May 16th, 9:45 AM

Keynote Address: New Poverty-Related Neglected Diseases ('The NTDs')

Peter Hotez
Baylor College of Medicine



Baylor College of Medicine

Texas Children's Hospital

New Poverty-Related Neglected Diseases ('The NTDs')

Peter Hotez, M.D., Ph.D.

Texas Children's Hospital Endowed Chair in Tropical Pediatrics

Dean, National School of Tropical Medicine at Baylor College of Medicine

Former U.S. Science Envoy
@PeterHotez

From the MDGs to the SDGs

2000-15 MDGs

The Millennium Development Goals

1. Eradicate extreme poverty and hunger.
2. Achieve universal primary education.
3. Promote gender equality and empower women.
4. Reduce child mortality.
5. Improve maternal health.
6. Combat HIV/AIDS, malaria, and other diseases.
7. Ensure environmental sustainability.
8. Develop a global partnership for development.

Gavi
The Vaccine Alliance

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The Global Burden of Disease Study

Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010

Rafael Lozano, Mohsen Naghavi, Kyle Foreman, Stephen Lim, Kenji Shibuya, Victor Aboyans*, Jerry Abraham*, Timothy Adair*, Rakesh Aggarwal*, Stephanie Y Ahn*, Miriam Alvarado*, H Ross Anderson*, Laurie M Anderson*, Kathryn G Andrews*, Charles Atkinson*, Larry M Baddour*, Suzanne Barker-Collo*, David H Bartels*, Michelle L Bell*, Emelia J Benjamin*, Derrick Bennett*, Kavi Bhalla*, Boris Bikbov*, Aref Bin Abdulhak*, Gretchen Birbeck*, Fiona Blyth*, Ian Bolliger*, Soufiane Boufous*, Chiara Bucello*, Michael Burch*, Peter Burney*, Jonathan Carapetis*, Honglei Chen*, David Chou*, Sumeet S Chugh*, Luc E Coffeng*, Steven D Colan*, Samantha Colquhoun*, K Ellicott Colson*, John Condon*, Myles D Connor*, Leslie T Cooper*, Matthew Corriere*, Monica Cortinovis*, Karen Courville de Vaccaro*, William Couser*, Benjamin C Cowie*, Michael H Criqui*, Marita Cross*, Kaustubh C Dabhadkar*, Nabila Dahodwala*, Diego De Leo*, Louisa Degenhardt*, Allyne Delossantos*, Julie Denenberg*, Don C Des Jarlais*, Samath D Dharmaratne*, E Ray Dorsey*, Tim Driscoll*, Herbert Duber*, Beth Ebel*, Patricia J Erwin*, Patricia Espindola*, Majid Ezzati*, Valery Feigin*, Abraham D Flaxman*, Mohammad H Forouzanfar*, Francis Gerry R Fowkes*, Richard Franklin*, Marlene Fransen*, Michael K Freeman*, Sherine E Gabriel*, Emmanuela Gakidou*, Flavio Gaspari*, Richard F Gillum*, Diego Gonzalez-Medina*, Yara A Halasa*, Diana Haring*, James E Harrison*, Rasmus Havmoeller*, Roderick J Hay*, Bruno Hoen*, Peter J Hotez*, Damian Hoy*, Kathryn H Jacobsen*, Spencer L James*, Rashmi Jasrasaria*, Sudha Jayaraman*, Nicole Johns*, Ganesan Karthikeyan*, Nicholas Kassebaum*, Andre Keren*, Jon-Paul Khoo*, Lisa Marie Knowlton*, Olive Kobusingye*, Adofo Koranteng*, Rita Krishnamurthi*, Michael Lipnick*, Steven E Lipshultz*, Summer Lockett Ohno*, Jacqueline Mabweijano*, Michael F MacIntyre*, Leslie Mallinger*, Lyn March*, Guy B Marks*, Robin Marks*, Akira Matsumori*, Richard Matzopoulos*, Bongani M Mayosi*, John H McAnulty*, Mary M McDermott*, John McGrath*, George A Mensah*, Tony R Merriman*, Catherine Michaud*, Matthew Miller*, Ted R Miller*, Charles Mock*, Ana Olga Mocumbi*, Ali A Mokdad*, Andrew Moran*, Kim Mulholland*, M Nathan Nair*, Luigi Naldi*, K M Venkat Narayan*, Kiumarss Nasseri*, Paul Norman*, Martin O'Donnell*, Saad B Omer*, Katrina Ortblad*, Richard Osborne*, Doruk Ozgediz*, Bishnu Pahari*, Jeyaraj Durai Pandian*, Andrea Panozo Rivero*, Rogelio Perez Padilla*, Fernando Perez-Ruiz*, Norberto Perico*, David Phillips*, Kelsey Pierce*, C Arden Pope III*, Esteban Porrini*, Farshad Pourmalek*, Murugesan Raju*, Dharani Ranganathan*, Jürgen T Rehm*, David B Rein*, Guiseppe Remuzzi*, Frederick P Rivara*, Thomas Roberts*, Felipe Rodriguez De León*, Lisa C Rosenfeld*, Lesley Rushton*, Ralph L Sacco*, Joshua A Salomon*, Uchechukwu Sampson*, Ella Sanman*, David C Schwebel*, Maria Segui-Gomez*, Donald S Shepard*, David Singh*, Jessica Singleton*, Karen Sliwa*, Emma Smith*, Andrew Steer*, Jennifer A Taylor*, Bernadette Thomas*, Imad M Tleyjeh*, Jeffrey A Towbin*, Thomas Truelsen*, Eduardo A Undurraga*, N Venketasubramanian*, Lakshmi Vijayakumar*, Theo Vos*, Gregory R Wagner*, Mengru Wang*, Wenzhi Wang*, Kerrianne Watt*, Martin A Weinstock*, Robert Weintraub*, James D Wilkinson*, Anthony D Woolf*, Sarah Wulf*, Pon-Hsiu Yeh*, Paul Yip*, Azadeh Zabetian*, Zhi-Jie Zheng*, Alan D Lopez†, Christopher J L Murray†‡

The Global Burden of Disease 2013

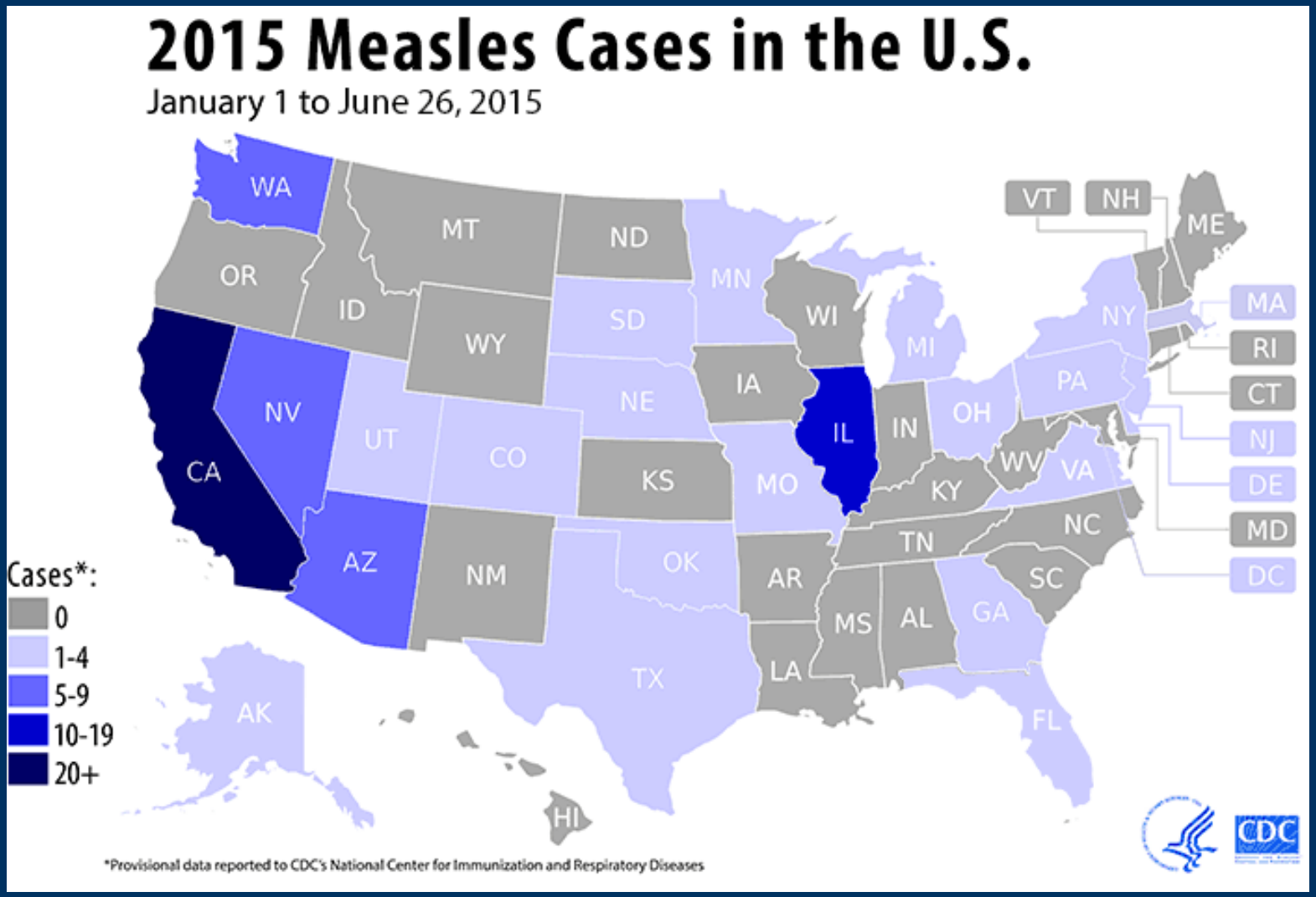
Expanded use of vaccines

- 83% reduction in measles deaths
- 82% reduction in tetanus deaths
- 57% reduction in diphtheria/pertussis deaths
- 45% reduction in Hib deaths

Development new vaccines

- Pneumococcal disease (36% reduction in deaths)
- Rotavirus (63% reduction in deaths)

2.5 million childhood lives saved through these initiatives



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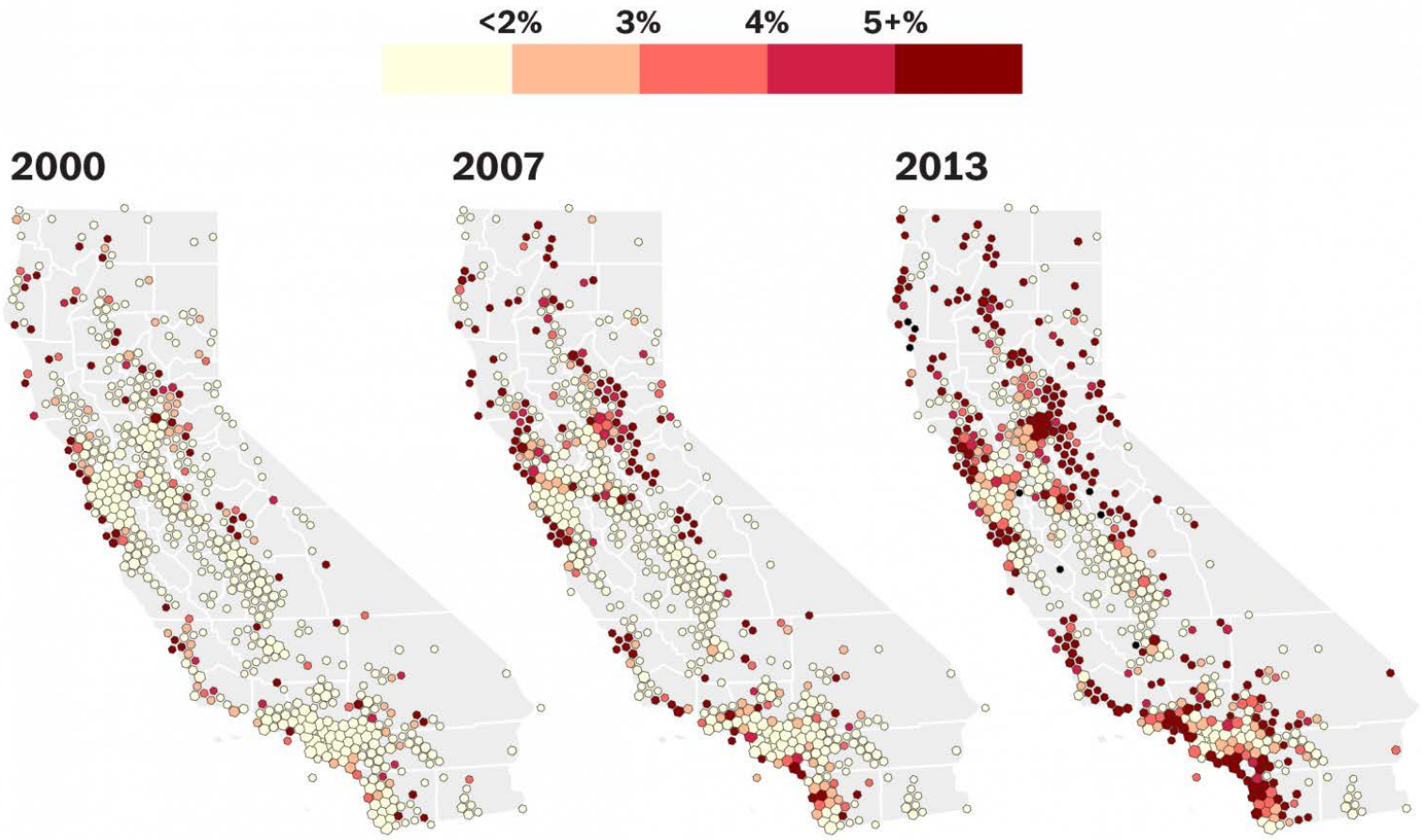
The spread of anti-vax sentiment in California

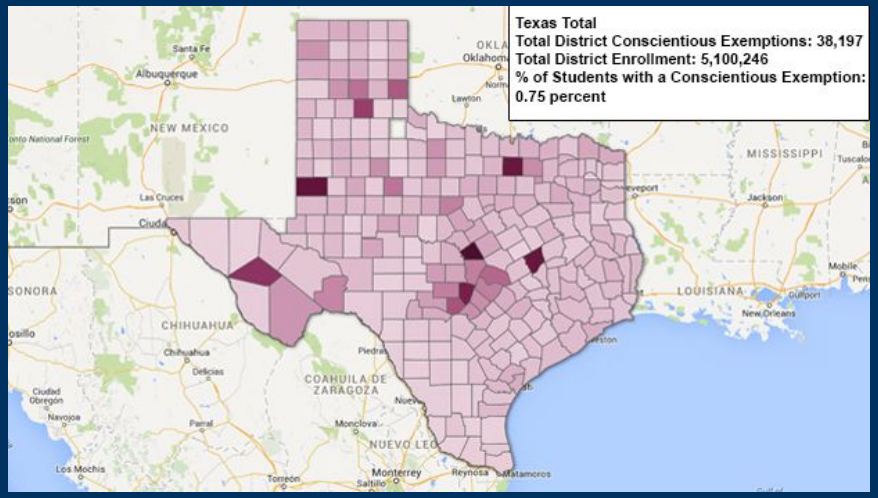
Share of public school kindergartners with personal belief exemptions to vaccination requirements

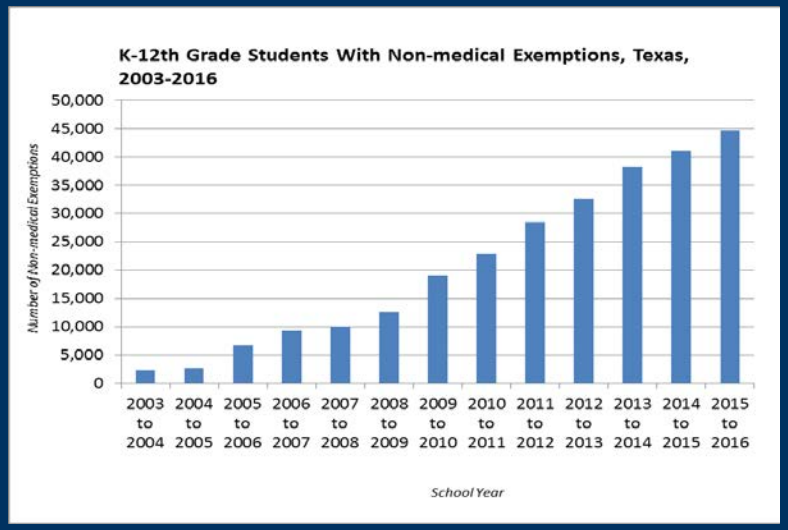


WASHINGTONPOST.COM/**WONKBLOG**

Source: California Department of Public Health

TEXANS for Vaccine Choice





- Texas ranks at the bottom of fully immunized children
- 45,000 Personal Belief Exemptions in Texas

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Patches of Disorganization in the Neocortex of Children with Autism

Rich Stoner, Ph.D., Maggie L. Chow, Ph.D., Maureen P. Boyle, Ph.D., Susan M. Sunkin, Ph.D., Peter R. Mouton, Ph.D., Subhojit Roy, M.D., Ph.D., Anthony Wynshaw-Boris, M.D., Ph.D., Sophia A. Colamarino, Ph.D., Ed S. Lein, Ph.D., and Eric Courchesne, Ph.D.

