NGDI.ubc.ca
Neglected Global Diseases Initiative
a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA

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Co-Founder & Co-Director NGDI-UBC

Website: https://ngdi.ubc.ca/
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The Neglected Global Diseases Initiative at UBC

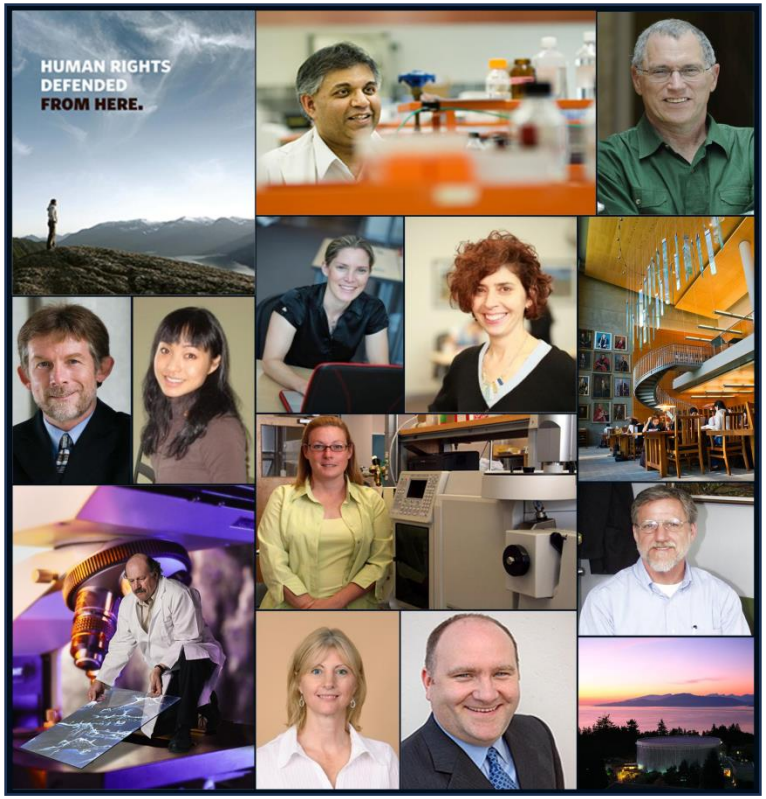
Developing Interventions for Developing Countries

How can the Poorest of the Poor Share in University Discoveries?

- Need mechanisms for encouraging and funding expensive research and development for Neglected Diseases.
- Must creatively protect early discoveries.
- Delivery!!!!

Mission: Developing interventions for neglected global diseases and ensuring their delivery to those in need.

www.ngdi.ubc.ca



The NGDI brings together a variety of disciplines, including bench science, biotechnology, pharmaceutical , health, social sciences, business, social policy and law.

Researchers work collaboratively to develop ways to most effectively generate affordable, life-sustaining medicines that can be brought to scale, thus reaching those most in need.

What are neglected global diseases?

Hookworm
Leprosy
Elephantitis
Sleeping Sickness
Chagas
Dengue Fever
Leishmaniasis
Soil Transmitted Helminthes

one in seven people
worldwide
is affected by a
neglected tropical disease

HIV/AIDS
Malaria
Tuberculosis

Why are they neglected?

TOTAL R&D FUNDING BY DISEASE IN 2007

HIV/AIDS	MALARIA	TUBERCULOSIS	OTHER*
$1,083,018,193	$468,449,438	$410,428,698	$598,172,420
42.3%	18.3%	16%	23.4%

*OTHER

Disease	Amount (USD)	%
KINETOPLASTIDS	$125,122,839	4.9
DIARRHOEAL DISEASES	$113,889,118	4.4
DENGUE	$82,013,895	3.2
HELMINTHS (WORMS & FLUKES)	$51,591,838	2.0
BACTERIAL PNEUMONIA & MENINGITIS	$32,517,311	1.3
TYPHOID & PARATYPHOID FEVER	$9,117,212	0.4
LEPROSY	$5,619,475	0.2
BURULI ULCER	$2,412,950	0.1
TRACHOMA	$1,679,711	0.1
RHEUMATIC FEVER	$1,670,089	0.1
CORE FUNDING OF A MULTI-DISEASE R&D ORGANIZATION	$110,921,673	4.3
PLATFORM TECHNOLOGIES	$9,997,189	0.4
UNSPECIFIED DISEASE	$51,619,120	2.0
Total R&D Funding	$2.560.068.749	100.0

Why are they important?

Top 10 Causes of Death	Approximate Deaths
Ischaemic heart disease	7,029,300
Stroke and other cerebro-vascular disease	5,874,200
Chronic obstructive pulmonary disease	2,899,900
Lower Respiratory Infections	**2,814,400**
Trachea, bronchus, lung cancers	1,527,100
HIV/AIDS	**1,465,400**
Diarrhoeal Diseases	**1,445,800**
Road traffic accidents	1,328,500
Diabetes mellitus	1,281,300
Tuberculosis	**1,196,000**

Statistics from Global Burden of Disease, 2010

How has UBC responded to this?

UNIVERSITY-INDUSTRY LIAISON OFFICE

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ACCESS

INNOVATION

How did we do?

