Políticas de Saúde de Países em Desenvolvimento: Qual o papel da ciência, tecnologia e inovação?

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Instituto Nacional de Ciência e Tecnologia de Inovação em Doenças Negligenciadas (INCT-IND)
Health Policies of Developing Countries: What role for science, technology and innovation?

Carlos M. Morel
Center for Technological Development in Health (CDTS)
National Institute of Science and Technology on Innovation on Neglected Diseases (INCT-IND)
Overview of this presentation

• The heterogeneity of developing countries
• Health and social/economic development
• What is innovation?
• Health innovation
  – Historical evolution
  – Challenges
  – Opportunities
• Health innovation at Fiocruz,
Different history, different trajectories, different outcomes

DEVELOPING COUNTRIES
The world is no longer bipolar.

The world of the 1950s: The "North" and the "South"

The world today: The "North", the "South" and countries in transition

Income per person (GDP/capita, inflation adjusted)

http://www.gapminder.org/
Map of countries according to HDI

http://www.canadiangeographic.ca/worldmap/cida/cidaworldmap.aspx
Heterogeneity of developing countries

World Bank income groups

IMF and UN groups
Heterogeneity of developing countries

Newly industrialized countries

Least developed countries (also known as “Failed States”)

Also used:
- BRICs/BRICS: Brazil, Russia, India, China (South Africa often also included)
- IDCs: Innovative Developing Countries (Morel et al, Science, 2005, 309:401-404)
Some countries are moving towards social and economic development. Brazil, Russia, India and China (the “BRICs”) in 2007 and some “Innovative Developing Countries” (IDCs) in 2007.
Trajectories of developing countries: some lessons to take home
HEALTH AND DEVELOPMENT
Health: consequence of, but also a requisite for, social and economic development

• "Improving the health and longevity of the poor is an end in itself, a fundamental goal of economic development. But it is also a means to achieving the other development goals relating to poverty reduction. The linkages of health to poverty reduction and to long-term growth are powerful, much stronger than is

Commission on Macroeconomics and Health,
Health as an Input into Economic Development

Commission on Macroeconomics and Health, 2000
Worldmapper: area of countries proportional to physicians working

Figure 3. Physicians Working: Worldmapper Poster 219
Source of data used to create map: World Health Organization, 2004, Human Resources for Health, Basic data.
**Worldmapper**: area of countries proportional to HIV/AIDS prevalence

*Figure 5. HIV/AIDS Prevalence: Worldmapper Poster 227*

Worldmapper: area of countries proportional to malaria cases

Figure 6. Malaria Cases: Worldmapper Poster 229
Worldmapper: area of countries proportional to deaths due to Chagas disease (2002)
WHAT IS INNOVATION?
What is innovation?

• “Innovation is not a new phenomenon. Arguably, it is as old as mankind itself. There seems to be something inherently ‘human’ about the tendency to think about new
What is innovation?

- **Invention** is the first occurrence of an idea for a new product or process.
- **Innovation** is the first attempt to carry it out into practice.
- Sometimes invention and innovation are closely linked; in many cases, however, there is a considerable
Example of time lag between invention and innovation

• **Invention**
  • 1947: Dias and Pellegrino in Brazil and Romaña and Abalos in Argentina demonstrate the efficacy of organochlorine insecticides against domiciliated triatomine bugs

• **Innovation**
  • 1990s: Political decisions at the highest level
Joseph Schumpeter and ‘creative destruction’

- New products
- New methods of production
- New sources of supply
- Exploitation of new markets
- New ways to organize business
Types of innovation

- Technological Innovation
  - Product Innovation
    - Incremental
    - Major
  - Process Innovation
- Non-technological Innovation
  - Advanced Management Techniques
  - Changes in Corporate Strategy
  - Changes in Organizational Structure

Introduction

HEALTH INNOVATION
Health innovation

- **Products**
  - New vaccines, drugs, diagnostics, devices

- **Processes**
  - Alternative ways to synthesize or administer a drug

- **Policies**
  - “National Immunization Days”