ABSTRACT

BACKGROUND

Autism involves early brain overgrowth and dysfunction, which is most strongly evident in the prefrontal cortex. As assessed on pathological analysis, an excess of neurons in the prefrontal cortex among children with autism signals a disturbance in prenatal development and may be concomitant with abnormal cell type and

The Millennium Development Goals

1. Eradicate extreme poverty and hunger.
2. Achieve universal primary education.
3. Promote gender equality and empower women.
4. Reduce child mortality.
5. Improve maternal health.
6. Combat HIV/AIDS, malaria and other diseases.
7. Ensure environmental sustainability.
8. Develop a global partnership for development.

Articles

Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013

Christopher J L Murray*, Katrina F Ortblad, Caterina Guinovart, Stephen S Lim, Timothy M Wolock, D Allen Roberts, Emily A Dansereau, Nicholas Graetz, Ryan M Barber, Jonathan C Brown, Haidong Wang, Herbert C Duber, Mohsen Naghavi, Daniel Dicker, Lalit Dandona, Joshua A Salomon, Kyle R Heuton, Kyle Foreman, David E Phillips, Thomas D Fleming, Abraham D Flaxman, Bryan K Phillips, Elizabeth K Johnson, Megan S Coggeshall, Foad Abd-Allah, Semaw Ferede Aberat, Jerry P Abraham, Ibrahim Abubakar, Laith J Abu-Raddad, Niveen Me Abu-Rmeileh, Tom Achoki, Austine Olufemi Adeyemo, Arsène Kouablan Adou, José C Adsuar, Emilie Elisabet Agardh, Dickens Akena, Mazin J Al Kahbouri, Deena Alasfoor, Mohammed I Albittar, Gabriel Alcalá-Cerra, Miguel Angel Alegretti, Zewdie Aderaw Alemu, Rafael Alfonso-Cristancho, Samia Alhabib, Raghib Ali, Francois Allal, Peter J Allen, Ubai Alsharif, Elena Alvarez, Nelson Alvis-Guzman, Adansi A Amankwaa, Azmeraw T Amare, Hassan Amini, Walid Ammar, Benjamin O Anderson, Carl Abelardo T Antonio, Palwasha Anwari, Johan Ärnlöv, Valentina S Arsic Arsenijevic, Ali Artaman, Rana J Asghar, Reza Assadi, Lydia S Atkins, Alaa Badawi, Kalpana Balakrishnan, Amitava Banerjee, Sanjay Basu, Justin Beardsley, Tolesa Bekele, Michelle L Bell, Eduardo Bernabe, Tariku Jibat Beyene, Neeraj Bhala, Ashish Bhalla, Zulfiqar A Bhutta, Aref Bin Abdulhak, Agnes Binagwaho, Jed D Blore, Dipan Bose, Michael Brainin, Nicholas Breitborde, Carlos A Castañeda-Orjuela, Ferrán Catalá-López, Vineet K Chadha, Jung-Chen Chang, Peggy Pei-Chia Chiang, Ting-Wu Chuang, Mercedes Colomar, Leslie Trumbull Cooper, Cyrus Cooper, Karen J Courville, Benjamin C Cowie, Michael H Criqui, Rakhi Dandona, Anand Dayama, Diego De Leo, Louisa Degenhardt, Borja Del Pozo-Cruz, Kebede Deribe, Don C Des Jarlais, Muluken Dessalegn, Samath D Dharmaratne, Ugur Dilmen, Eric L Ding, Tim R Driscoll, Adnan M Durrani, Richard G Ellenbogen, Sergey Petrovich Ermakov, Alireza Esteghamati, Emerito Jose A Faraon, Farshad Farzadfar, Seyed-Mohammad Fereshtehnejad, Daniel Obadare Fijabi, Mohammad H Forouzanfar, Urbano Fra Paleo, Lynne Gaffikin, Amiran Gamkrelidze, Fortuné Gbètoho Gankpé, Johanna M Geleijnse, Bradford D Gessner, Katherine B Gibney, Ibrahim Abdelmageem Mohamed Ginawi, Elizabeth L Glaser, Philimon Gona, Atsushi Goto, Hebe N Gouda, Harish Chander Gugnani, Rajeev Gupta, Rahul Gupta, Nima Hafezi-Nejad, Randah Ribhi Hamadeh, Mouhanad Hammami, Graeme J Hankey, Hilda L Harb, Josep Maria Haro, Rasmus Havmoeller, Simon I Hay, Mohammad T Hedayati, Ileana B Heredia Pi, Hans W Hoek, John C Hornberger, H Dean Hosgood, Peter J Hotez, Damian G Hoy, John J Huang, Kim M Iburg, Bulat T Idrisov, Kaire Innos, Kathryn H Jacobsen, Panniyammakal Jeemon, Paul N Jensen, Vivekanand Jha, Guohong Jiang, Jost B Jonas, Knud Juel, Haidong Kan, Ida Kankindi, Nadim E Karam, André Karch, Corine Kakizi Karema, Anil Kaul, Norito Kawakami, Dhruv S Kazi, Andrew H Kemp, Andre Pascal Kengne, Andre Keren, Maia Kereselidze, Yousef Saleh Khader, Shams Eldin Ali Hassan Khalifa, Ejaz Ahmed Khan, Young-Ho Khang, Irma Khonelidze, Yohannes Kinfu, Jonas M Kinge, Luke Knibbs, Yoshihiro Kokubo, S Kosen, Barthelemy Kuate Defo, Veena S Kulkarni, Chanda Kulkarni, Kaushalendra Kumar, Ravi B Kumar, G Anil Kumar, Gene F Kwan, Taavi Lai, Arjun Lakshmana Balaji, Hilton Lam, Qing Lan, Van C Lansingh, Heidi J Larson, Anders Larsson, Jong-Tae Lee, James Leigh, Mall Leinsalu, Ricky Leung, Yichong Li, Yongmei Li, Graça Maria Ferreira De Lima, Hsien-Ho Lin, Steven E Lipshultz, Shiwei Liu, Yang Liu, Belinda K Lloyd, Paulo A Lotufo, Vasco Manuel Pedro Machado, Jennifer H Maclachlan, Carlos Magis-Rodriguez, Marek Majdan, Christopher Chabila Mapoma, Wagner Marcenes, Melvin Barrientos Marzan, Joseph R Masci, Mohammad Taufiq Mashal, Amanda J Mason-Jones, Bongani M Mayosi, Tasara T Mazorodze, Abigail Cecilia Mckay, Peter A Meaney, Man Mohan Mehndiratta, Fabiola Mejia-Rodriguez, Yohannes Adama Melaku,

6

COMBAT HIV/AIDS, MALARIA AND OTHER DISEASES

- 19 million lives saved from AIDS
- 30% reduction in Malaria

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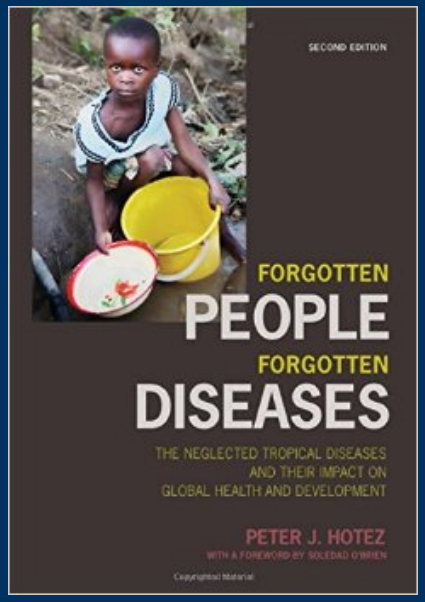
"Other Diseases"

The Neglected Tropical Diseases

- 13-14 tropical infections:
  - Highly prevalent among the poor
  - Endemic in rural areas of low-income countries
  - Ancient afflictions
  - Chronic
  - Disabling (growth delays, blindness or disfigurement)
  - Stigmatizing
  - Poverty promoting



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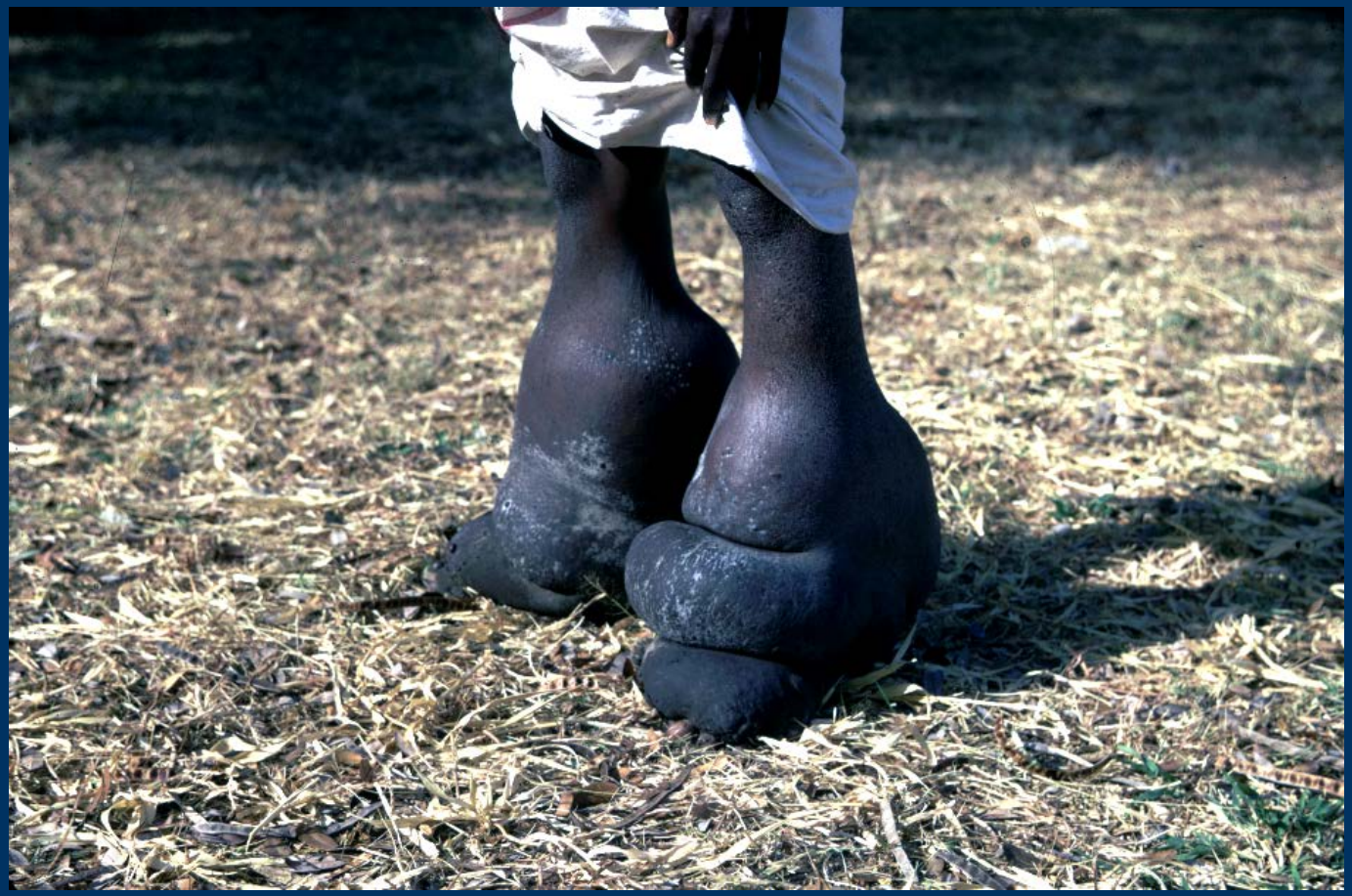
NEGLECTED TROPICAL DISEASES:

NTDs infect more than 1 BILLION of the world's poorest people

Ascariasis	761.9 million	Trachoma	3.6 million
Trichuriasis	463.7 million	Cysticercosis	1.9 million
Hookworm Disease	428.8 million	Echinococcosis	1.4 million
Schistosomiasis	252.2 million	Hansen's Disease	514,200
Dengue and other arboviruses	79.6 million	Rabies	17,400
		African Trypanosomiasis	10,700
Food-borne trematodiases	71.1 million	Guinea worm	<1,000
		Yaws	Not determined
Lymphatic Filariasis	38.5 million	Buruli ulcer	Not determined
Onchocerciasis	15.5 million	Mycetoma	Not determined
Chagas disease	6.7 million	*Zika*	*4 million*
Leishmaniasis	3.9 million	*Ebola*	*2,800*

“It’s quite a problem for me when I have to stand at work for long periods.”



Lymphatic Filariasis (“Elephantiasis”)

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NTDs and Girls & Women

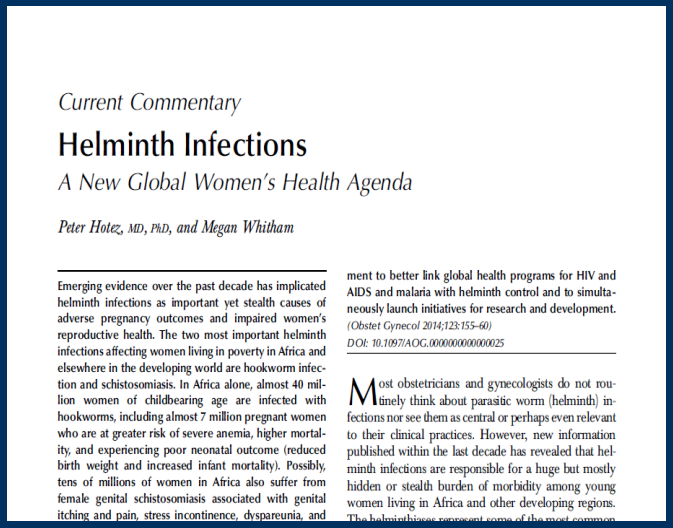
Female Genital Schistosomiasis

Zimbabwe
OR = 3 increase in HIV/AIDS
Kjetland et al. AIDS 2006

Tanzania
OR = 4 increase in HIV/AIDS
Downs et al. AJTMH 2011

100 million girls & women

Africa's most common gynecologic condition?



