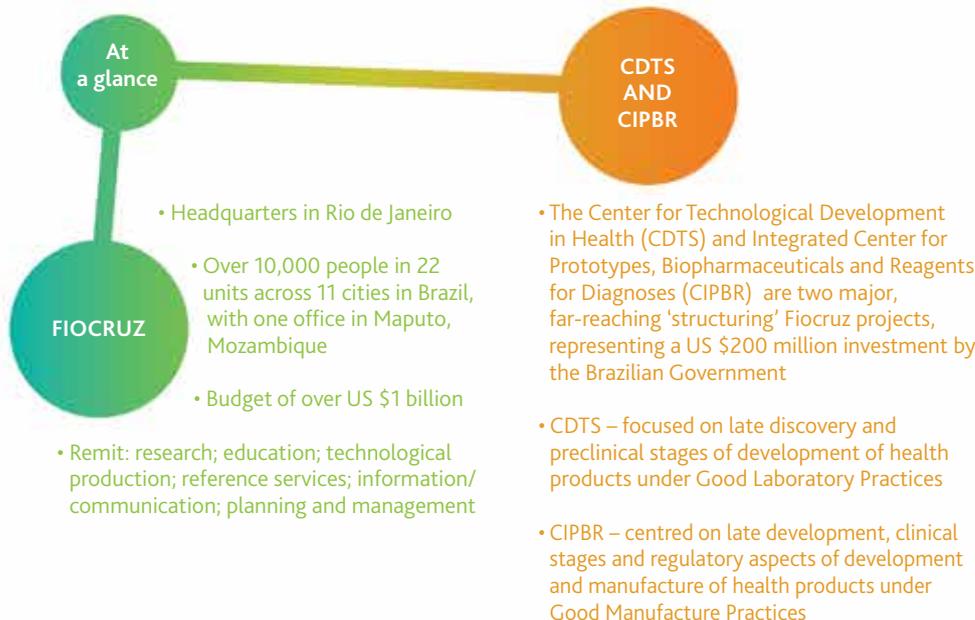
The work focused on HIV-infected individuals has become very influential as well. Under

the umbrella of INCT-IDN, Dr Márcio Rodrigues' lab is primarily concerned with halting the deleterious effects of *Cryptococcus neoformans*; a fungus which causes opportunistic infection in HIV patients and others. Rodrigues' team has centred efforts on the fungus' ability to produce polysaccharides, ultimately determining through a series of studies that the regulators of the fungus' unconventional secretion methods – allowing it to expel polysaccharides into the extracellular milieu – are a key to its virulence, and are therefore a likely target for new therapeutic drugs.

This is only a tiny snapshot of the wide-ranging medical research output at Fiocruz. Similarly broad is the Foundation's collaborative network, which includes organisations and bodies at both national and international levels. INCT-IDN collaborates with many of the other INCTs set up by the same programme, and the work carried out as part of this new institute is nothing short of phenomenal.

LATIN AMERICAN LEADERS

As the Brazilian Government has recognised, major organisational changes are required in order to ensure that, going forward, Brazil's prodigious research power is directed towards better serving its citizens. The new programmes underway at Fiocruz are a vital step towards this goal, and the institution's effort to lead the country by example is as commendable as its continued contribution to the research landscape both at home and abroad.



INTELLIGENCE

TRANSLATIONAL SCIENCE FOR NEGLECTED DISEASES IN NEGLECTED POPULATIONS

OBJECTIVES

The Center for Technological Development in Health (CDTS) and National Institute of Science and Technology for Innovation in Neglected Diseases (INCT-IDN) are dedicated to developing new tools for the improvement of interventions, policies and strategies relevant to public health through collaboration with academia, product development partnerships and industry. Major emphasis is placed on the control, prevention and treatment of neglected diseases that perpetuate poverty.

CORE TEAM

A P O Brum; A S Campos; N Carels; C I Chamas; C S De-Macedo; S G De-Simone; F T S Elias; R C Hauegen; J Junker; M Lenzi; F H A Lima-e-Silva; D S Marinho; E V Martins; C Penido; P C G Pieroni; D W Provance Jr; C L Rodrigues; C N P Romero; G F Silva; M D S Souza, Fiocruz/CDTS, Rio de Janeiro, Brazil

KEY PARTNERS

Fiocruz units: **ENSP; ICICT; IOC; IPEC; CPqGM** • R&D institutions: **CLAP/SMR**, Montevideo, Uruguay; **FMT-HVD**, Manaus, Brazil; **IS-SES/SP**, São Paulo, Brazil; **Kitasato Institute**, Tokyo, Japan; **INMETRO; FGV; INPI**, Rio de Janeiro, Brazil

Universities: **UFRJ; INCT-INOFAR**, Rio de Janeiro, Brazil; **UnB**, Brasilia, Brazil; **USP**, São Paulo, Brazil

Product Development Partnerships (PDPs): **DNDi; FIND; MMV**, Geneva, Switzerland • **TB Alliance**, New York, USA

FUNDING

Brazilian Government (CAPES, CNPq, Decit/ SCTIE/Ministry of Health) • Rio de Janeiro State Government (FAPERJ) • EC projects Elan2Life (FP6) and Access to Pharmaceuticals (FP7)

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CARLOS MEDICIS MOREL, MD, DSc is a senior scientist and former President of Fiocruz. As Director of TDR at the World Health Organization, Geneva (1998-2003) he supported the creation of the PDPs DNDi, FIND, MMV and TB Alliance.