Overcoming the Translational Barrier in Drug Repositioning

Nibedita Rath, Ph.D., Scientific Director, OSPF

WHAT IS OPEN SOURCE PHARMA?
HOW CAN PHARMA, A MEAT SPACE ENDEAVOUR, BE OPEN SOURCE?

- Idea mooted in 2006 Nature paper by OSPF co-founder Bernard Munos https://www.nature.com/articles/nrd2131
- Idea implemented in Government of India's CSIR's Open Source Drug Discovery by Professor Samir K. Brahmachari, now mentor and GN Ramachandran Fellow at OSPF
- OSPF is same idea as OSDD, but outside government, and more international www.ospfound.org. Core approach: Apply open source techniques of computation, crowdsourcing, open data, and open IP to drug R&D https://doi.org/10.1371/journal.pmed.1002276
- Emerging process:
  - Computation-led early stage drug discovery + distributed pro/low bono wet lab work + open source style clinical trials (with open data) + generics manufacture
  - With crowd commentary and open IP

OPEN SOURCE PHARMA FOUNDATION PROFILE

- Global nonprofit, founded 2016, with principal drug discovery lab at NIAS-Bangalore, and a presence in New York and Paris
- In four words, OSPF is “Affordable Medicine for All.” In three words, “Linux for drugs”
- We seek to discover drugs, and a new way to discover drugs
- Our goal is to revolutionize the process of drug discovery using open source principles, and to deliver affordable new treatments in areas of great health need
- Major areas: 1) discover medicines for neglected diseases, via computation-led drug discovery, clinical trials, 2) create open ecosystem, via conferences, education, platforms
- Completed phase 2B clinical trials for tuberculosis, in partnership with ICMR’s NIRT, https://bmjopen.bmj.com/content/9/3/e024363.info , repurposing off patent metformin, at 95% cost savings and 50% time savings over classic big pharma de novo models
- Other progress: multiple scientific papers published, three global conferences held, collaborator in phase 3 trials for two vaccines and one medicine against COVID-19, co-founder of global repurposing hub with US NIH, Gov’t of Brazil, EU-backed EATRIS

PARTNERS AND COLLABORATORS

AXIOMEDIX
THE FUTURE OF PRECISION MEDICINE

BROAD INSTITUTE

CRI

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FIOCRUZ
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NIAS

NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS

NIH National Center for Advancing Translational Sciences

eatris

TDU
INSTITUTE OF TRANSDISCIPLINARY HEALTH SCIENCES & TECHNOLOGY

TB ALLIANCE

OPEN SOURCE PHARMA FOUNDATION

FUNDERS

Note: Welcome, OSF, Rockefeller funding provided to North American affiliates.

OSPF PRESS CLIPS

THE NEW YORKER

BEYOND THE BOOSTER SHOT

Could a "broad spectrum" booster increase our immunity to

BBC NEWS

We Should Own Our Own Livelihood and Our Own Dream

FAST COMPANY

FAST COMPANY WORLD CHANGING IDEAS 2020

HONORABLE MENTION | OPEN SOURCE PHARMACEUTICAL RESEARCH

Newsweek

America's 50 Greatest Disruptors:
Collaborative Tech to Develop New, Affordable Drugs - Open Pharma

THE LANCET

Can open-source drug development deliver?

FAST COMPANY

How open-source medicine could prepare us for the next pandemic

The old drug discovery system was built to benefit shareholders, not patients. But a new, Linux-like platform could transform the way medicine is developed—and energize the race against COVID-19.

NDTV

Can Open-Source Vaccines Become A Reality For India?

theguardian

Why Open Source Pharma is the Path to both New and Cheaper Medicines

The New York Times

Why a Century-Old Vaccine Offers New Hope Against Pathogens

(#3 on NYT daily most shared articles list)

Forbes

Beyond Heroism And Denial: How To Fortify Our Response To Ebola

TC

What is Open Source Pharma (and Why Should You Care)?