Current Commentary

Helminth Infections

A New Global Women's Health Agenda

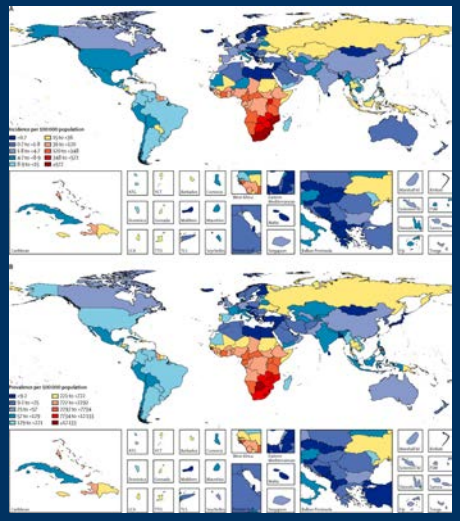
Peter Hotez, MD, PhD, and Megan Whitham

Emerging evidence over the past decade has implicated helminth infections as important yet stealth causes of adverse pregnancy outcomes and impaired women's reproductive health. The two most important helminth infections affecting women living in poverty in Africa and elsewhere in the developing world are hookworm infection and schistosomiasis. In Africa alone, almost 40 million women of childbearing age are infected with hookworms, including almost 7 million pregnant women who are at greater risk of severe anemia, higher mortality, and experiencing poor neonatal outcome (reduced birth weight and increased infant mortality). Possibly, tens of millions of women in Africa also suffer from female genital schistosomiasis associated with genital itching and pain, stress incontinence, dyspareunia, and

ment to better link global health programs for HIV and AIDS and malaria with helminth control and to simultaneously launch initiatives for research and development.

(Obstet Gynecol 2014;123:155–60)
DOI: 10.1097/AOG.0000000000000025

Most obstetricians and gynecologists do not routinely think about parasitic worm (helminth) infections nor see them as central or perhaps even relevant to their clinical practices. However, new information published within the last decade has revealed that helminth infections are responsible for a huge but mostly hidden or stealth burden of morbidity among young women living in Africa and other developing regions.



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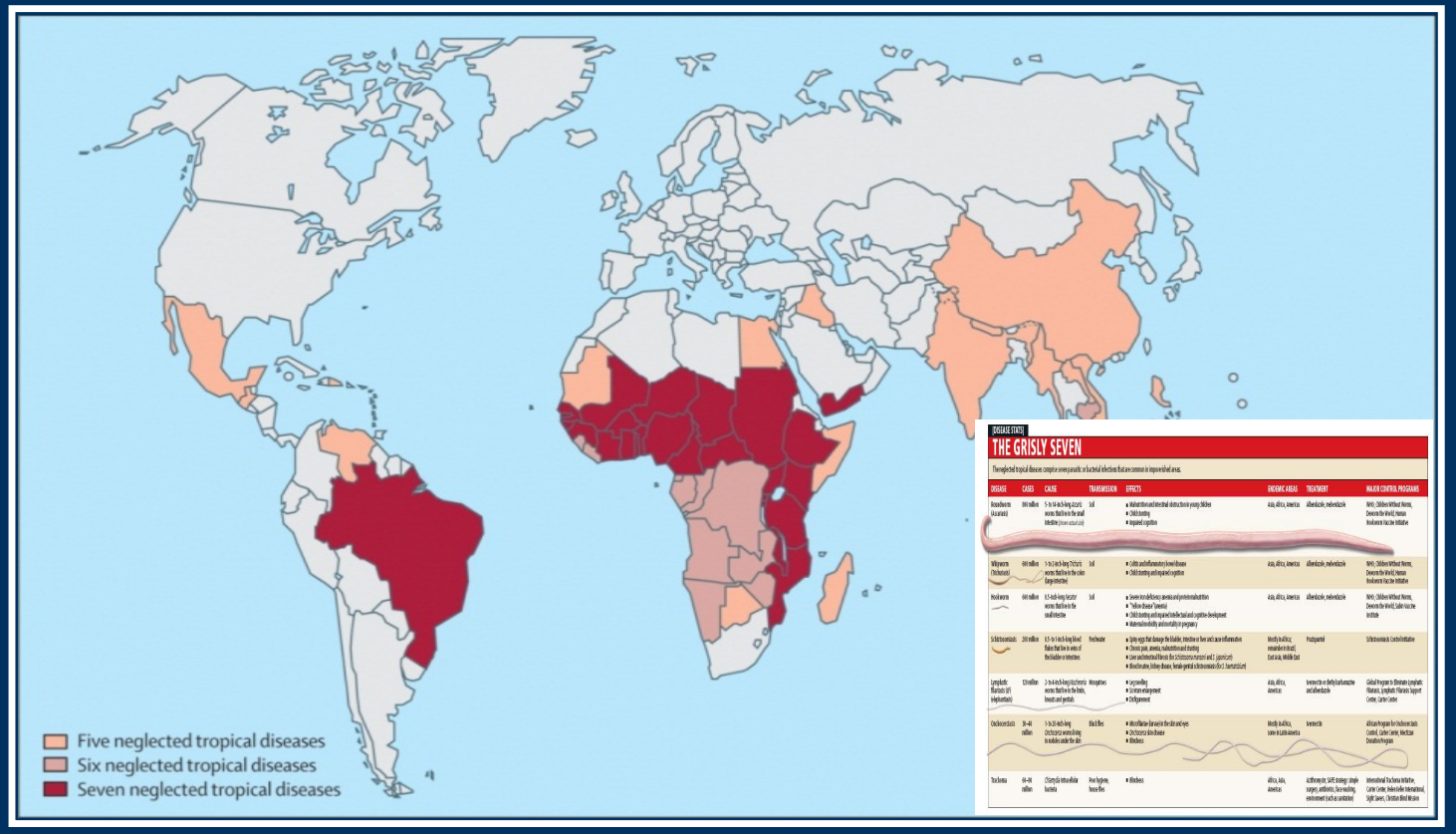
The Bottom Billion Suffers from Multiple NTDs!

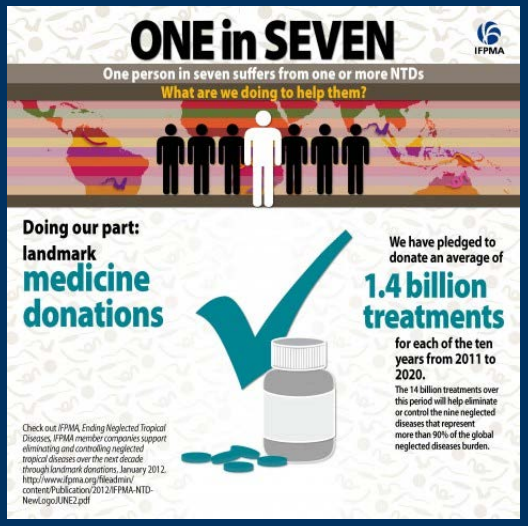
Ascariasis, Trichuriasis, Hookworm, Schistosomiasis, LF, Onchocerciasis, Trachoma



Hotez PJ et al. *Lancet* 2009

NTD Scale up with the U.S. Government + Drug Donations from


"Rapid-Impact Interventions": How a Policy of Integrated Control for Africa's Neglected Tropical Diseases Could Benefit the Poor




Incorporating a Rapid-Impact Package for Neglected Tropical Diseases with Programs for HIV/AIDS, Tuberculosis, and Malaria

INTERNATIONAL BUSINESS TIMES

TECHNOLOGY (HTTP://WWW.IBTIMES.COM/TECHNOLOGY) SCIENCE (HTTP://WWW.IBTIMES.COM/TECHNOLOGY/SCIENCE)

How Three Scientists 'Marketed' Neglected Tropical Diseases And Raised More Than $1 Billion

By Amy Nordrum (/reporters/amy-nordrum)
@amynordrum (http://www.twitter.com/amynordrum)
a.nordrum@ibtimes.com (mailto:a.nordrum@ibtimes.com)

on May 14 2015 1:55 PM EDT

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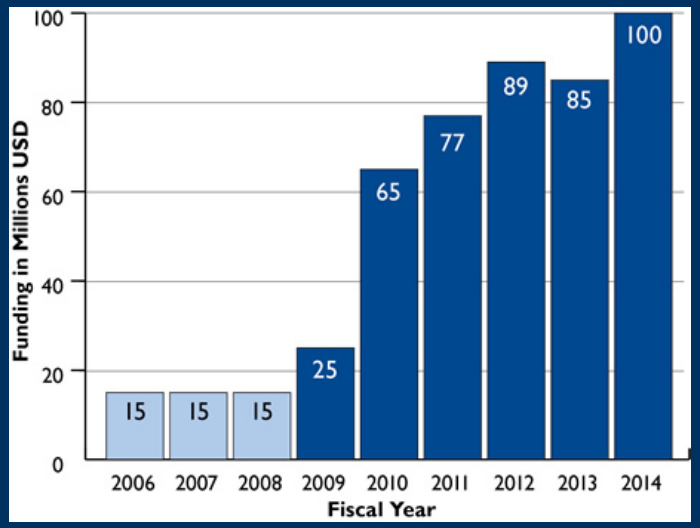
USAID NTD Program



Africa:

Benin
Burkina Faso
Cameroon
DRC
Ghana
Guinea
Mali
Mozambique
Niger
Nigeria
Sierra Leone
Senegal
Tanzania
Togo
Uganda

Asia:

Bangladesh
Cambodia
Indonesia
Philippines
Lao PDR
Nepal
Vietnam

Americas:

Haiti

>450 million People Rx: Elimination of some NTDs

10 SIGNIFICANT GAINS

Mass Drug Administration (MDA)

Lymphatic filariasis
-52% (2005-15)

Onchocerciasis
-52% (1990-2013)

Trachoma
-65% (1990-2013)

Ascariasis
-20% (2005-2015)

Yaws
Not determined

Case detection + Rx + Vector control

African trypanosomiasis
-78%
(2005-2015)

WASH

Dracunculiasis
-99%
(1990-2013)

Other approaches

Rabies (Canine)
-53%
(2005-2015)

Cysticercosis
-21%
(2005-2015)

Leprosy

Elimination targets:
LF
Trachoma
Yaws
African trypanosomiasis
Dracunculiasis
Leprosy (Hansen's Disease)

Source: GBD 2015 and GBD 2013

9 MAJOR SETBACKS

Mass Drug Administration (MDA)	Case detection + Rx + Vector control	WASH	Other approaches
Schistosomiasis +30% (1990-2013)	**Leishmaniasis** +174% (1990-2013)	**Ebola** +28,000% (2005-2015)	**Food-borne Trematodiases** +51% (1990-2013)
Hookworm -5% (1990-2013)	**Chagas disease** +22% (1990-2013)	**Coronaviruses**	
Trichuriasis -12% (1990-2013)	**Dengue & Other Arbovirus Infections** +610% (1990-2013)		

Losing the Battle:

Vector-borne Neglected Diseases
- Arthropods
- Snails

Zoonotic Neglected Diseases
- Viral Diseases

Source: GBD 2015 and GBD 2013

Are we playing "global health whack-a-mole"?

MDGs

AIDS
Malaria
Some NTDs
Childhood dz

SDGs

NTDs V.2.0
Vector-borne NTDs
Zoonotic NTDs

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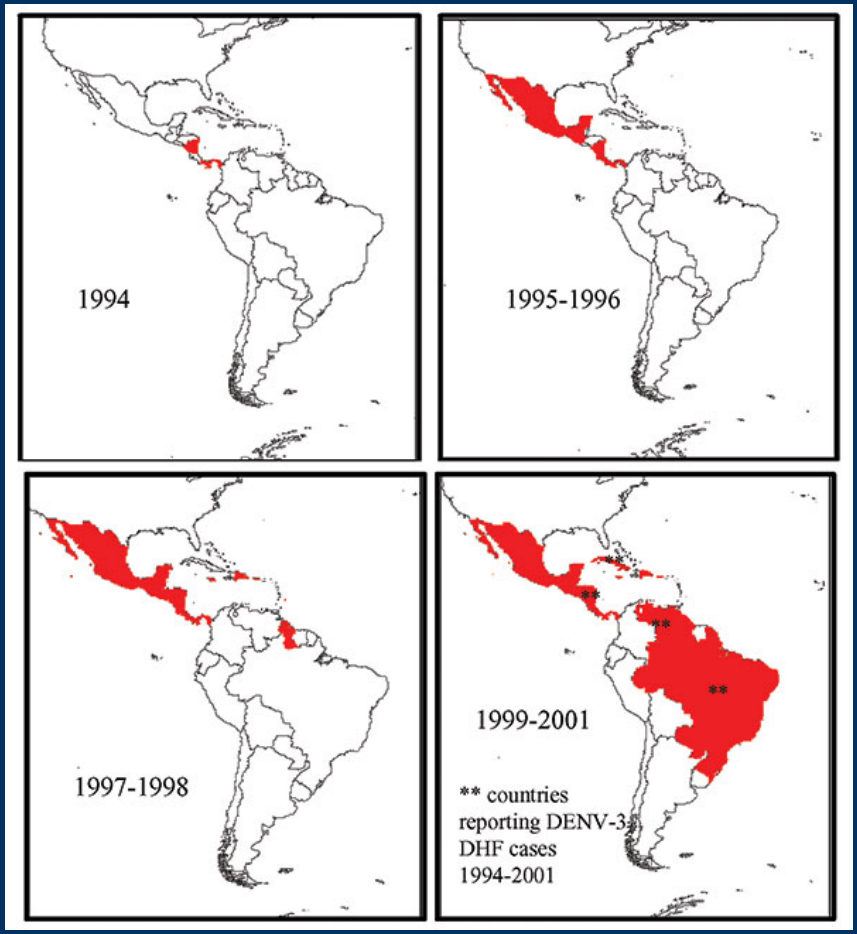
Explosive Outbreaks in the Americas



Emergence of Dengue in the New World in 1980s, 1990s

Zika Path: Explosive Pacific Outbreaks

Emergence of Chikungunya in New World in 2013 (Saint Martin)

