

Creating a global community for clinical drug repurposing and development

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Neglected tropical diseases

1) Repurposing and developing new drugs

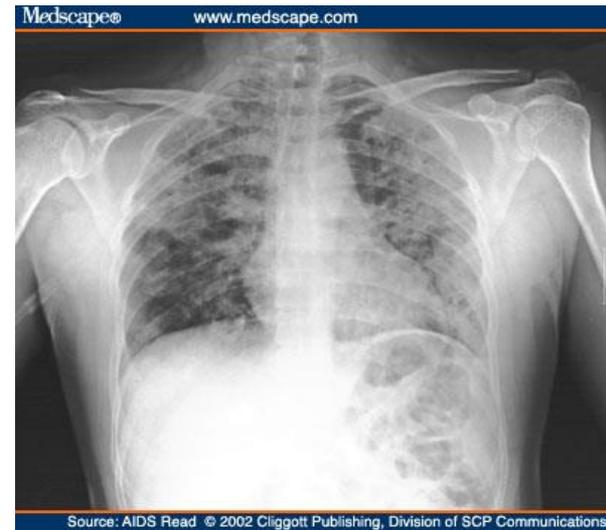


2) Improving patient care



How has drug repurposing worked?

- 1983- worldwide outbreak of pneumocystis
- Effective drugs:
 - Cotrimoxazole
 - Pentamidine
 - Clindamycin
 - Primaquine
 - Dapsone
 - Atovaquone



Lack of satisfactory drugs

- Concern in medical community about lack of drug development for NTDs
- No economic incentive for drug manufacturers to invest
- Many drugs are old, many are toxic
- For a number of neglected tropical diseases, there are no treatments approved by regulatory agencies
- Many eradicable diseases still plague millions of patients in tropical communities around the world

Some of the tropical diseases with limited or no approved treatments in USA

Disease	Number of FDA Approved Drugs	
African Trypanosomiasis (HAT)	0	
Chagas disease	0	
Lymphatic Filariasis	0	
Ebola	0	
Dengue	0	
Rabies	0	
Japanese encephalitis	0	
Buruli Ulcer	0	
Anasikiasis	0	
Fascioliasis	0	
Echinococcosis	1	Albendazole
Neurocysticercosis	1	Albendazole
Onchocerciasis	1	Ivermectin
Leishmaniasis	2	AmBisome, miltefosine
Leprosy	3	Thalidomide, Dapsone, Clofazamine
Tuberculosis (TB)	11	Bedaquiline, Isoniazid, Rifampin, Ethambutol, Pyrazinamide, Rifapentine, Rifabutin, Capreomycin, Para-aminosalicylic acid (PAS), Cycloserine, Streptomycin

37 FDA approved drugs/combinations for HIV since 1987

When patients with NTDs have no satisfactory treatment options...

Doctors often need to:

- Borrow drugs from other condition
- Use drugs in new combinations
- Alter dosages and durations of treatment

Examples of drug repurposing for NTDs

New use	Drug name	Original use
Malaria	Tetracycline Atovaquone	Bacterial infections Pneumocystis
Tuberculosis	Fluoroquinolones Linezolid	Bacterial infections Gram positive bacterial infections
Strongyloidiasis Onchocerciasis	Ivermectin	Veterinary antihelminthic
Leishmaniasis	Amphotericin Miltefosine	Antifungal Cancer
Amebiasis	Metronidazole	Anaerobic bacterial infections
Filariasis	Tetracycline (Wolbachia)	Bacterial infections
Cysticercosis	Praziquantal	Schistosomiasis
Babesiosis	Quinine	Malaria
African trypanosomiasis	Nifurtimox	Chaga's disease

Numbers of repurposed drugs reported

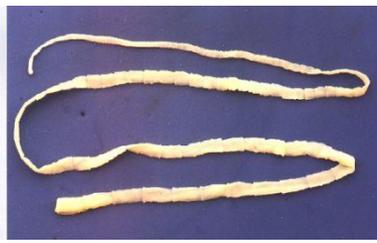
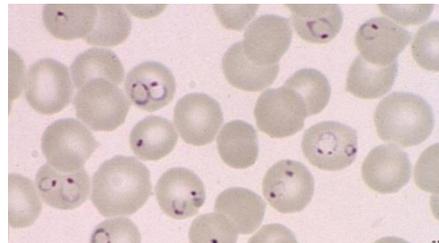
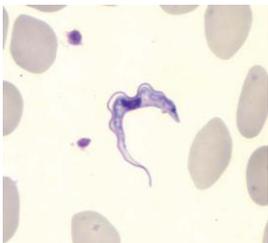
Disease	Number of Repurposed Drugs (literature)
Buruli Ulcer	23
Leishmaniasis	22
Onchocerciasis	20
Tuberculosis (TB)	14
Chagas	11
Lymphatic Filariasis	10
Leprosy	8
African Trypanosomiasis (HAT)	6
Echinococcosis	5
Neurocysticercosis	5