UNIVERSITY GLOBAL HEALTH IMPACT REPORT CARD

1.	U. OF BRITISH COLUMBIA	A-
2.	CASE WESTERN RESERVE	B+
3.	JOHNS HOPKINS U.	B
4.	U.C. IRVINE	B
5.	HARVARD U.	B-
6.	EMORY U.	B-
7.	DUKE U.	C+
8.	VANDERBILT U.	C+
8.	U. OF PENNSYLVANIA	C+
10.	U. OF MARYLAND BALTIMORE	C+

Developing interventions for neglected global diseases and ensuring their delivery to those in need.

INTERVENTIONS (Drug and Non-Drug)

DISCOVERY + **DEVELOPMENT** + **VECTOR CONTROL, TOOLS and DIAGNOSTICS**

DELIVERY (Social Determinants & Health Equity Approach)

SUPPLY CHAIN DYNAMICS

+

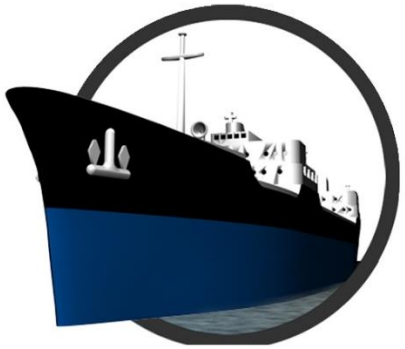
HEALTH SYSTEMS RESEARCH

IMPLEMENTATION RESEARCH

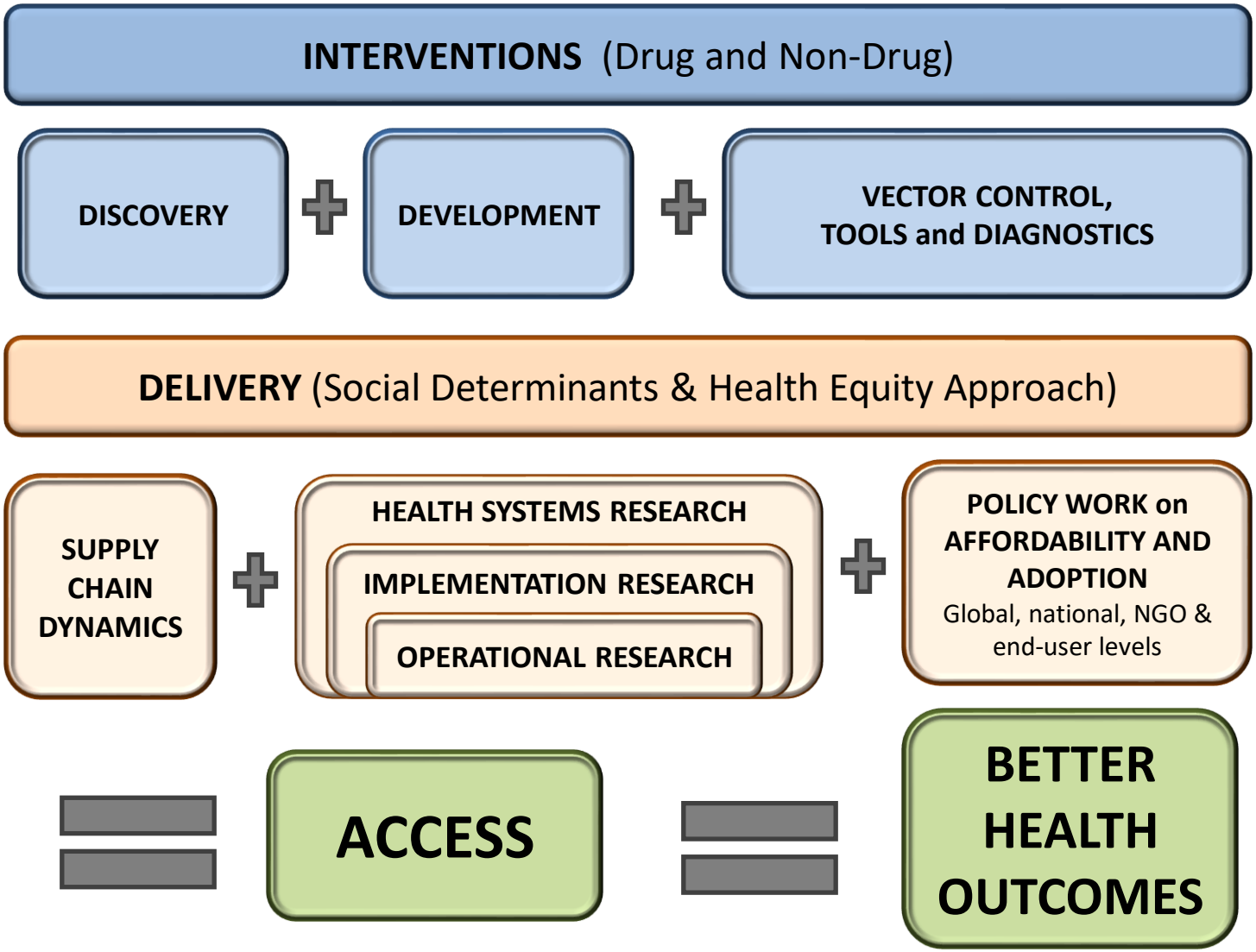
OPERATIONAL RESEARCH

+

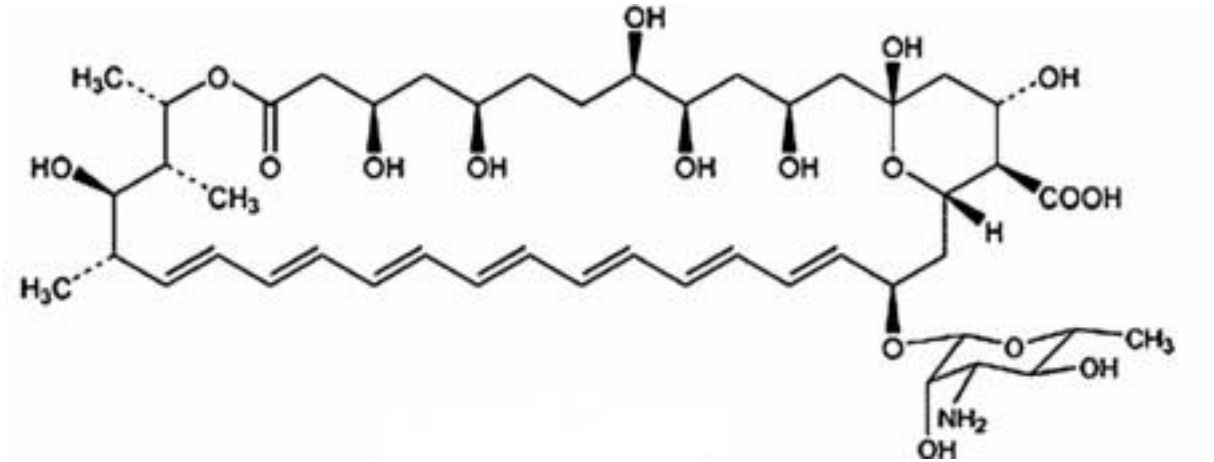
POLICY WORK on AFFORDABILITY AND ADOPTION