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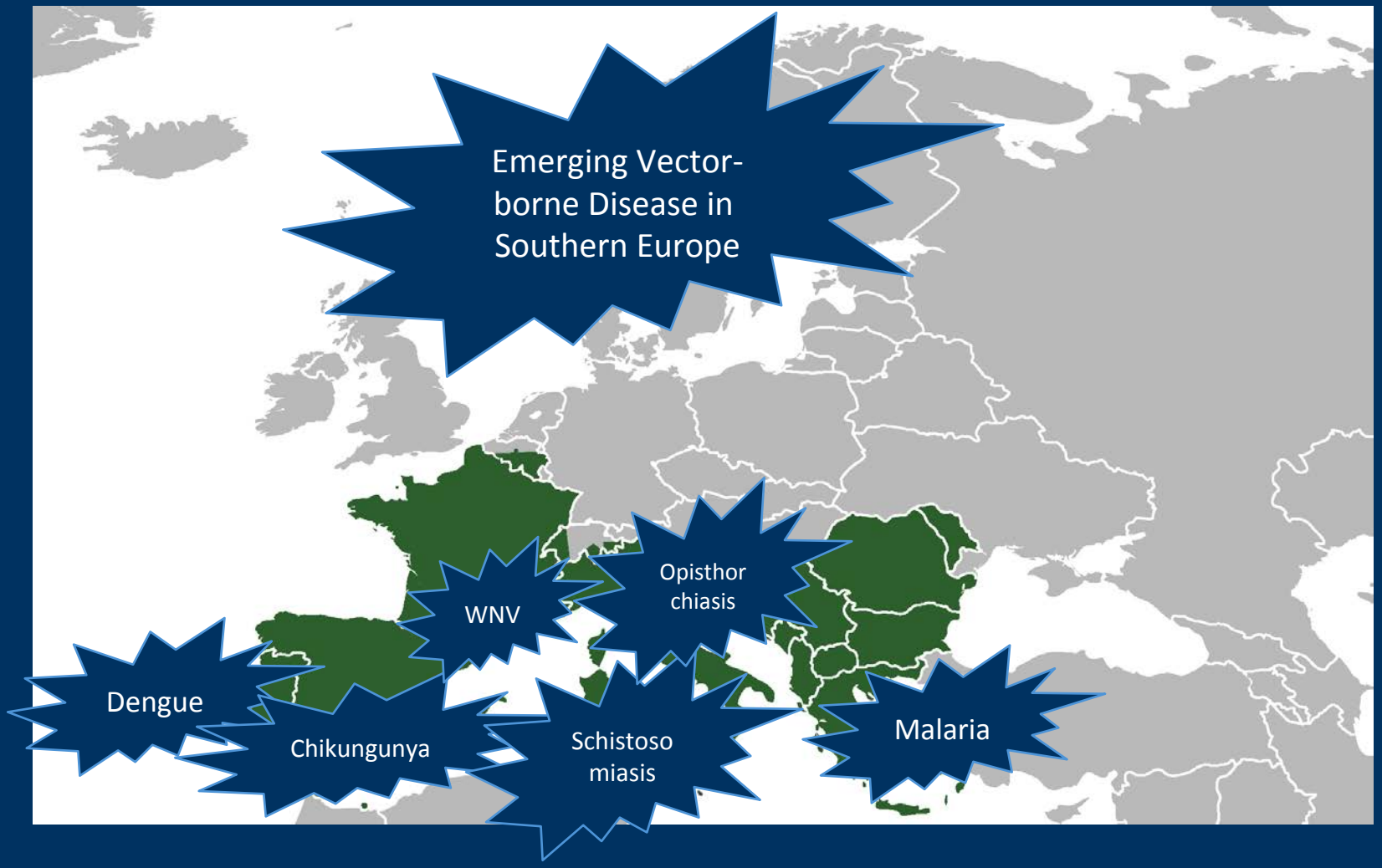
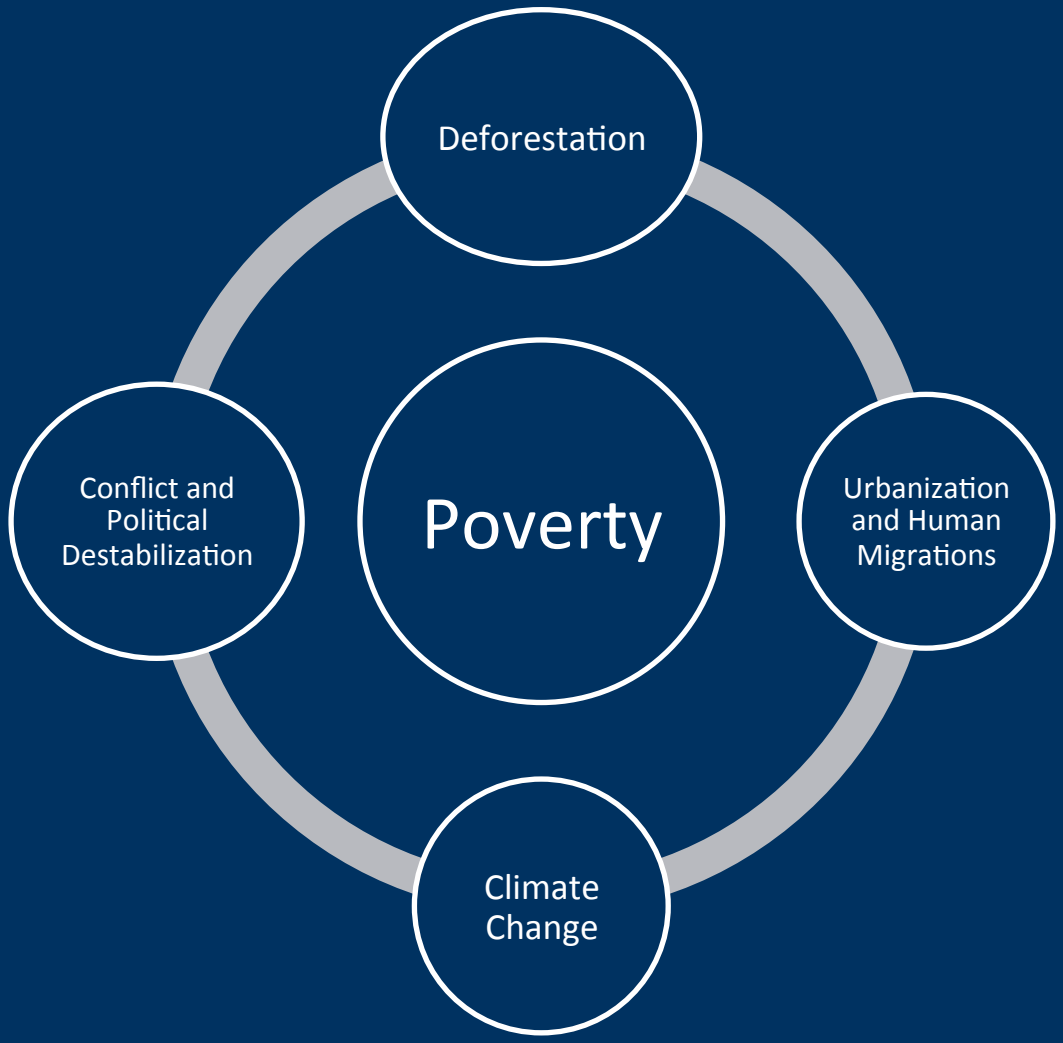


EMERGING VECTOR BORNE NEGLECTED DISEASE IN SOUTHERN EUROPE

The Anthropocene

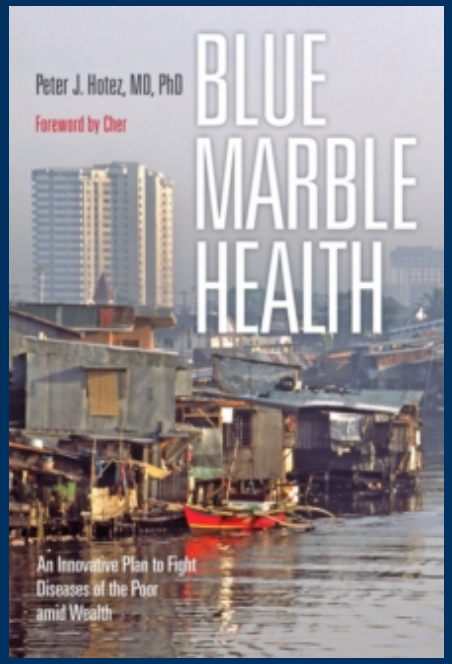
The **Anthropocene** is a proposed epoch that begins when human activities started to have a significant global impact on Earth's geology and ecosystems.

Anthropocene forces promoting NTDs



POVERTY: "Blue Marble Health"

- Neglected diseases of the poor living amidst wealth
- A new framework for global science policy and the poverty-related diseases



Blue Marble Health:

The poor living among the wealthy (G20 + Nigeria)

WHO + GBD 2013

- 73-78% Leprosy
- 61-78% Chagas
- 60-61% Dengue
- 57-60% TB
- 45-67% VL
- 50-52% Helminths

- STH
- Schistosomiasis
- Lymphatic Filariasis
- Onchocerciasis

G20 + Nigeria = 54% Population and 86% Global Economy

Hotez PJ (2013) NTDs V.2.0: "Blue Marble Health"—Neglected Tropical Disease Control and Elimination in a Shifting Health Policy Landscape. PLoS Negl Trop Dis 7(11): e2570. doi:10.1371/journal.pntd.0002570
http://www.plosntd.org/article/info:doi/10.1371/journal.pntd.0002570

PLOS | NEGLECTED TROPICAL DISEASES

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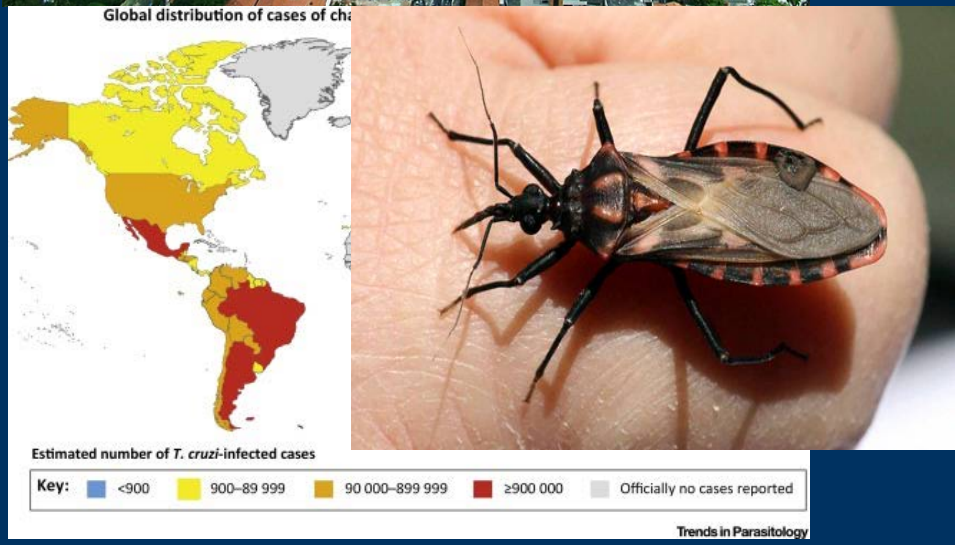
Chagas disease in Argentina, Brazil, Mexico

- Ranking By GDP
  - 1. Brazil
  - 2. Mexico
  - 3. Argentina

- Ranking By Chagas
  - 1. Argentina 1.5 million
  - 2. Brazil 1.2 million
  - 3. Mexico 0.9 million



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Brazil and Blue Marble Health

Introduction to Brazil

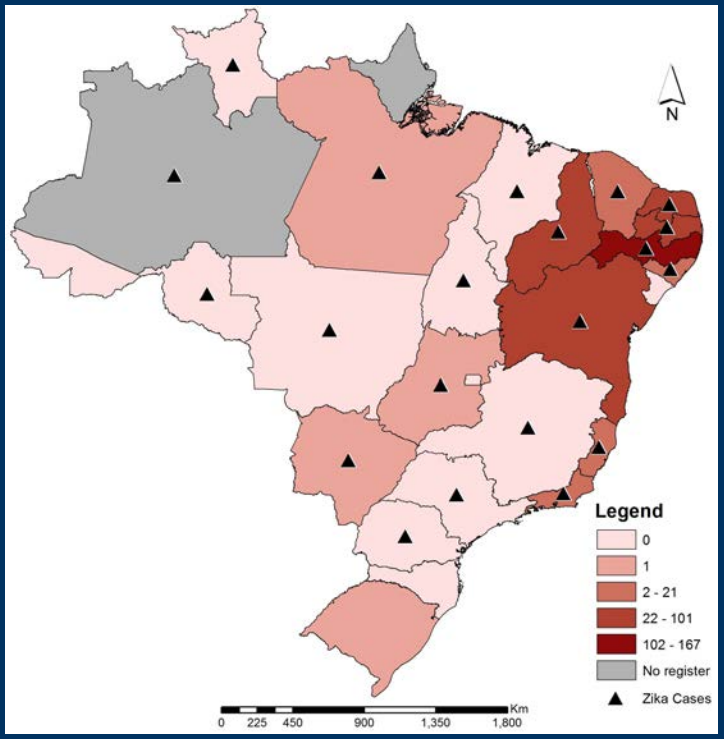
LARGEST Economy in Latin America

5th Largest country by land mass + population

7th Largest economy by nominal GDP

MERCOSUL Member

BRICS Member



Poverty & Disease NE Brazil:
Schistosomiasis, Leishmaniasis, Chagas, Dengue

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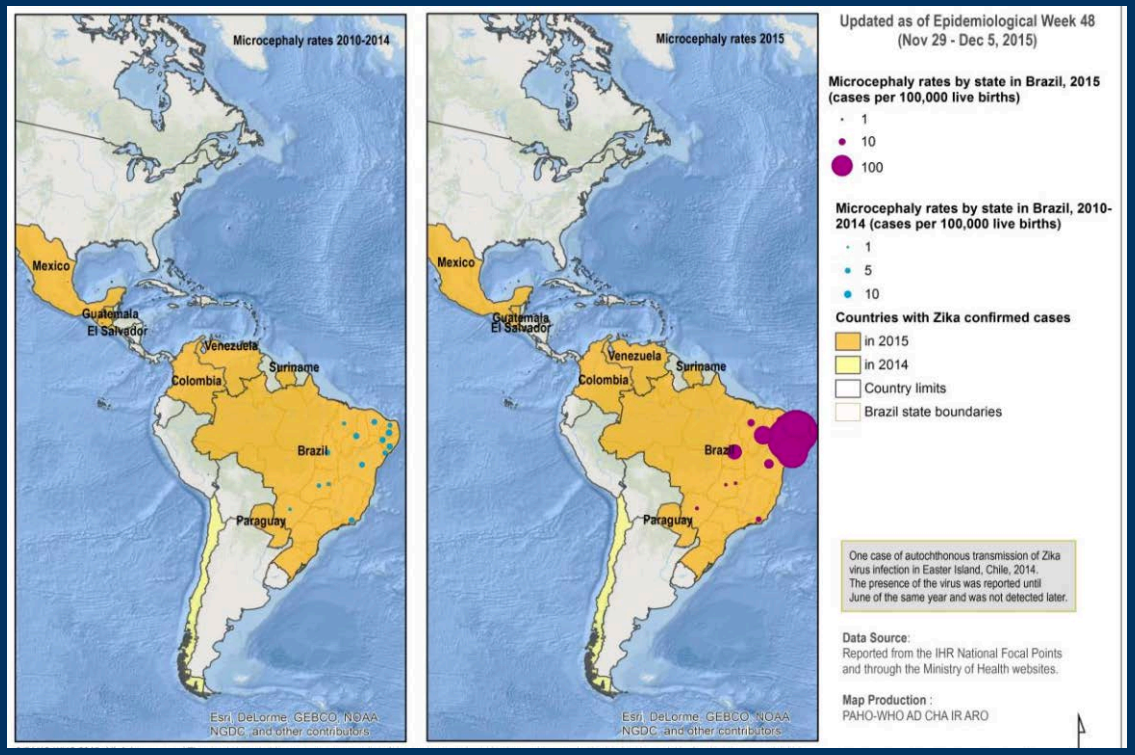
Zika Microcephaly cases in NE Brazil



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Poverty in Northeastern Brazil

Recife

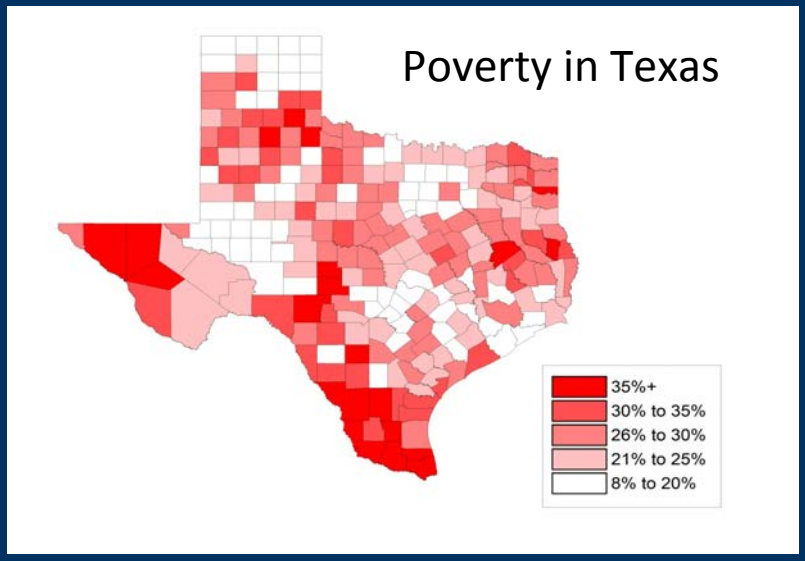
Salvador de Bahia

Spread of Zika in the Americas

POVERTY IN TEXAS

Hotez PJ (2017) The Rise of Neglected Tropical Diseases in the 'New Texas'

Fifth Ward, Houston Texas
Anna Grove



South Texas "Colonias" Shaghayegh Tajvidi.