Collecting the worldwide experience of clinicians using existing drugs in new ways

- This would allow identification of promising treatments which can then be formally developed in clinical trials
- This would help identify ineffective or harmful treatments
- This would advance the clinical knowledge of these diseases and their treatments
- This would allow caregivers to rapidly communicate treatment experience in outbreaks and emergencies e.g. Ebola, Mers CoA, SARS

Rationale for Clinical Repurposing

- Many organisms share drug targets with other organisms



Some share human targets

Drug	Target	Neglected tropical disease
Miltefosine (Cancer)	AKT (protein kinase B) inhibitor	leishmaniasis
Methotrexate (cancer)	Folate antagonist	P vivax
Gleevac (imatinib) (cancer)	Tyrosine kinase inhibitor (ABL)	Filaricide, B Malayi
Lansoprazole (PPI)	Cytochrome bc1 inhibitor	Tuberculosis

The challenge

- To develop a website/mobile app where physicians around the world could submit their experience using existing drugs in new ways, new combinations or new dosing regimens

Heatmap type: Case Reports Heatmap Clinical Trials Heatmap

Search for drug or disez

	ALBENDAZOLE	ALLOPURINOL	AMIKACIN	AMPHOTERICIN B	AZITHROMYCIN	BENZNIDAZOLE	BETAMETHASONE	CEFTRIAZONE	CIPROFLOXACIN	CLARITHROMYCIN	DAPSONE	DIETHYLCARBAMAZINE
Buruli Ulcer	0	0	6	0	1	0	0	0	7	25	1	0
Chagas Disease	1	1	0	0	0	1	0	0	0	0	0	0
Ebola	0	0	0	0	0	0	0	0	0	0	0	0
Fungal Meningitis	0	0	0	0	0	0	0	0	0	0	0	0
African Trypanosomiasis	0	0	0	0	0	0	0	2	0	0	0	0
Loa Loa	13	0	0	0	0	0	0	0	0	0	0	174
Leishmaniasis	0	0	0	3	1	0	0	0	0	0	0	0
Leprosy	0	0	0	0	0	0	0	0	0	0	0	0
Lymphatic Filariasis	14	0	0	0	0	0	0	0	0	0	0	14
MERS-CoV	0	0	0	0	0	0	0	0	0	0	0	0

Show All Case Reports

Multi-cell select Show Empty Rows/Columns

Case Reports Clinical Trials

Found 13 case studies for Loa Loa and ALBENDAZOLE

Show 10 entries Search:

Disease	Organism/Strain	Drug	Year	Country	Outcome	Contact Author	Link
Loa Loa	Loa loa	ALBENDAZOLE		Cameroon	Success	Contact	link
Loa Loa	Loa Loa	DIETHYLCARBAMAZINE ALBENDAZOLE	2011		Unspecified	Publication	link
Loa Loa	Loa loa	IVERMECTIN ALBENDAZOLE	2011	Gabon	Success	Publication	link
Loa Loa	Loa loa	ALBENDAZOLE	2012	Congo	Success	Publication	link



Case Reports

Clinical Trials

Found **13** case studies for **Loa Loa** and **ALBENDAZOLE**Show **10** entriesSearch:

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Loa Loa	Loa loa	ALBENDAZOLE	2012	Congo	Success	Publication	link
Loa Loa	Loa loa and Mansonella perstans	ALBENDAZOLE	2001	Cameroon	Success	Publication	link
Loa Loa	Loa loa	ALBENDAZOLE	2007	Congo		Publication	link
Loa Loa	Loa loa	ALBENDAZOLE	2002	Cameroon	Success	Publication	link
Loa Loa	Loa loa	ALBENDAZOLE	1999	Gabon	Success	Publication	link
Loa Loa	Loa loa	ALBENDAZOLE	1999	Gabon	Success	Publication	link
Loa Loa	Loa Loa	ALBENDAZOLE	2003	Cameroon	Success	Publication	link

Showing 1 to 10 of 13 entries

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Sharing global experience

- A patient comes to your clinic with drug-resistant malaria.
 - Enter website
 - Browse repurposing database
 - Enter the treatment forum to discuss your problem case with disease experts around the world

An email with your query immediately goes out to all users and/or institutions around the world who have chatted, or submitted cases with that disease



Sharing global experience

- Now you can report your case on the internet to the CURE database
- Become a part of the global community of doctors treating malaria



What about emerging threats?

- SARS, MERS, Anthrax, Fungal meningitis, Ebola, Chickungunya, Bornavirus
- We need to hear immediately what is working and what is not



What about drug-resistance?

Drug-resistant organisms

Unlike all other drugs, antimicrobial efficacy changes. What worked 10 years ago for malaria does not work today. As antimicrobial sensitivities change, we need to hear from affected parts of the world what is working and what is not.

Summary

- Global reporting tool in development
- May fuel drug development NTDs
- May develop global communities of disease experts for patients all over the world
- Will depend on participation of doctors around the world