Global, national, NGO & end-user levels



NGDI Model of Collaboration



Amphotericin B

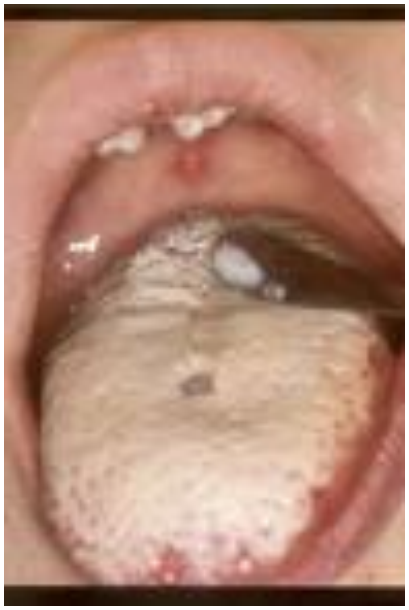


- AmB is a BCS Class IV drug
  - Low solubility and low permeability
  - Low oral bioavailability
  - Intravenous administration

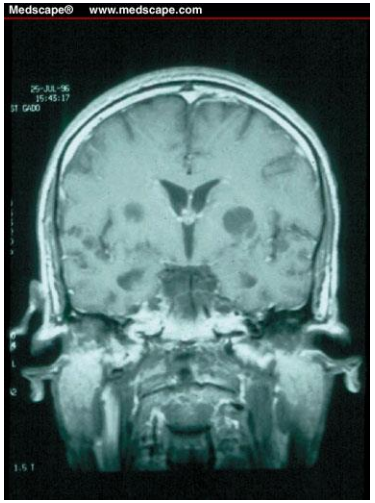
Demonstrated Efficacy

Cryptococcosis

Fungal infections



Candidiasis



Aspergillosis

Global Access

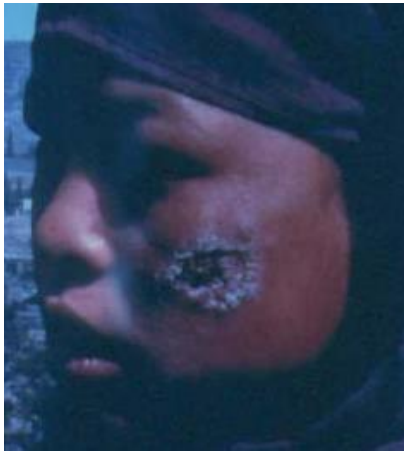
- Lobbying by strong UBC **UAEM chapter** and Grand Challenges funding led to consideration of new policy
- UBC **first Canadian university** to put forward a broad strategy to provide global access to appropriate technologies.
- Provide flexibility for tailored, technology-specific strategies.
- **Principles versus policy**; adopted by UBC in Fall 2007.