- **Strategies**
  - TRIPS compulsory licenses
  - Taxation on financial transactions → purchase of antiretrovirals
Health innovations & smallpox eradication

- **Product** innovation
  - Lyophilized vaccine → avoidance of cold-chains

- **Process** innovation
  - Bifurcated needle

- **Policy** innovation
  - Maximum use of underutilized health personnel
  - Community participation: teachers, religious leaders, elders

- **Strategy** innovation
  - “Circle” vaccination, instead of mass vaccination
Types of innovation

Technological And Social Innovation: A Unifying New Paradigm For Global Health

Developing countries need R&D partnerships and implementation research networks to play a more prominent role in global health.

by Charles A. Gardner, Tara Acharya, and Derek Yach

Health Innovation: evolution

Historical periods
Health innovation: Major historical periods

- 1850–early 1900s': **Era of the public sector**
  - Epitomized by the work of Pasteur
- 1900s’–1970s’: **Era of the private sector**
  - Emerged in Germany & chemical companies
- 1970s’–2000: **Era of public sector reawakening**
  - United Nations: WHO Special Programmes (HRP, TDR)
  - USA: Bayh–Dole Act; NIH budget increase
- 2000–: **Era of public–private partnerships (PPPs)**
  - Innovative Developing Countries (IDCs)

Health innovation: Major historical periods

• 1850–early 1900s’: *Era of the public sector*
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• 2000– : *Era of public–private partnerships (PPPs) & Product Development Partnerships (PDPs)*

  
The era of the public sector
The era of the public sector
Health innovation: Major historical periods

- 1850–early 1900s’: Era of the public sector
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- 2000–: Era of public–private partnerships (PPPs)
  - Innovative Developing Countries (IDCs)
  - Product Development Partnerships (PDPs)

The era of the private sector
The era of the private sector
Neglected diseases, neglected populations
Health innovation: Major historical periods

• 1850–early 1900s’: Era of the public sector
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• 2000–: Era of public–private partnerships (PPPs)
  – Product Development Partnerships (PDPs)
  – Innovative Developing Countries (IDCs)

Research on neglected priority needs

Building on our 30 year history, TDR is supporting innovative research on neglected priority needs for disease control. Through focused, time-limited activities, our goal is to support research in the countries where the diseases are prevalent that fosters:

- innovation for product discovery and development
- research on development and evaluation of interventions in real-life settings
- research to increase access to interventions.

TDR has restructured its operations, creating nine research lines, which may vary over time. Some are functionally specific, while others are focused on specific diseases.
Health innovation: Major historical periods

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  - USA: Bayh–Dole Act; NIH budget increase

- 2000–: **Era of public–private partnerships (PPPs)**
  - Innovative Developing Countries (IDCs)
The era of PDPs: Partnerships for the Development of Products
The Sisyphus Challenge
The Valley of Death

Health Innovation: Challenges
The Sisyphus challenge of the 21st century

The Sisyphus challenge in Chile

Low awareness of the link between science and innovation affects public policies in developing countries: The Chilean case

MANUEL KRAUSKOPF, a,b ERWIN KRAUSKOPF, a,b,c BERNARDITA MÉNDEZ a,b,c

a Universidad Andrés Bello, Santiago (Chile)
b Millenium Institute for Fundamental and Applied Biology, Santiago (Chile)
c Fundación Ciencia para la Vida, Santiago (Chile)

Scientometrics, Vol. 72, No. 1 (2007) 93–103
DOI: 10.1007/s11192-007-1737-5

Scientometrics
The Sisyphus challenge in Chile

• "Developing countries share disbelief about the benefits of the endogenous production of science as a tool for economical growth. Hence, public policies to strengthen science and technology and promote the culture of innovation are, in general, weak."
The Sisyphus challenge in Brazil

Translational research: “Crossing the Valley of Death”

The path from health innovation to application: Six components/determinants (*)

1. Capacity for and undertaking R&D
2. Capabilities to manufacture products to appropriate standards
3. Promoting and sustaining domestic markets
4. Promoting and sustaining export markets
5. Creating and implementing systems for intellectual property management