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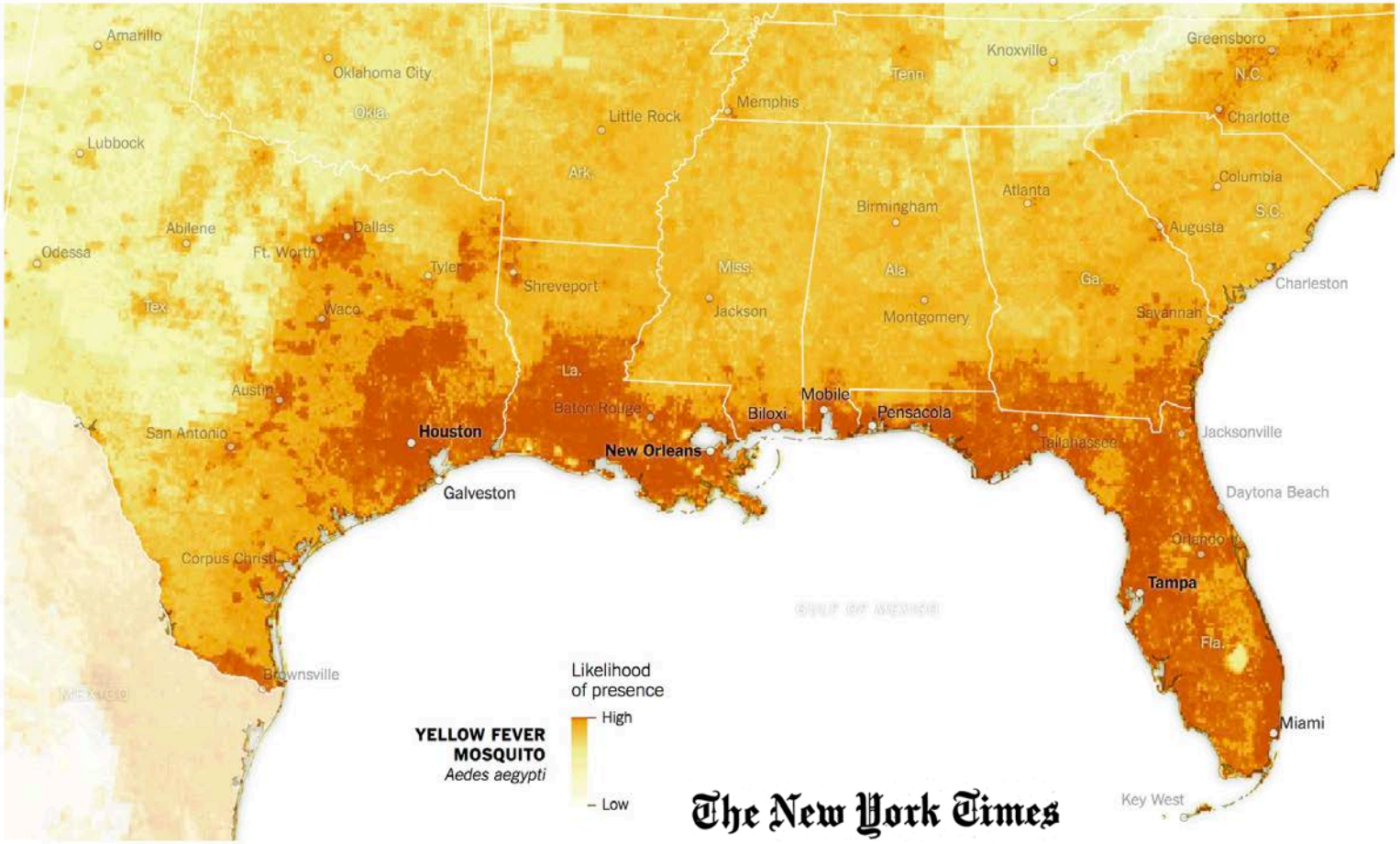
Hotez PJ "Zika is Coming"
The New York Times April 9, 2016

The Most Vulnerable

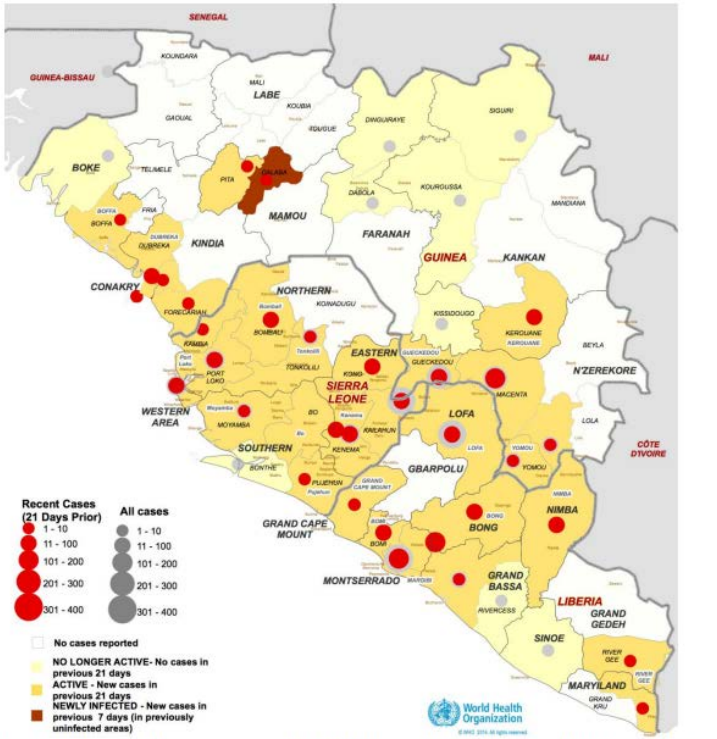
Predicted locations of the yellow fever mosquito, which transmits the Zika virus and other diseases.



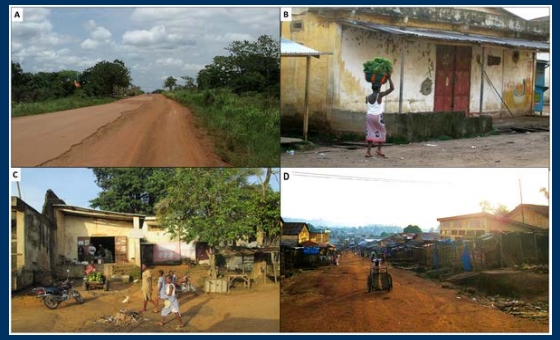
Source: Moritz U. G. Kraemer et al., eLife Sciences; Simon Hay, University of Oxford

By The New York Times

WAR & POLITICAL DESTABILIZATION: Ebola



Data are based on reported cases up to the end of 13 September 2014 for Guinea and Sierra Leone. Data for Liberia are based on reported cases up to the end of 9 September 2014. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.



ISIS-Occupied Syria, Iraq, Libya Yemen

Measles/Polio

Leishmaniasis

Schistosomiasis

Brucellosis

MERS CoV

Dengue

Malaria/TB

Rift Valley Fever

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Vaccinating Against The Anthropocene's NTDs

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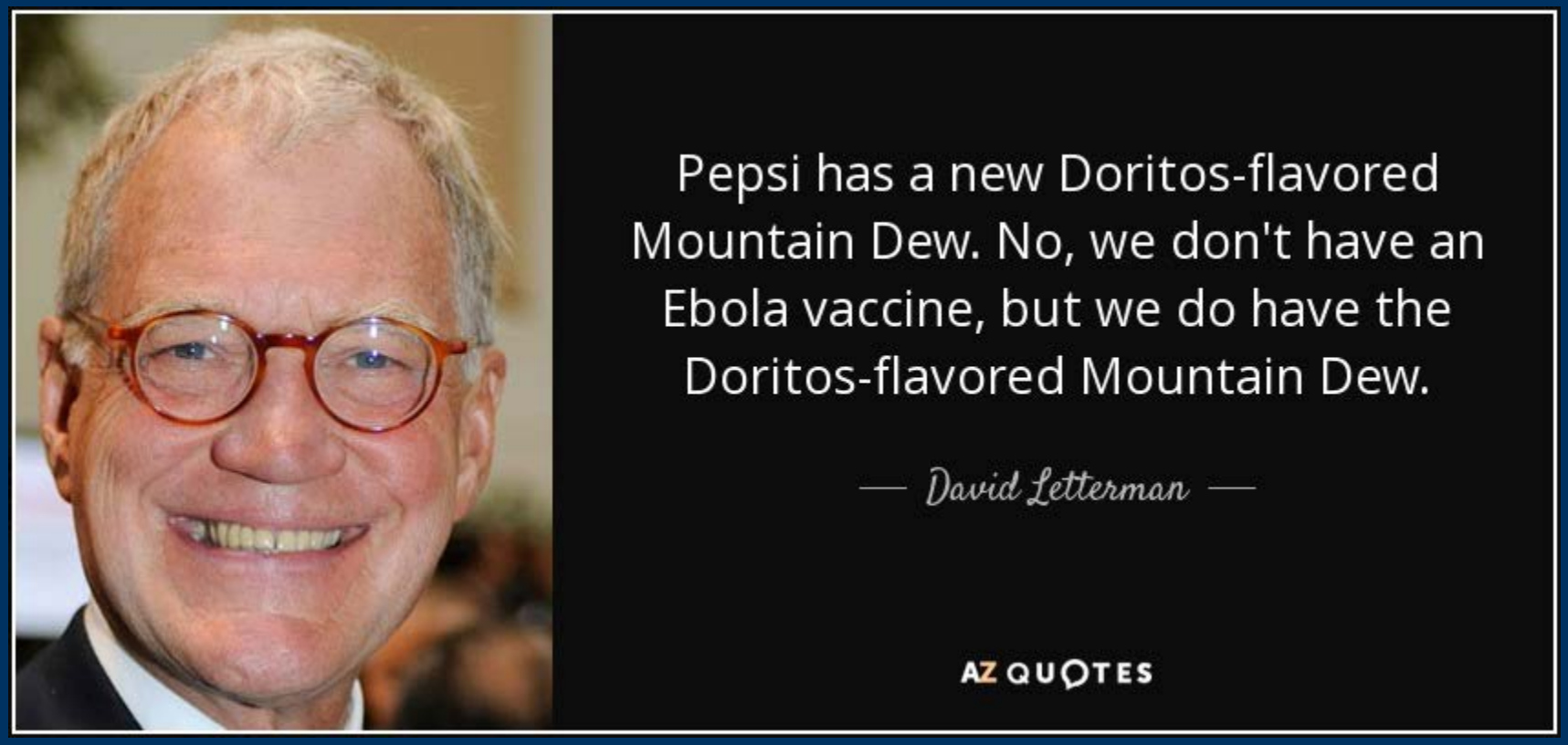

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Coalition for Epidemic Preparedness Innovations (CEPI)

Coalition for Epidemic Preparedness Innovations (CEPI)

Presentation to the WHO

21 July, 2017

Professor John-Arne Røttingen, Interim CEO, CEPI

Norwegian Ministry of Foreign Affairs · Bill & Melinda Gates foundation · wellcome trust · World Economic Forum · Department of Biotechnology, Ministry of Science & Technology

- Building on the WHO R&D blueprint
- Need for improved R&D preparedness for diseases of epidemic potential
- Prioritization of pathogens
- Identification of R&D priorities
- Exploration of funding models for R&D preparedness and response
  - Nipah
  - Lassa
  - MERS CoV

The Economist

Vaccines

Putting shots in the locker

How to anticipate epidemics

Sep 3rd 2016 | From the print edition

FOREWARNED, the proverb has it, is forearmed. But what happens when there is no warning? That was the case in December 2013, when an outbreak of Ebola haemorrhagic fever began in Guinea. It spread rapidly to Liberia and Sierra Leone and raged on for over a year. Around 29,000 people were infected. More than 11,000 of them died.

The world responded to this crisis, shipping in doctors, nurses and medical equipment. But what it could not ship in, for none existed, was the thing that would most quickly have stopped the epidemic: a vaccine. Such a vaccine was created eventually, but by the time it was ready, the outbreak was all but over. Had it been available from the beginning, things could have been different.

Next time, though, they might be, for on August 31st a new organisation came into being. CEPI, the Coalition for Epidemic Preparedness Innovations, was founded this week in London, at the headquarters of the Wellcome Trust, a medical charity. It is the joint brainchild of the Wellcome, the Bill and Melinda Gates Foundation, the World Economic Forum and the government of Norway, and its purpose is precisely to forearm the world against future outbreaks of disease, without foreknowledge of what those outbreaks will be.

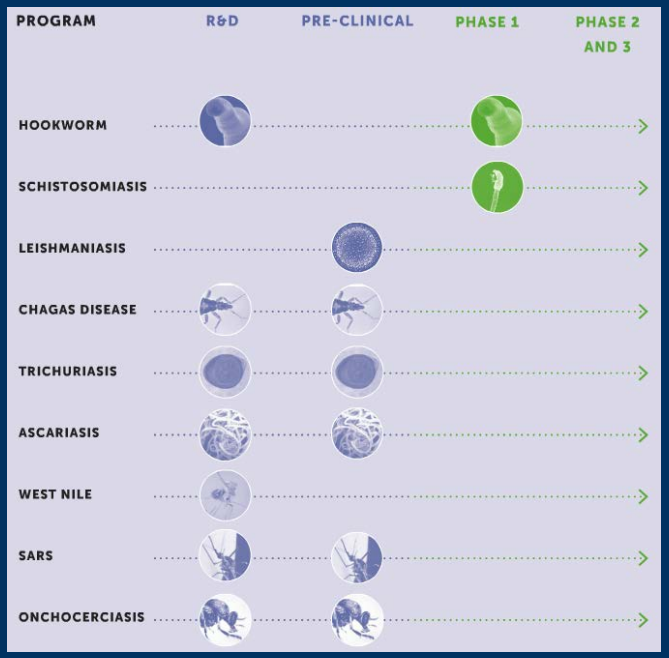
Paradoxically, part of the inspiration for CEPI's creation was not the failure to deliver an Ebola vaccine in time for it to be useful, but how close that project came to success. Creating a new vaccine from scratch is a long-winded undertaking, but in the case of Ebola several candidate vaccines were already on the shelf thanks to earlier, but stalled, work by America's army and that country's National Institutes of Health. There were also three pharma companies, GlaxoSmithKline, Johnson & Johnson and Merck, willing, *pro bono publico*, to take these candidates and try to turn them into the real thing as quickly as possible. That they succeeded in doing so by the summer of 2015 was, by most standards, extraordinary

Sabin PDP Pipeline and Disease Portfolio

2000 to 2004
- Built structure
- Launched Hookworm Program

2004 to 2011
- Expanded Hookworm Program
- Schisto Program
- Relocated to TMC

2011 to 2015
- Added 7 additional programs
- Expansion of capabilities



FIGHTING CRITICAL DISEASES

By Peter Hotez

A Handful Of 'Antipoverty' Vaccines Exist For Neglected Diseases, But The World's Poorest Billion People Need More

ABSTRACT So-called neglected tropical diseases are the most common infections of the world's poor. Almost all of the "bottom billion"—the 1.4 billion people who live below the poverty level defined by the World Bank—suffer from one or more neglected diseases including hookworm infection, sleeping sickness, or Chagas disease. These diseases are actually a cause of poverty because of their adverse effects on child growth and development and worker productivity. Vaccines to combat such diseases have come to be known as "antipoverty vaccines." Unfortunately, the recent surge in the development and delivery of vaccines to combat the major childhood killers—such as pneumococcal pneumonia and measles—has bypassed neglected diseases. Nevertheless, some vaccines for these neglected diseases are now entering the clinical pipeline. In this article I describe how some antipoverty vaccine development is proceeding and offer recommendations for stimulating further development such as through pooled funding for innovation, developing-country manufacturers, and public-private partnerships for product development.