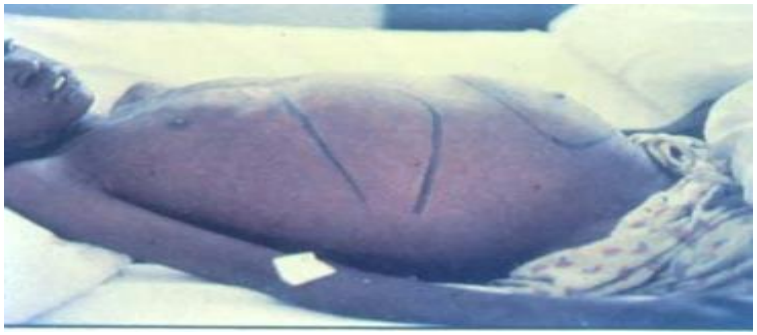
e.g. Reserved 4 of our patents with >50,000 immunomodulatory and antimicrobial peptides for the exclusive use of the Grand Challenges projects; One of these now optioned to a US company **with developing country rights reserved**

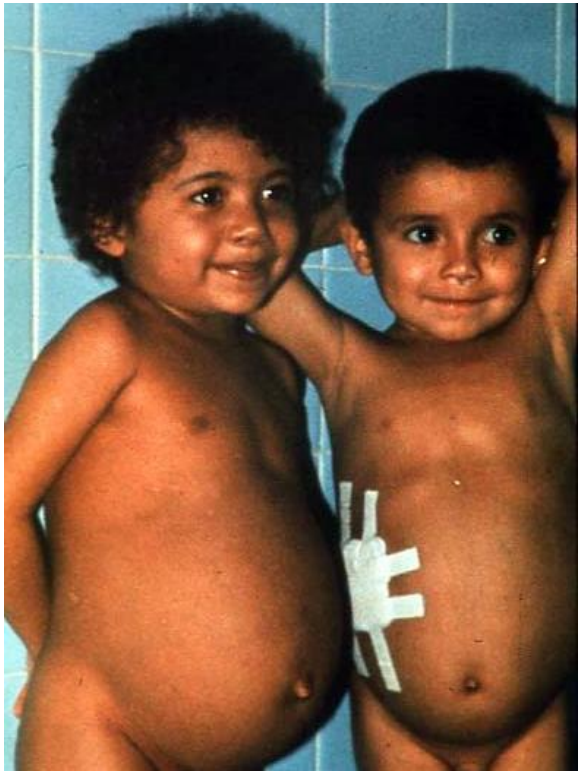
http://www.uilo.ubc.ca/about/initiatives/global.html