LDCs → IDCs → OECD and the six components of health innovation

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Manufacture</th>
<th>Domestic Market</th>
<th>Export Market</th>
<th>R&amp;D</th>
<th>IP System</th>
<th>Drug Regulatory System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assembly of imported components</td>
<td>Small market</td>
<td>Very little except as toll manufacturers</td>
<td>Very little</td>
<td>Very limited understanding of IP, no IP protection</td>
<td>Very limited</td>
<td></td>
</tr>
</tbody>
</table>

| Stage 2 | Manufacture or domestically developed high technology products with significant cost advantages over Northern products | Growing domestic market of increasing interest to foreign companies; some import substitution; significant share of exports go to other developing countries | Growing trade companies learning how to establish export markets; significant share of exports go to other developing countries | Local government and foreign donor-funded R&D to understand technology either to produce on license or to copy | Parents allowed for local inventors, but foreign inventors and investors still not interested because of lack of markets and IP protection; few local public-private partnerships (PPPs) | Limited services without enforcement capabilities |

| Stage 3 | Manufacture of domestically developed high technology products with significant cost advantages over Northern products, growing source of outsourcing | Rapidly growing domestic market of interest to foreign companies | Increasing exports make significant contribution to GDP; significant share of exports go to other developing countries | Scientifically advanced, funded predominantly by local government, and carried out predominantly by local public research institutions capable of innovation | Advanced IP system, but poorly enforced; moderate experience with technology management in local PPPs | Advanced capabilities but not at highest level because of need to strengthen capabilities as appropriate |

| Developed countries | Most developed capabilities to produce high technology drugs, vaccines and devices | Highly profitable market in both the public and private sectors generating profits to support R&D; advanced research | Global companies | Generous support for health research from basic to applied. Large research investment by private companies, including large pharmaceutical manufacturers and biotechnology companies | Established system of IP protection, and management of technology in local PPPs (e.g., university-industry R&D agreements) | A dedicated agency overseeing regulatory approvals of drugs and vaccines. In addition, the government oversees clinical trials & production facilities and enforces rules and regulations |

http://www.biodevelopments.org/innovation/index.htm
National Health Innovation System

Networks and partnerships

Health Innovation: Opportunities
Evolution of the scientific enterprise. **(Left)** For centuries, creative individuals were embedded in an invisible college, that is, a community of scholars whose exchange of ideas represented the basis for scientific advances. Although intellectuals built on each other’s work and communicated with each other, they published alone. Most great ideas were attributed to a few influential thinkers: Galileo, Newton, Darwin, and Einstein. Thus, the traditional scientific enterprise is best described by many isolated nodes (blue circles). **(Middle)** In the 20th century, science became an increasingly collaborative enterprise, resulting in such iconic pairs as the physicist Crick and the biologist Watson (left), who were responsible for unraveling DNA’s structure. The joint publications documenting these collaborations shed light on the invisible college, replacing the hidden links with published coauthorships. **(Right)** Although it is unlikely that large collaborations—such as the D0 team in particle physics or the International Human Genome Sequencing Consortium pictured here—will come to dominate science, most fields need such collaborations. Indeed, the size of collaborative teams is increasing, turning the scientific enterprise into a densely interconnected network whose evolution is driven by simple universal laws.
GROUP THEORY

What makes a successful team? John Whitfield looks at research that uses massive online databases and network analysis to come up with some rules of thumb for productive collaborations.

455:720–723
Health Innovation Networks to Help Developing Countries Address Neglected Diseases
C. M. Morel et al.
Health Innovation Networks to Help Developing Countries Address Neglected Diseases


Gross inequities in disease burden between developed and developing countries are now the subject of intense global attention. Public and private donors have marshaled resources and created organizational structures to accelerate the development of new health products and to procure and distribute drugs and vaccines for the poor. Despite these encouraging efforts directed primarily from and funded by industrialized countries, sufficiency and sustainability remain enormous challenges because of the sheer magnitude of the problem. Here we highlight a complementary and increasingly important means to improve health equity: the growing ability of some developing countries to undertake health innovation.