A full year has passed since the launch of the "Decade of Vaccines," which was articulated when the Bill & Melinda Gates Foundation made a ten-year commitment to ensuring the development and delivery of new vaccines for the poorest people living in the world's low- and middle-income countries. Since then, enormous progress has been made in increasing global access to vaccines that combat the great childhood killer diseases such as pneumococcal pneumonia, rotavirus, *Haemophilus influenzae* type b, and measles.

That progress was made possible through enhanced cooperation between the GAVI Alliance, the multinational pharmaceutical companies, and organizations supported by the Bill & Melinda Gates Foundation such as the Program for Appropriate Technology in Health, known as PATH. New financial incentives including a $1.5 billion advance market commitment have also contributed to the progress.[1]

Lagging far behind those global efforts against the major killer childhood diseases, are parallel activities to produce and deliver a new generation of vaccines for so-called neglected diseases (these are sometimes known as neglected tropical diseases).[2] These neglected diseases are the most common infections of the world's poor, and almost all of the "bottom billion"—the 1.4 billion people who live below the poverty level defined by the World Bank—suffer from one or more of the neglected diseases.[3,4]

The World Health Organization now identifies seventeen conditions as "neglected tropical diseases."[4] The most common neglected diseases are caused by parasitic worms, including hookworm infection, ascariasis (intestinal roundworm), trichuriasis (whipworm), schistosomiasis (bilharzia), lymphatic filariasis (elephantiasis), and onchocerciasis (river blindness); by parasitic protozoa, including Chagas

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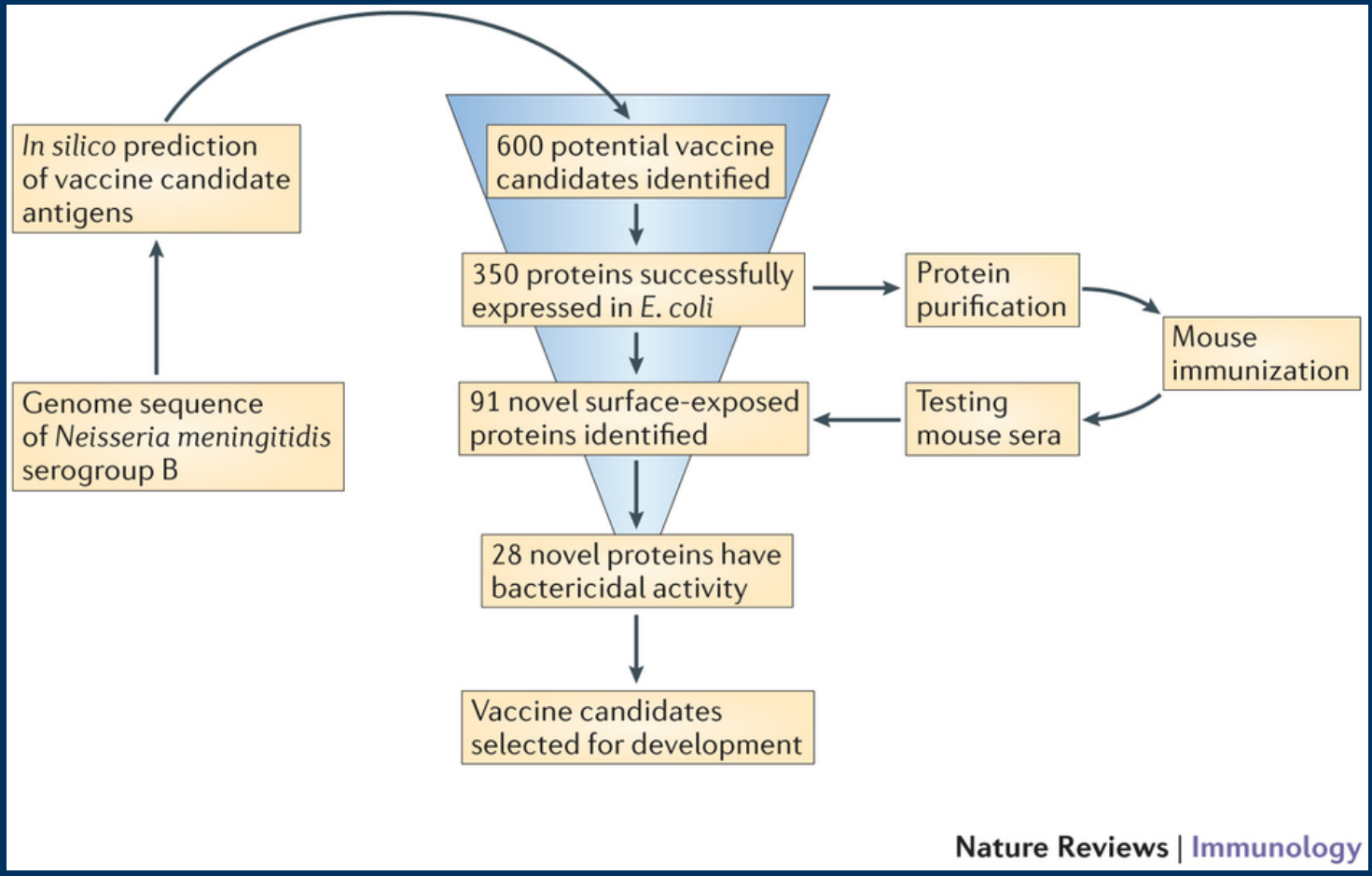
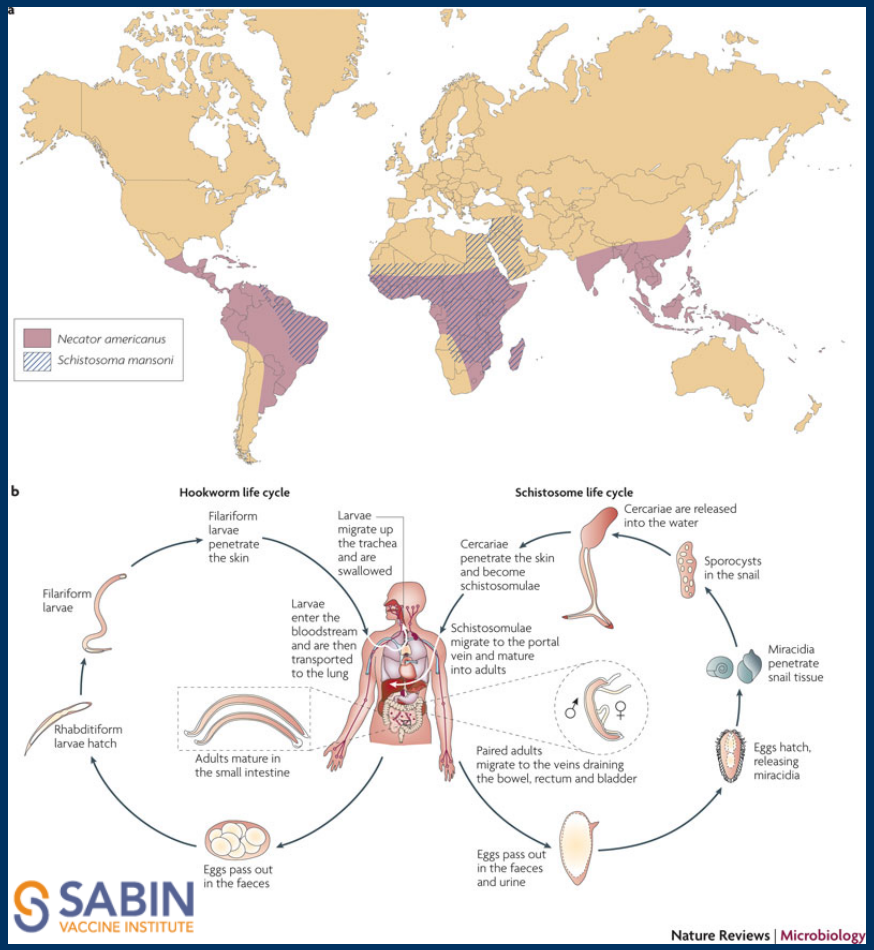
Rino Rappuoli: Reverse Vaccinology



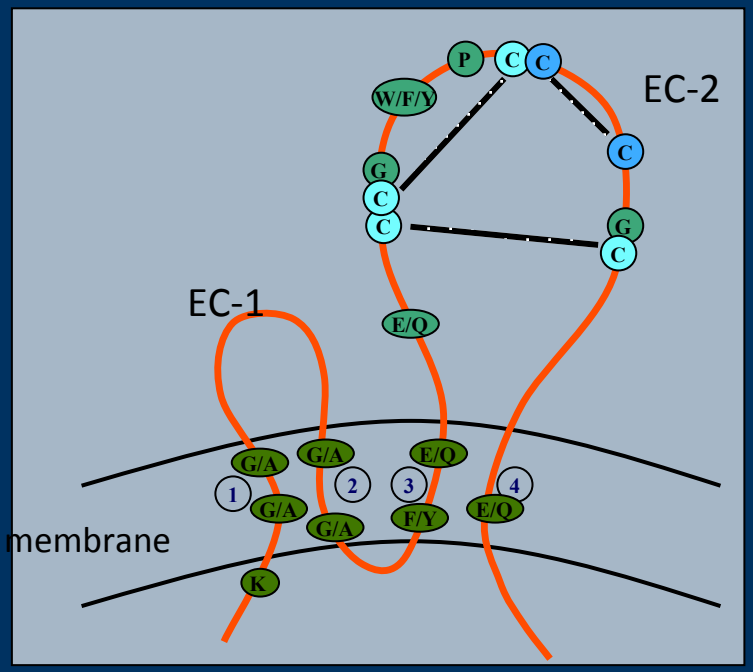
Reverse vaccinology as a ‘holy grail’ for complex eukaryotic organisms

- Large genomes of similar complexity to human genome
- Inadequacy of bacterial expression systems for eukaryotic antigens
- Low throughput not high throughput
- Deficiencies in animal models

Vaccine Targeting
Hookworm and Schistosomiasis Co-Infections



A MULTIVALENT
VACCINE TARGETING
HOOKWORM + SCHISTO



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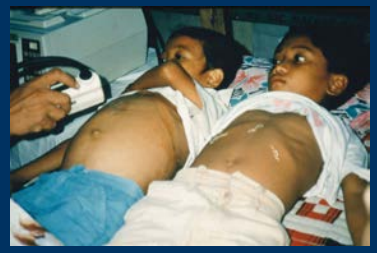
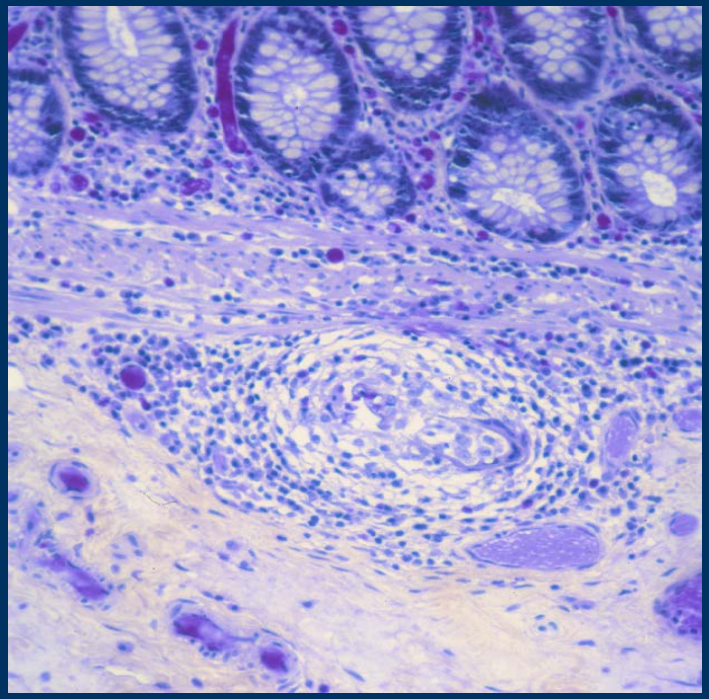
Goals of Anti-schistosome Vaccine

- **Worm burden reduction**
- **Egg reduction**
- **Reduced end-organ pathology**
- **Reduction in inflammation**
- **Reduction in anemia and malnutrition**





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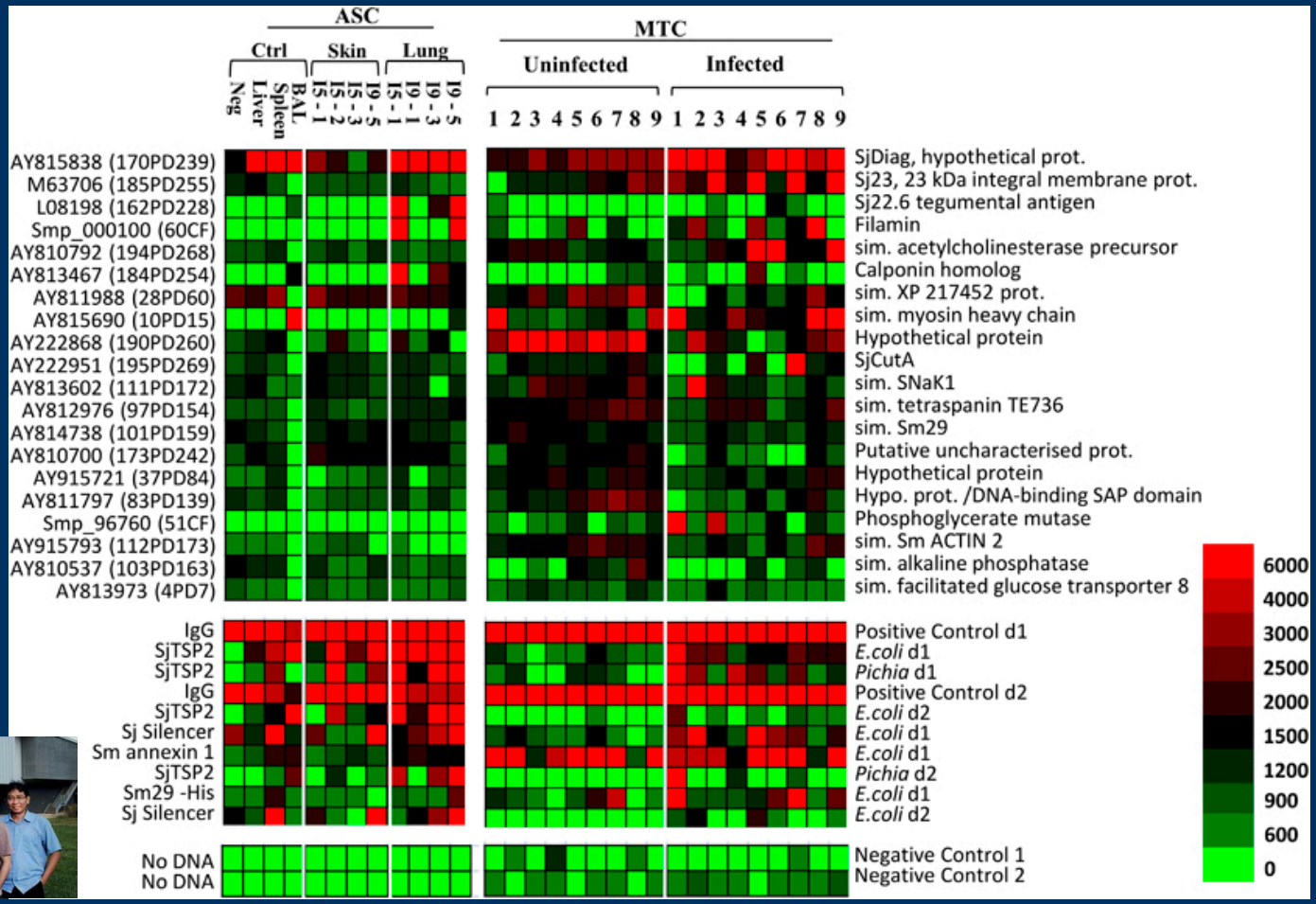
Immunomics Approach: Schistosome protein microarrays