PRINCIPLES FOR GLOBAL ACCESS TO UBC TECHNOLOGIES

Leishmaniasis: Current Disease Status



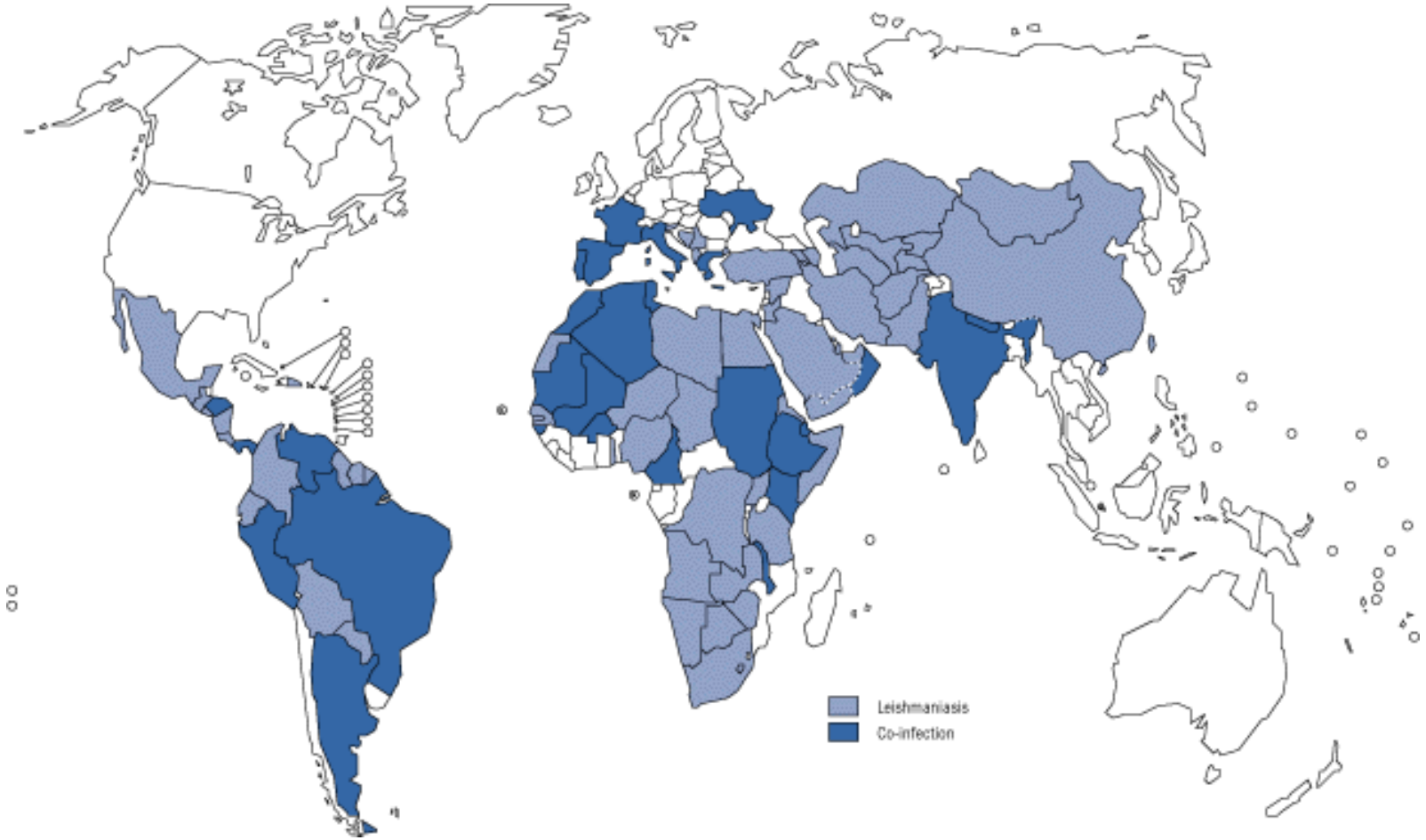




Source: WHO/TDR/Marsden

- Spectrum of disease which affects approximately 12 million people in 88 countries
  - About 2 million new cases annually
  - 75% involve cutaneous leishmaniasis, with the remainder being visceral leishmaniasis (VL)
- Mortality rate for VL is close to 100% in the absence of treatment

“Real World” Efficacy



2 million new cases reported every year (WHO)

Visceral leishmaniasis causes ~59 000 deaths annually

Current Treatments of VL

	Liposomal amphotericin	Miltefosine	Paromomycin
Efficacy in VL	**~99 %**	**~97%**	**~95%**
Safety	Safe	G-I intolerance Potential foetotoxicity	Reversible ototoxicity 2% Painful injection
Administration	Intravenous infusion	Oral tablet. Contraception in child-bearing -age women	Intramuscular injection
Price for 35 kg Indian VL adult	~US $140 –220	~US$ 61 – 75	~US$ 15

Wasan & Thornton 2009

Implications for Developing Countries

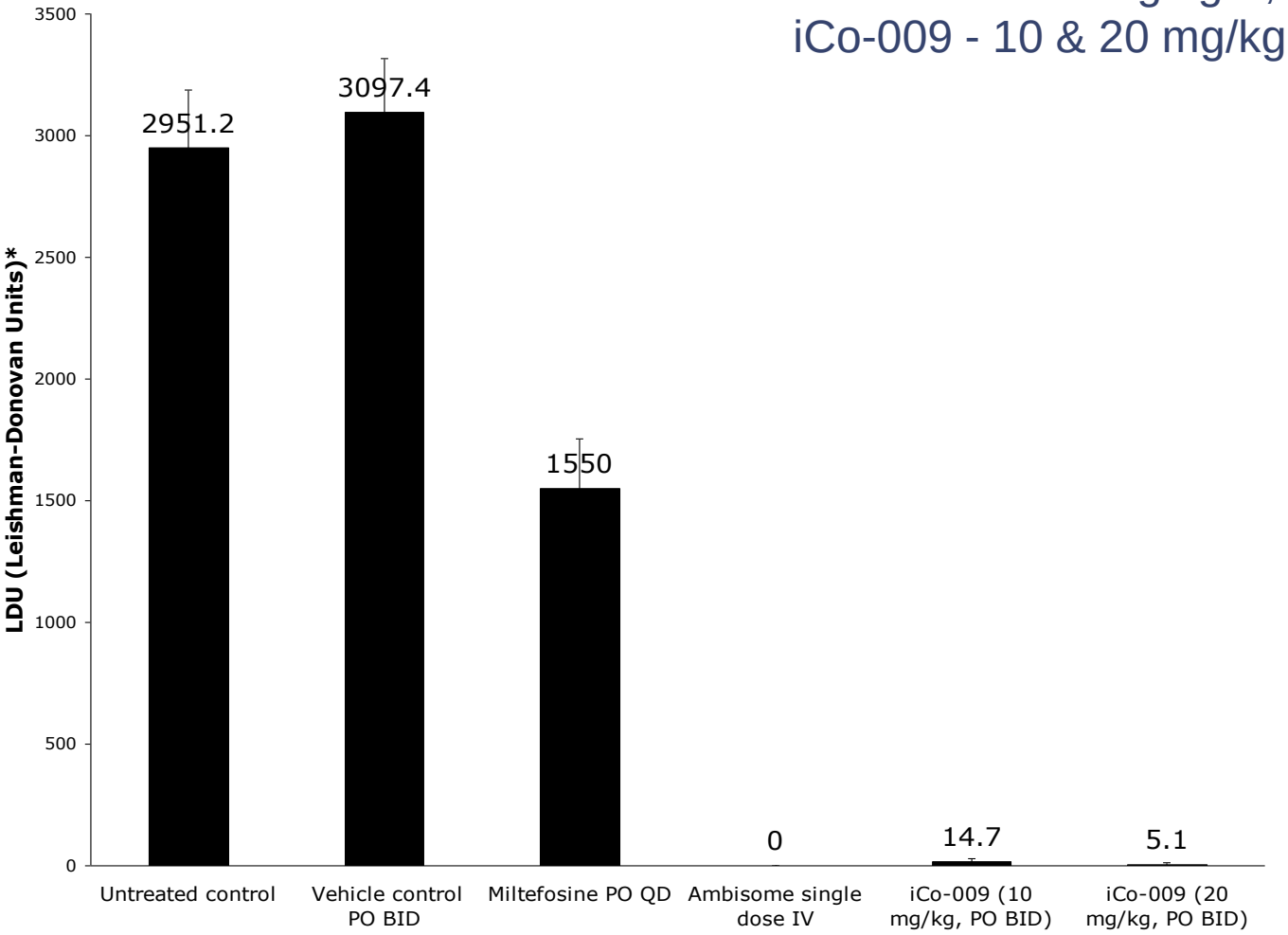
Parenteral administration results in:

- Loss of income
- Increased cost of administration
- Increased risk of side effects
- Decreased availability of treatment

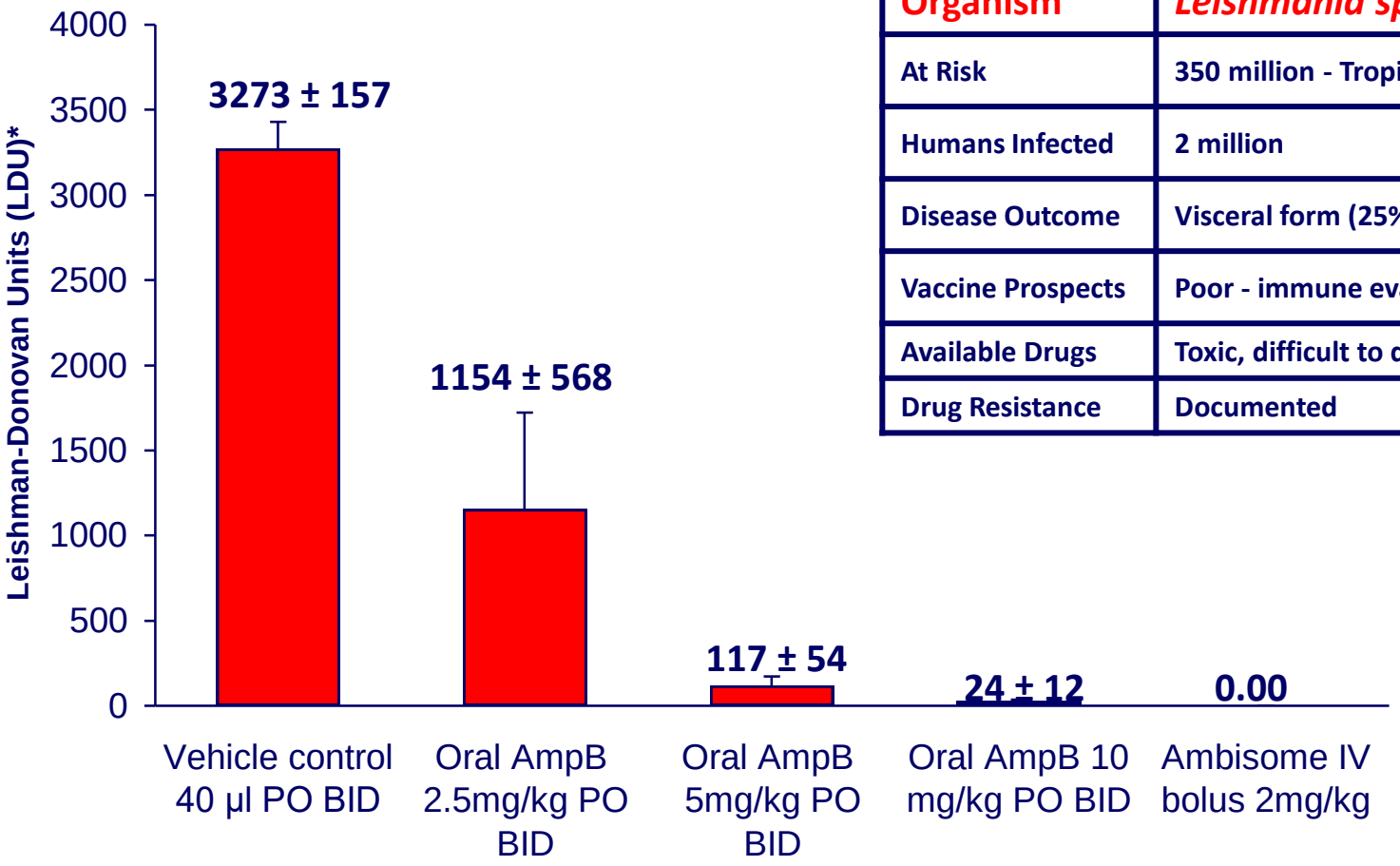
Data Overview
Visceral Leishmania (VL)

- Mice were infected i.v. with 1×10^7 *Leishmania donovani*
- Treatment begins on Day 7 post infection
- Oral Amp B administered bid for 5 consecutive days
- Mice were sacrificed Day 14 post infection
- Livers were then weighed and impression smears prepared
- The number of *Leishmania* amastigotes per liver cell nuclei was determined microscopically
- studies performed in independent laboratory
  - part of the Consortium for Parasitic Drug Development, a Gates Foundation funded organization

Miltefosine - 3mg/kg PO, qd x 5 d
Ambisome - 2 mg/kg iv, once
iCo-009 - 10 & 20 mg/kg PO, bid x 5 d



A new oral amphotericin B formulation (iCo 009) works well vs. visceral Leishmanaisis in animals