• Developing Country Vaccine Manufactures’ Network
  - Brazil, Cuba, China, India, Indonesia, Mexico

• WHO Developing Countries’ Vaccine Regulators Network
  - Brazil, China, Cuba, India, Indonesia, Russia, South Africa, South Korea, Thailand

Sources amounts to more than all that was spent in 2004 by the above-mentioned PDPs engaged in the development of drugs, vaccines, and diagnostics for diseases of the poor (8, 9).

Patents and well-cited publications indicate the productivity of research investments, and in this light, IDCs have made major progress. The number of U.S. patents per capita is a common proxy used to measure the relative innovation.
DNDi networks: ‘LEAP’
(DNDi: Drugs for Neglected Diseases initiative)
MINISTRY OF HEALTH

KIMALEL HEALTH CENTRE

P.O. Box. 71, MARIGAT.

DNDi / KEMRI

Drugs for Neglected Diseases initiative.

Kenya Medical Research Institute.

Kala-azar Research & Treatment Centre.
DNDi networks: HAT, PAN4ND

- **THE HAT PLATFORM**

  - **Target disease:** HAT
  - **Core partners:** STI; national HAT control programmes of most affected endemic countries (see map on left); national and international research groups (e.g. ITMA, INRB, CDC, and KARI-TRC); NGOs like MSF; FIND; WHO; TDR; regional networks (e.g. EANET, PAEIN, AMANET)
  - **DNDI contact:** Augustin K. Ebeja
  - **Project start:** August 2005; Kinshasa, DRC

- **DISCOVERY RESEARCH PAN-ASIAN NETWORK FOR NEGLECTED DISEASES (PANNID) NATURAL SUBSTANCES SCREENING**

  - **Target disease:** HAT, VL, Chagas
  - **Core partners:** Central Drug Research Institute (CDRI), India; Eskitis Institute, Australia; Forest Research Institute Malaysia (FRIM); Institut Pasteur Korea (IPK); Kitasato Institute (KII), Japan; Malaysian Institute of Pharmacoeconomics and Neutrocoletics (MIPN), Malaysia; Novartis Institute of Tropical Diseases (NITD), Singapore; Shanghai Institute of Materia Medica (SIMM), China.
  - **DNDI contact:** Jean-Robert Isset
  - **Project start:** May 2006; Tokyo, Japan
“African Network for Drugs and Diagnostics Innovation”, ANDI

Learning from history, planning the future

HEALTH INNOVATION, FIOCRUZ
2009
Learning from History — Nancy Stepan:
Beginnings of Brazilian Science

© Science History Publications, 1976

© Editora Artenova S.A., 1976
Beginnings of Brazilian Science

- In its research, barriers between basic and applied science broke down; many investigations originally undertaken for their scientific value yielded unexpected practical results, while practical studies often led to new research. There was as a result a
Origens da ciência biomédica brasileira

... As barreiras entre a ciência básica e aplicada se romperam; muitas investigações realizadas originalmente, por seu valor científico, produziram resultados práticos inesperados, ao passo que estudos práticos levaram muitas vezes a novas pesquisas. Houve, em consequência, uma realimentação contínua e benéfica de
Center for Technological Development in Health
CDTS/FIOCRUZ
Product Development

Partnerships with international partners/networks

**Fiocruz-DNDi:** Artesunate-Mefloquine (AS/MQ) against malaria

**Fiocruz-Genzyme:** R&D agreement on neglected diseases
Fiocruz–Genzyme partnership: Current projects on **Chagas disease**

- Identification of biochemical targets by genomics and bioinformatics
- Synthesis of small molecules with therapeutic potential against *T. cruzi*
- Screening Genzyme compounds against *T. cruzi* both *in vitro* and *in vivo*
- Role of the Transforming Growth Factor beta (TGF-β) on *T. cruzi*
Target identification