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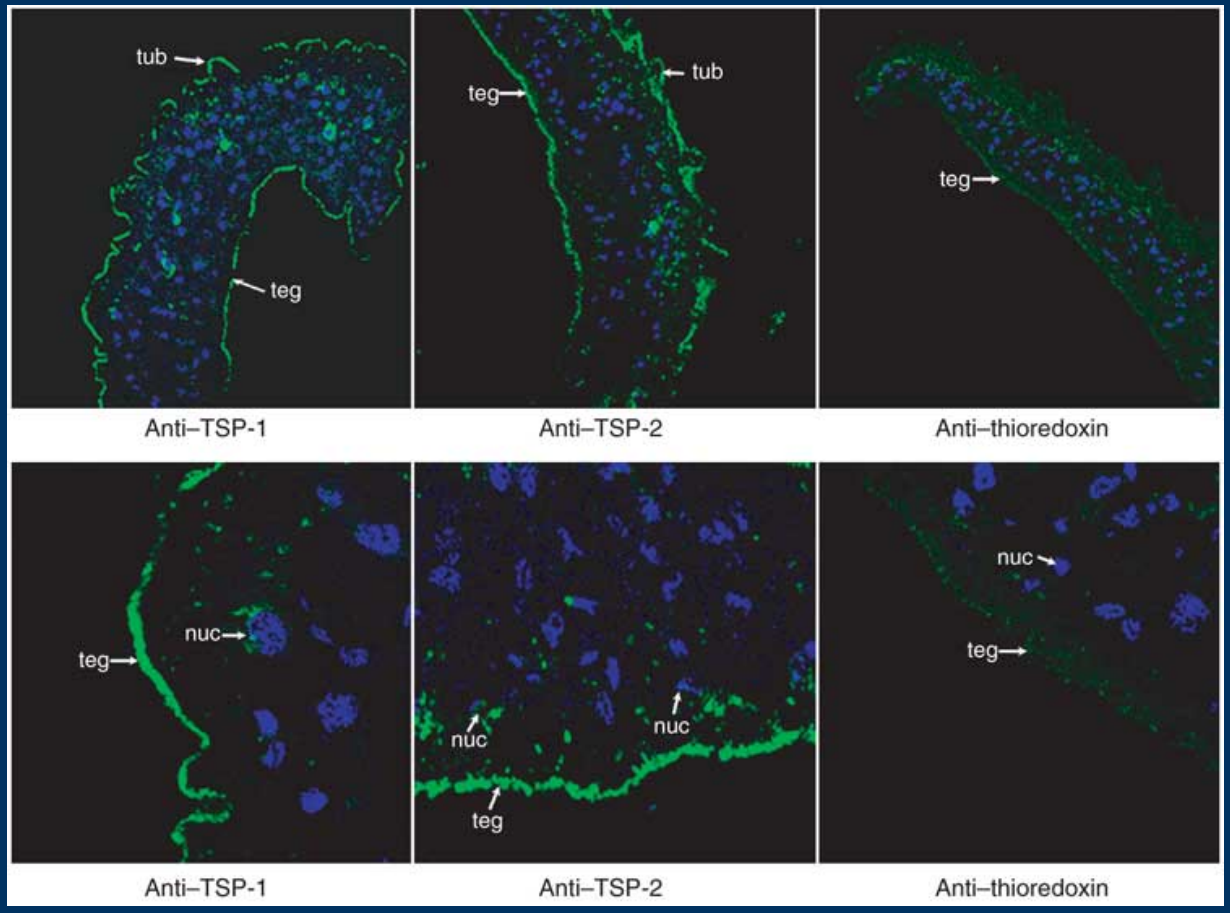
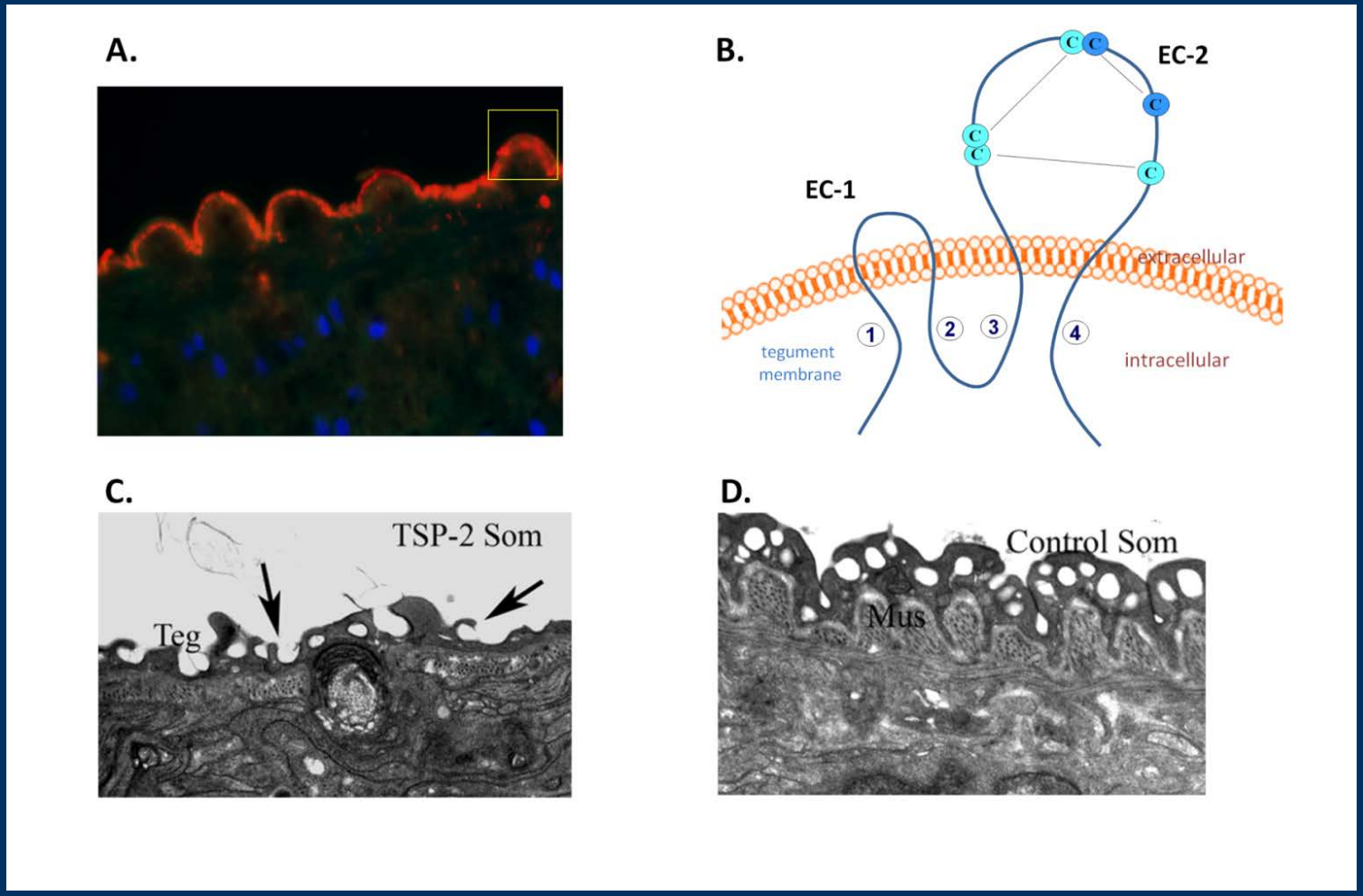
Immune localization of *Sm*-TSP-2



Suppression of tsp-2 mRNA expression results in impaired tegument turnover *in vitro*



Tran et al. *PLoS Path* 2010

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Intestinal Schistosomiasis Vaccine

Human Vaccines & Immunotherapeutics 9:11, 2342–2350; November 2013; © 2013 Landes Bioscience

Expression at a 20L scale and purification of the extracellular domain of the *Schistosoma mansoni* TSP-2 recombinant protein

A vaccine candidate for human intestinal schistosomiasis

Elena Curti[1,2], Clifford Kwityn[1,2,3], Bin Zhan[1,2], Portia Gillespie[1,2], Jill Brelsford[1], Vehid Deumic[1], Jordan Plieskatt[1], Wanderson C Rezende[1,2], Eric Tsao[4], Bose Kalampanayil[4], Peter J Hotez[1,2,5], and Maria Elena Bottazzi[1,2,*]

[1]Departments of Pediatrics and Molecular Virology and Microbiology; National School of Tropical Medicine; Baylor College of Medicine; Houston, TX USA; [2]Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development; Houston, TX USA; [3]Department of Microbiology; Immunology and Tropical Medicine; the George Washington University; Washington, DC USA; [4]Aeras; Rockville, MD USA; [5]James A. Baker III Institute for Public Policy; Rice University; Houston, TX USA

[*]Current affiliation: Beckman Coulter Inc.; Chaska, MN USA

Keywords: Schistosomiasis, *Schistosoma mansoni*, neglected tropical diseases, vaccine, *Sm*-TSP-2, *Pichia Pastoris*, recombinant protein

A novel recombinant protein vaccine for human schistosomiasis caused by *Schistosoma mansoni* is under development. The *Sm*-TSP-2 schistosomiasis vaccine is comprised of a 9 kDa recombinant protein corresponding to the extracellular domain of a unique *S. mansoni* tetraspanin. Here, we describe the cloning and the expression of the external loop of *Sm*-TSP-2 recombinant protein secreted by *Pichia Pink*™ the process development at 20L scale fermentation, and the two-steps purification, which resulted in a protein recovery yield of 31% and a protein purity of 97%. The developed processes are suitable for the production of purified protein for subsequent formulation and Phase 1 clinical studies.

Introduction

Schistosomiasis is a parasitic infection caused by blood flukes of the genus *Schistosoma*. Today, human schistosomiasis is considered one of the most important human helminthic infections in terms of mortality and morbidity, especially in Africa, where more than 90% of the cases occur.[1,2] Recent studies indicate that approximately 200 million people are infected worldwide, with 800 million people at risk.[3-6] However, additional analyses indicate that this number may be an underestimate and as many as 400–600 million people may be infected with schistosomes.[7]

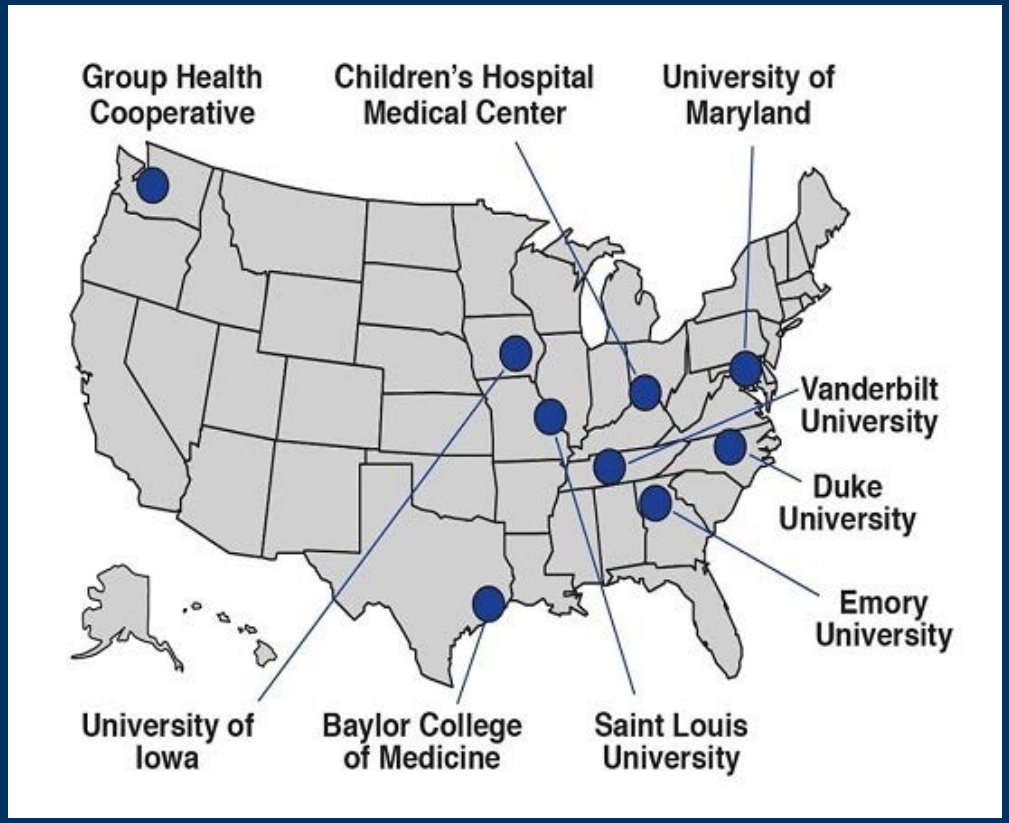
Although schistosomiasis is a treatable infection, the current treatment of choice does not provide an optimal strategy for controlling the disease.[8] Since 1990, praziquantel (PZQ) based mass chemotherapy has been the major approach in controlling schistosomiasis, by primarily targeting school-aged children with annual treatments.[9] However, the sustainability of PZQ treatment for the long-term control and elimination of schistosomiasis remains a concern and has limitations. For instance, PZQ does not prevent reinfection nor does it reduce transmission in

resistance to PZQ. Although there is no clear evidence for the existence of PZQ-resistant schistosome strains, decreased susceptibility to the drug has been observed in several countries.[13-15] To overcome these challenges, a prophylactic vaccine or a vaccine-linked chemotherapy would be ideal to complement the existing treatment initiatives.[16] Evidence for the feasibility of developing a schistosomiasis vaccine includes studies showing that immunization with irradiated schistosome cercariae regularly induces high levels of protection in experimental animal models, with boosts further increasing the level of protection.[17] In addition, a subset of human populations living in endemic areas has been shown to develop various degrees of natural resistance,[18] while veterinary recombinant vaccines against other platyhelminth parasites have been developed successfully and applied in practice.[19]

Expanded information on the mechanisms of immunity to schistosomiasis[20] and the recent availability of the schistosome genome for both *S. mansoni* and *S. hematobium*[21] have resulted in the discovery of several schistosome antigens, while additional candidates are now being found through proteomic approaches.[22-24] Within the last year results of a Phase 1 trial for

glutathione S-transferase)

the cause of urogenital



The Schistosome Tetraspanins

Entering phase 1 trials – Baylor VTEU

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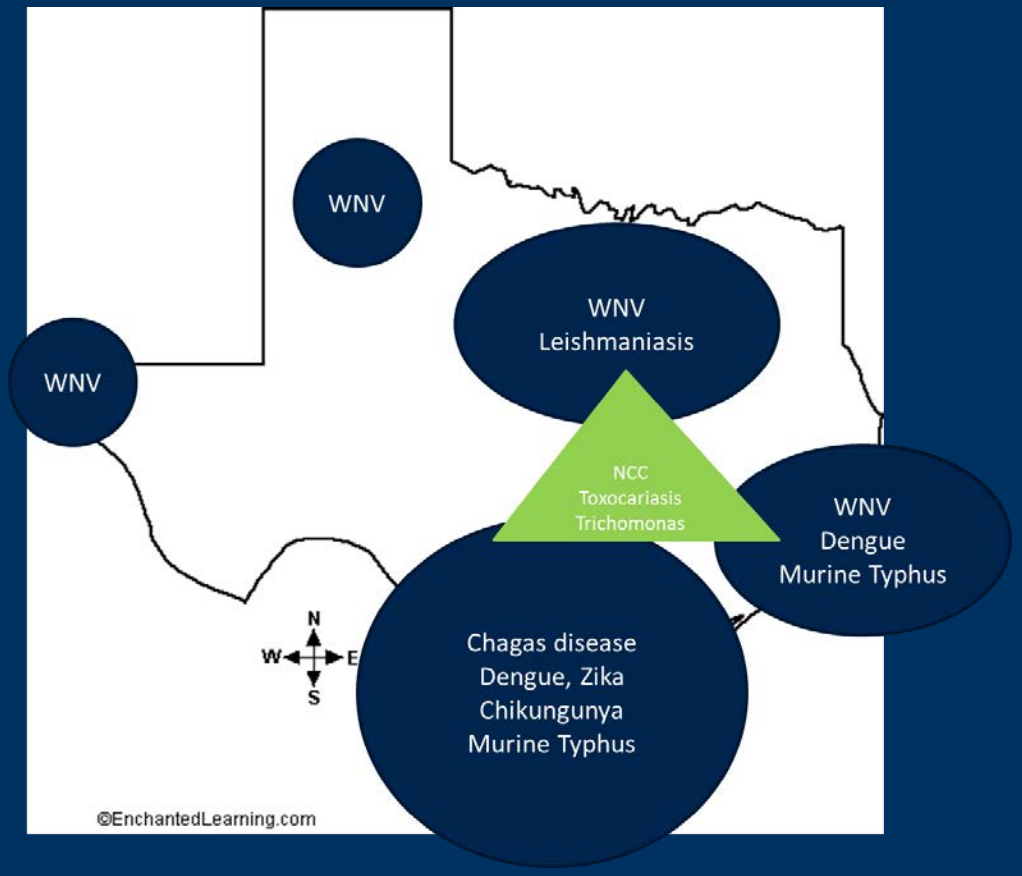
The Rise of Emerging + Neglected Diseases in the "New Texas"