Organism	*Leishmania spp.*
At Risk	350 million - Tropics and Subtropics
Humans Infected	2 million
Disease Outcome	Visceral form (25% above) fatal
Vaccine Prospects	Poor - immune evasion
Available Drugs	Toxic, difficult to deliver
Drug Resistance	Documented

Oral Amphotericin B Formulation Technology

- Proprietary blend of mono- and di-glycerides (FDA GRAS approved)
- Solubilized AmpB Formulations
- Nanosuspensions/dispersions
- Affordable lipid excipients
- Ease of formulation scale-up
- Formulation Stability over 120 days
- Drug Stability at 43˚C over 120 days

Advantages of Oral Amphotericin B Formulation

- Affordable
- Easy to store
- Easy to administer
- Lack of kidney toxicity
- Lack of Infusion-related side effects (i.e. fever, chills etc.)
- Lack of liver and GI toxicity

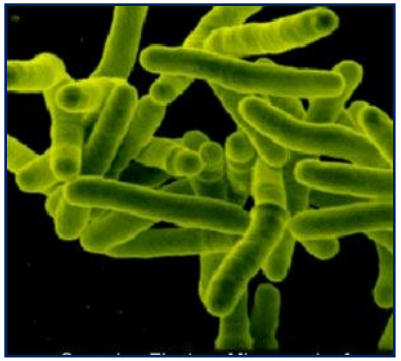
Advantages of Oral Amphotericin B Formulation

- Treating patients with drug-resistant strains (decrease hospitalization and eliminate IV AmpB Therapy)
- First available Oral Fungicidal Agent (only Fungistatic Agents, Diflucan® from Pfizer)
- Orphan Drug Designation FDA (2010)
- US Patent Issuances 2013 & 2014
- Positive Human Phase 1a/1b Safety Results

Centre for TB Research at UBC

Overall objectives:

1. Improve our basic understanding of the physiology of *M. tuberculosis*, especially those processes that are critical to pathogenesis.
2. Establish a pipeline for the development of novel inhibitors.



Why now?

1. With the emergence of XDR strains, TB is a global threat

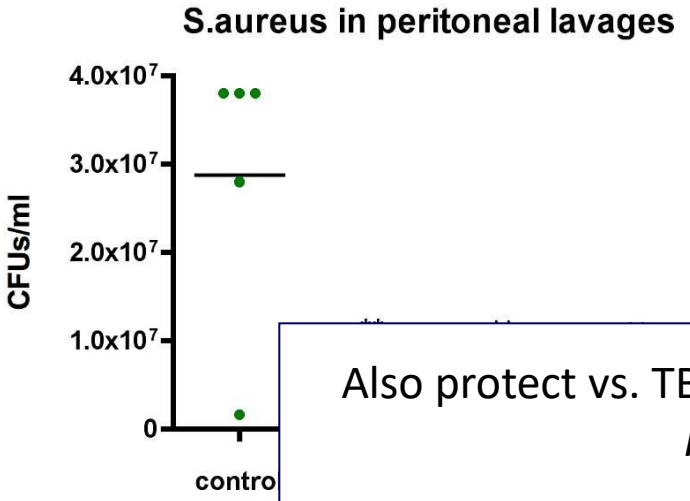
   novel treatment strategies are urgently required

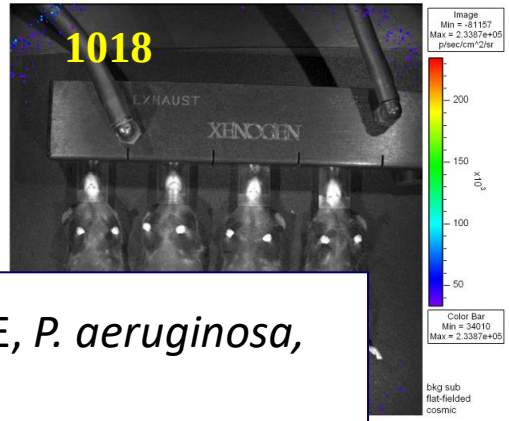
2. Researchers at UBC have recently discovered systems that contribute to *MTB*'s inherent resistance and unusual ability to persist in macrophages.