• Presumptive biochemical targets (sterol biosynthesis) identified by genomics and bioinformatics at Fiocruz
  - Genes for phosphomevalonate kinase (FMK) and isopentenyl diphosphate isomerase (IPP) cloned at Fiocruz and sent to Genzyme.
  - Expression of FMK in progress at Genzyme.
  - High throughput screening assay
Synthesis of rhenium, palladium and nickel complexes against *T. cruzi*

- Metal-containing small molecule inhibitors of cathepsin-B protease synthesized at Genzyme and shipped to Fiocruz (CPqRR, Belo Horizonte) for testing against *T.*
Metal-containing cathepsin-B protease inhibitors inhibit growth of *T. cruzi* in vitro

- Screening capabilities at Fiocruz used for testing activity of Genzyme compounds against *T. cruzi* both in vitro and in vivo

### Resultados

<table>
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<tr>
<th>Drogas</th>
<th>Código</th>
<th>Experimento 1</th>
<th>Experimento 2</th>
<th>Experimento 3</th>
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</table>

BZ: Benzonidazol.
TGFβ and *T. cruzi*

- Anti-TGFβ antibody sent from Genzyme to Fiocruz
  - Confirmed that host TGFβ is required for *T. cruzi* invasion and differentiation both in vitro and in vivo
  - Parasite TGFβ receptor may represent a possible drug target
Fiocruz-Genzyme partnership: Mutual capacity building

- Senior chemist from Fiocruz spent 6 months at Genzyme working on organic synthesis of cathepsin-B inhibitors.
- Two Fiocruz project managers spent 2 weeks at Genzyme working with other project managers and scientists.
- Senior biologist from Fiocruz to spend a month at Genzyme characterizing the *T. cruzi* TGFβ receptor.
- Senior scientist from Genzyme to spend 3 weeks at Fiocruz in fall '09.
- Several scientific exchanges both in Brazil and USA to review data, plan upcoming studies
Teams involved in collaborative networks

**DNDi**
- Bernard Pécoul
- Isabela Ribeiro
- Jean-Pierre Paccaud
- Jean-René Kiechel
- Michel Lotrowska

**Fiocruz**
- Alvaro Romanha
- Ana Paula Brum
- Eduardo Costa
- Jamaira Giora
- James Wardell
- Jorge Costa
- Jorge Mendonça
- Maria das Graças Henriques
- Mariana Waghabi
- Marcelo Ferreira
- Marcus Souza
- Nubia Boechat
- Patricia Seixas
- Renata Curi
- Renata Souza
- Solange Wardell
- Wim Degrave

**Genzyme**
- Carol Sherako
- Cassandra Celatka
- Clarence Wang
- Edmund Sybertz
- Elisabeth Tsilikounas
- Hanlan Liu
- Jeff Klinger
- James Geraghty
- Katherine Klinger
- Michael Booker
- Paulo Braga
- Renato Skerlj
- Rogerio Vivaldi
- Robert Barker
- Steve Ledbetter
- Sunil Mhaskar

**CAPES-Fiocruz Steering Committee**
- CAPES
  - Antonio Carlos C. Carvalho
  - Eliezer Barreiro
  - José Luiz de Lima Filho

- Fiocruz
  - Maria das Graças Henriques
  - Ricardo Galler
Fiocruz-Genzyme collaboration
Fiocruz-Genzyme partnership: Moving beyond neglected diseases?

- Discussions in progress around role for Genzyme in Fiocruz new Center for Technological Development in Health (CDTS) in collaboration with the Brazilian Network on Cell Therapy.
Center for Technological Development in Health
CDTS/FIOCRUZ
May 25, 2009

Photo taken at the construction site, May 2009

Video: CTDS maquette

Source: ATPeng

Photos: CDTS maquette
CDTS/Fiocruz: home of the CNPq/Decit/FAPERJ National Institute of Science and Technology on Innovation on Neglected Diseases

http://cdtsfiocruz.blogspot.com
http://cdtsfiocruz-english.blogspot.com
Doença de Chagas: Prevenção não BASTA!
Thank you

Muito obrigado

morel@cdts.fiocruz.br