- Leading TX NTDs
  - Toxocariasis 700,000
  - Trichomoniasis 450,000
  - Chagas disease 37,000
  - WNV 183-1,900
  - Intestinal protozoan 1,000
  - Cysticercosis 195-754
  - Murine Typhus >100
  - Dengue, Zika, Chik



ORIGINAL ARTICLE

Randomized Trial of Benznidazole for Chronic Chagas' Cardiomyopathy

Carlos A. Morillo, M.D., Jose Antonio Marin-Neto, M.D., Ph.D., Alvaro Avezum, M.D., Ph.D., Sergio Sosa-Estani, M.D., Ph.D., M.P.H., Anis Rassi, Jr., M.D., Ph.D., Fernando Rosas, M.D., Erick Villena, M.D., Roberto Quiroz, M.D., Rina Bonilla, M.D., Constança Britto, Ph.D., Felipe Guhl, M.Sc., Elsa Velazquez, Ph.D., Laura Bonilla, M.Sc., Brandi Meeks, M.Eng., Purnima Rao-Melacini, M.Sc., Janice Pogue, Ph.D., Antonio Mattos, M.Sc., Janis Lazdins, M.D., Ph.D., Anis Rassi, M.D., Stuart J. Connolly, M.D., and Salim Yusuf, M.D., Ph.D., for the BENEFIT Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

The role of trypanocidal therapy in patients with established Chagas' cardiomyopathy is unproven.

Trypanocidal therapy with benznidazole in patients with established Chagas' cardiomyopathy significantly reduced serum parasite detection but did not significantly reduce cardiac clinical deterioration through 5 years of follow-up.

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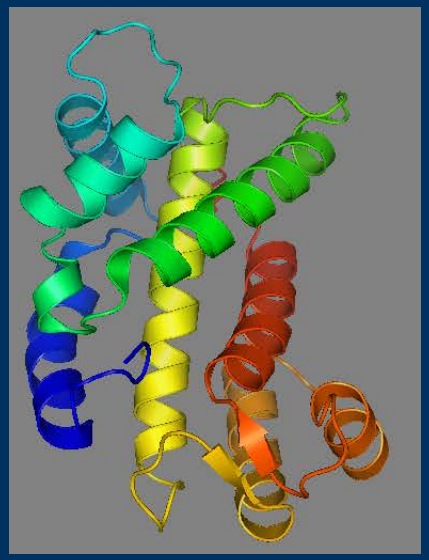
Tc24 protein combined with E6020 in a Stable Squalene Emulsion as a lead candidate vaccine

Candidate Antigen

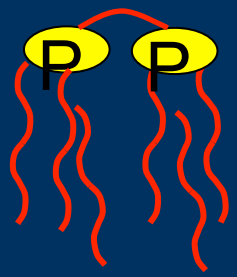
Tc24- 24kDa *Trypanosoma Cruzi* Flagellar Calcium Binding Protein



+

Candidate Adjuvant

TLR4 agonist:



E6020

Eisai

Additional antigens also under evaluation and development

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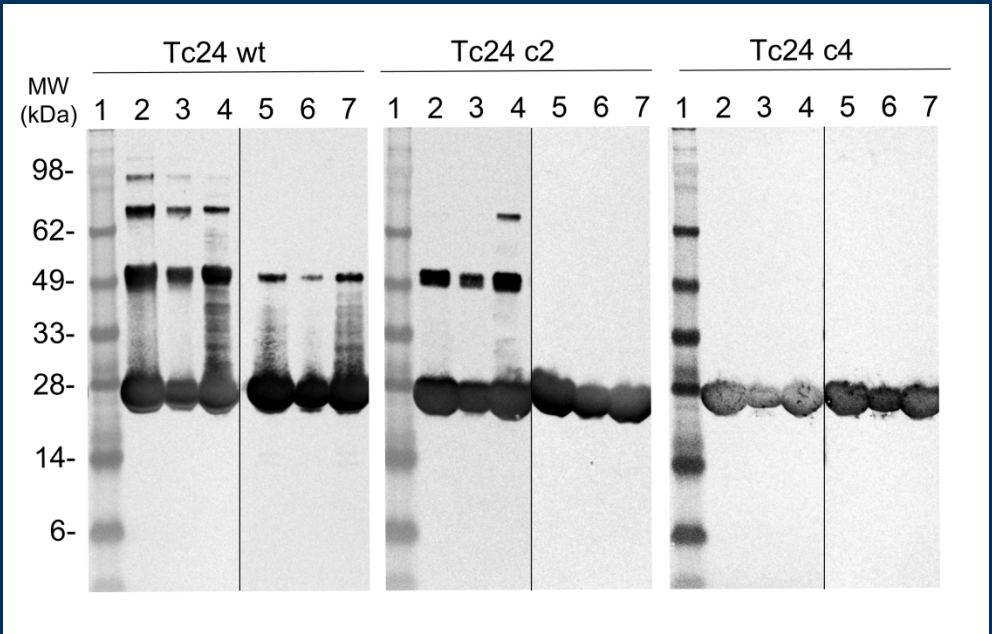
ADVANCES IN A THERAPEUTIC CHAGAS VACCINE INITIATIVE

- Preclinical Efficacy:
  - Pilot studies were performed to evaluate efficacy of recombinant Tc24 combined with imiquimod or MPLA when used as a preventative vaccine

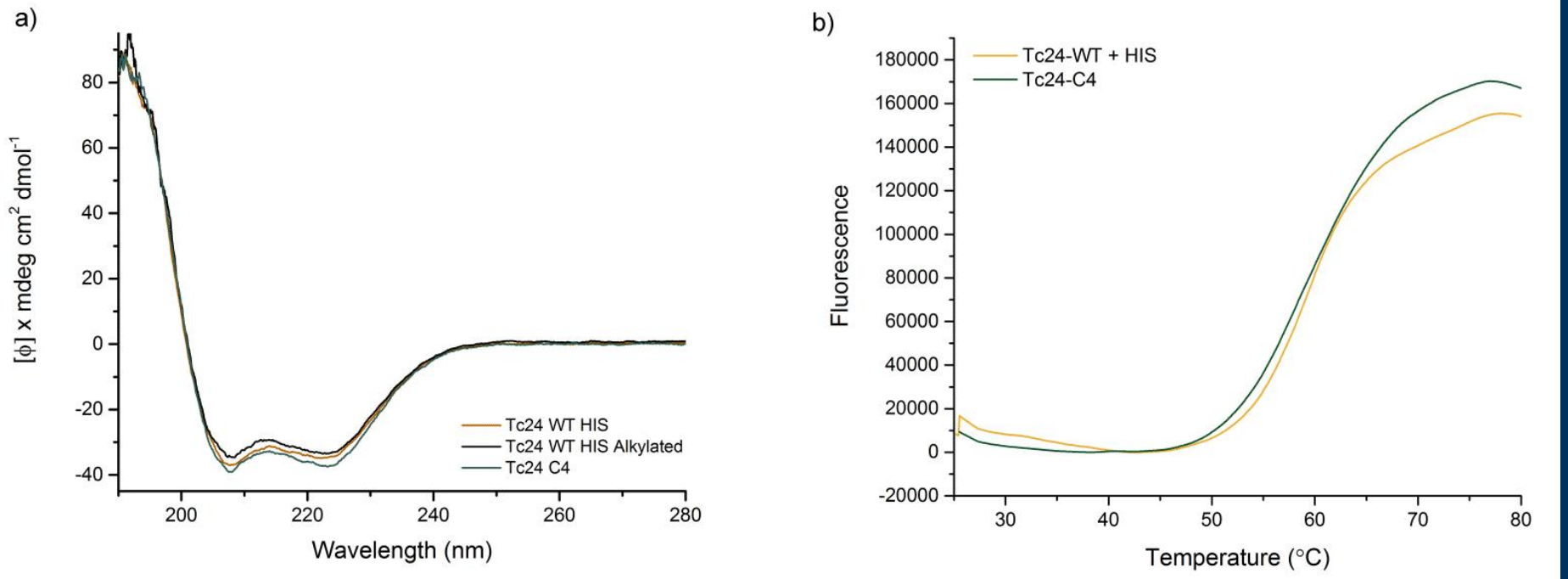
- Preliminary Results
  - Reduce parasitemia
  - Increase survival during acute phase
  - Antigen specific IgG2a
  - Antigen specific IFNγ
  - Reduced cardiac parasite burden

Oligomer Formation: Solving the problem?



Western Blot comparison of Tc24-WT (A), Tc24-C2 (B), and Tc24-C4 (C) purified proteins. Lanes 1-3: Non-Reduced. Lane 4: SeeBlue Plus Molecular Weight Marker. Lanes 5-7 Reduced. Lanes 1,5: Sample before size-exclusion chromatography (SEC) 8 µg load. Lanes 2,6: Post SEC low load (3 µg). Lanes 3,7: Post SEC high load (8 µg). Detection was performed using mouse polyclonal antibody against Tc24 expressed in *Pichia pastoris* as primary antibody diluted 1:2,500 in PBST and an alkaline phosphatase conjugated goat anti-mouse secondary antibody diluted 1:7,500 in PBST.

Maintaining secondary/tertiary structures



Structural comparison of Tc24 constructs. a) Circular Dichroism (CD). Far UV CD spectrum of different constructs of Tc24 were taken on a Jasco J-1500. All tested Tc24 protein have a virtual identical CD profile with overlapping spectra. Negative peaks at 222 nm and 208 nm and a positive peak at 193 nm indicate that Tc24 is an α-helical protein. b) Thermal melting profile of Tc24-WT and Tc24-C4 measured using Protein Thermal Shift™ kit (Life Technologies).

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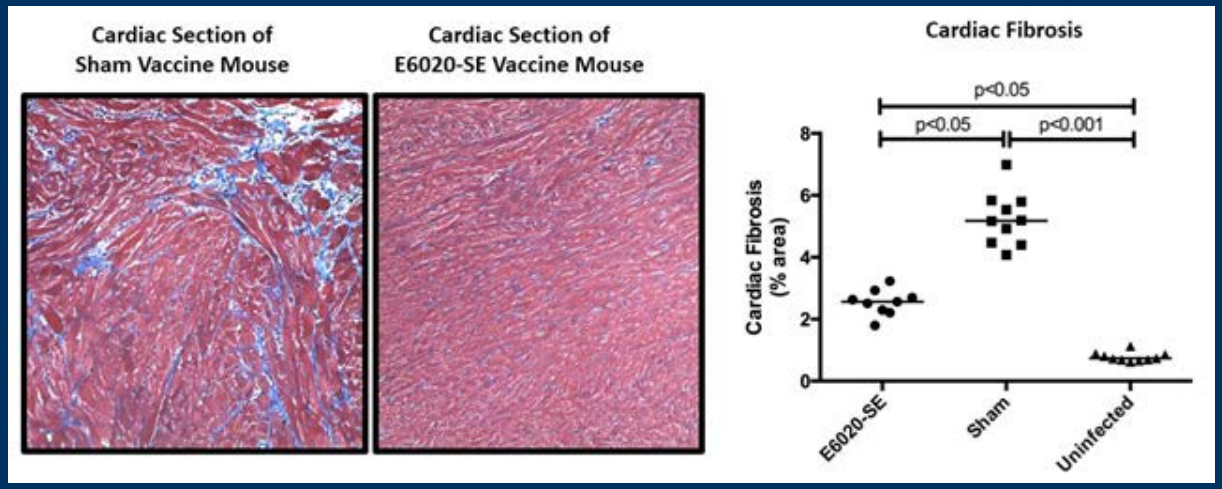
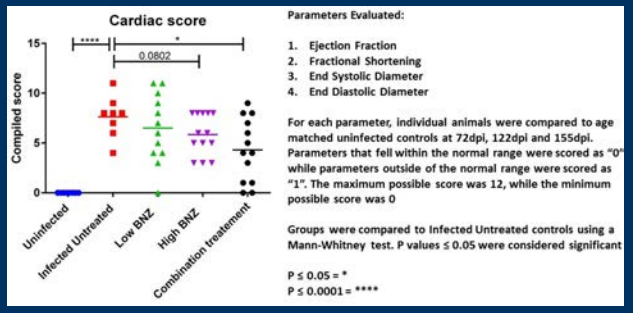
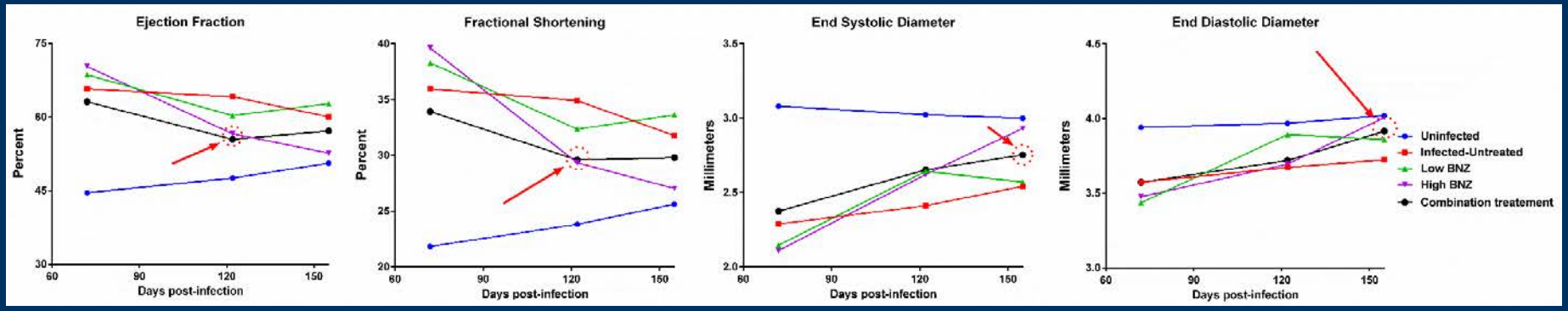
Therapeutic Chagas Disease Vaccine







Experimental Chagas disease vaccine improves Cardiac Echocardiography function

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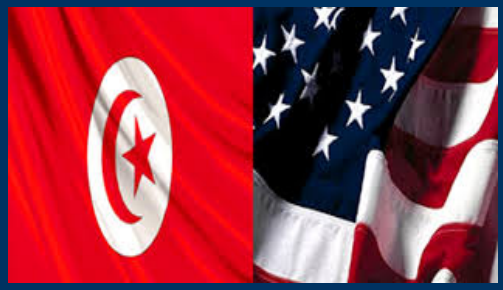
U.S. Science Envoy Program

Office of Science and Technology Policy



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