Undisputed leaders in Canada and internationally recognized

Centre for Microbial Diseases and Immunity Research

New immunomodulatory peptides show broad protection in mouse model infections

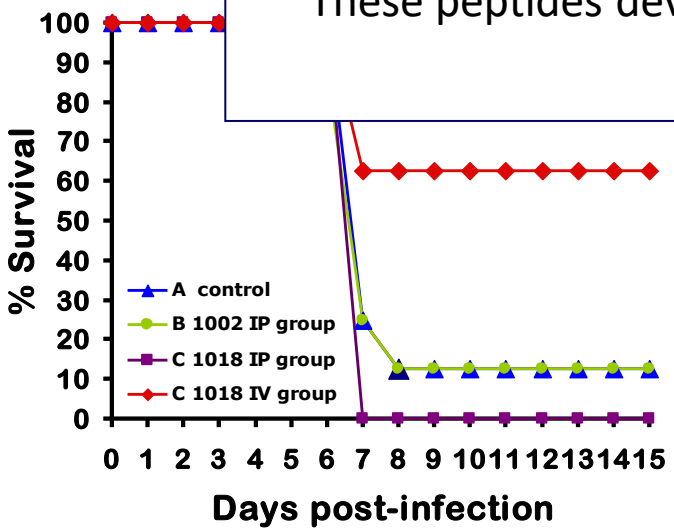


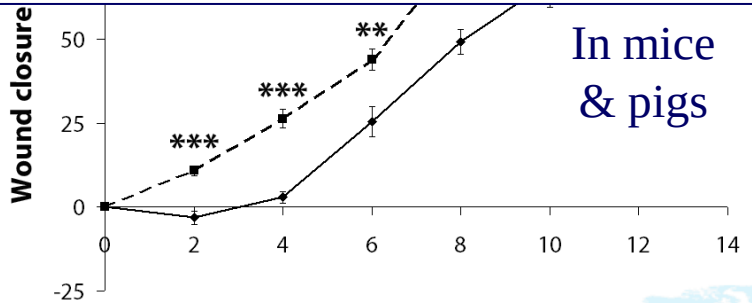


Also protect vs. TB, *E. coli, Salmonella,* MRSA, VRE, *P. aeruginosa, IBD* Sterile inflammation, etc.

A spin off company has completed Phase I clinical trials.

These peptides developed independently for Grand Challenges Program.





In mice & pigs

Grand Challenges in Global Health

THE UNIVERSITY OF BRITISH COLUMBIA

Neglected Global Diseases Initiative

Lars Steinstraesser, Louis Schofield, Sandra Pillat, Lisa Thorsen, Sarah Mullaly, Bruce Vallance, Brett Finlay, Bob Hancock

Prevention and Control of Dengue in Ecuador

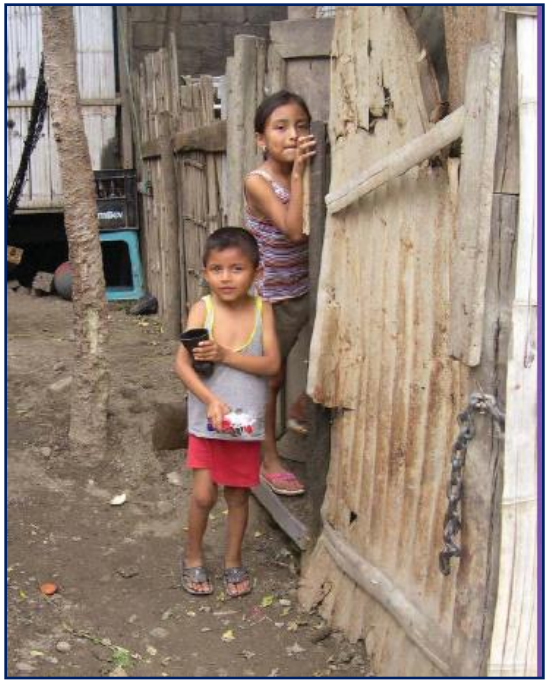
Sustainable capacity-building and scaling-up challenges

Dr. Jerry Spiegel, SPPH / Liu Institute and Kendra Foster, ISGP PhD student

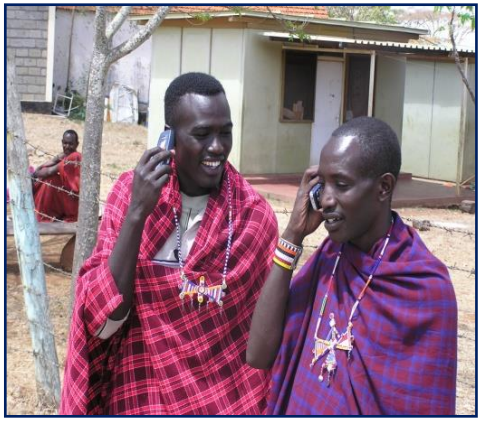
Funded by: IDRC CRDI
World Health Organization
TDR For research on diseases of poverty

Pilots an integrated community-based approach compared to reactive insecticide-based program

- comprehensive intervention effectiveness evaluation protocol
- information system for monitoring implementation & feasibility of transforming existing vector control programs



Global mHealth - WelTel



Richard Lester, MD, FRCPC

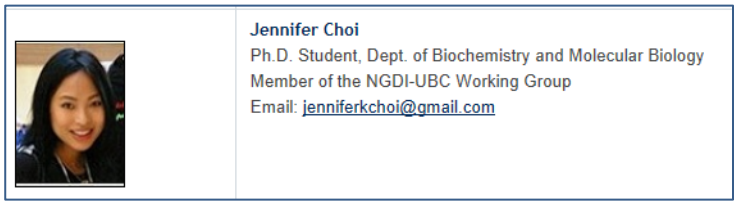
Infectious Diseases Physician (UBC)

STI/HIV control (BCCDC)

WHO Collaborative Centre for HIV/STD Research and Training (University of Manitoba / University of Nairobi, Kenya)

- Recently joined the UBC and the BCCDC after a 5 year HIV research fellowship in Kenya.
- Worked on discovery vaccine research around immunity to HIV in HIV-resistant sex-workers,
- Developed the Weltel mHealth program using cell phones to improve antiretroviral (ARV) adherence in urban and rural patients with HIV/AIDS.

What else can you do?



September, 2013
NGDI-UBC Newsletter

Advocate, Educate, Participate

Collaborate outside your discipline to expand your research

Initiate your own neglected disease research