Newsweek

COVER STORY:
How COVID Opened a 'Pandora's Box' of Monkeypox, Polio and Other Diseases

OPEN SOURCE PHARMA FOUNDATION

Drug Repositioning – A promise of rapid Clinical impact at a lower cost

Attractive and Pragmatic

- Large number of potential drugs never reach clinical testing
- Approved or failed drugs with established safety profile, finding new indications can be rapidly bring benefits to patients

Successful drug repurposing

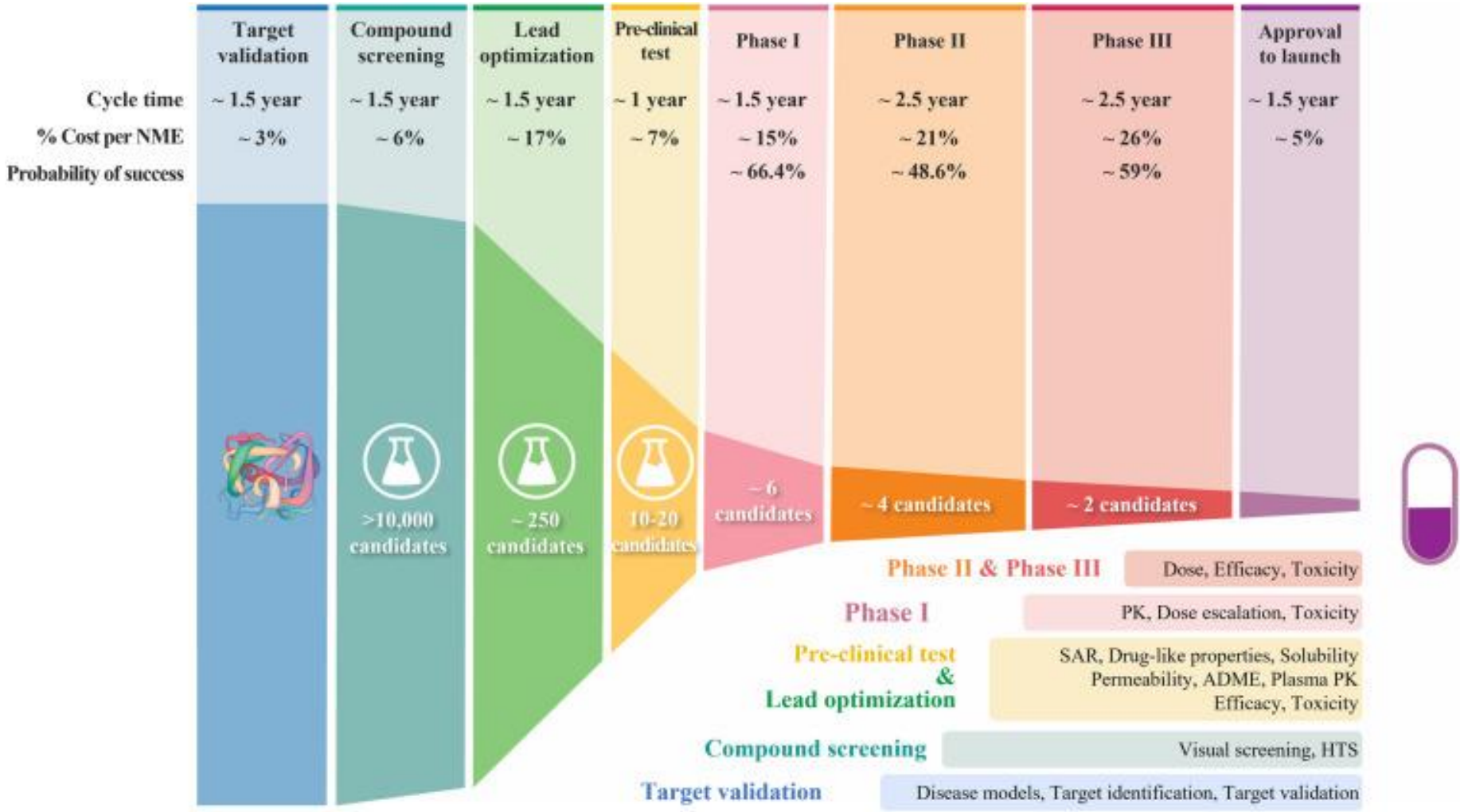
- Cyclooxygenease inhibitor Aspirin for coronary-artery disease Antiemetic thalidomide to treat multiple myeloma.

Successes thus far have been mostly serendipitous

Current academic and industrial efforts

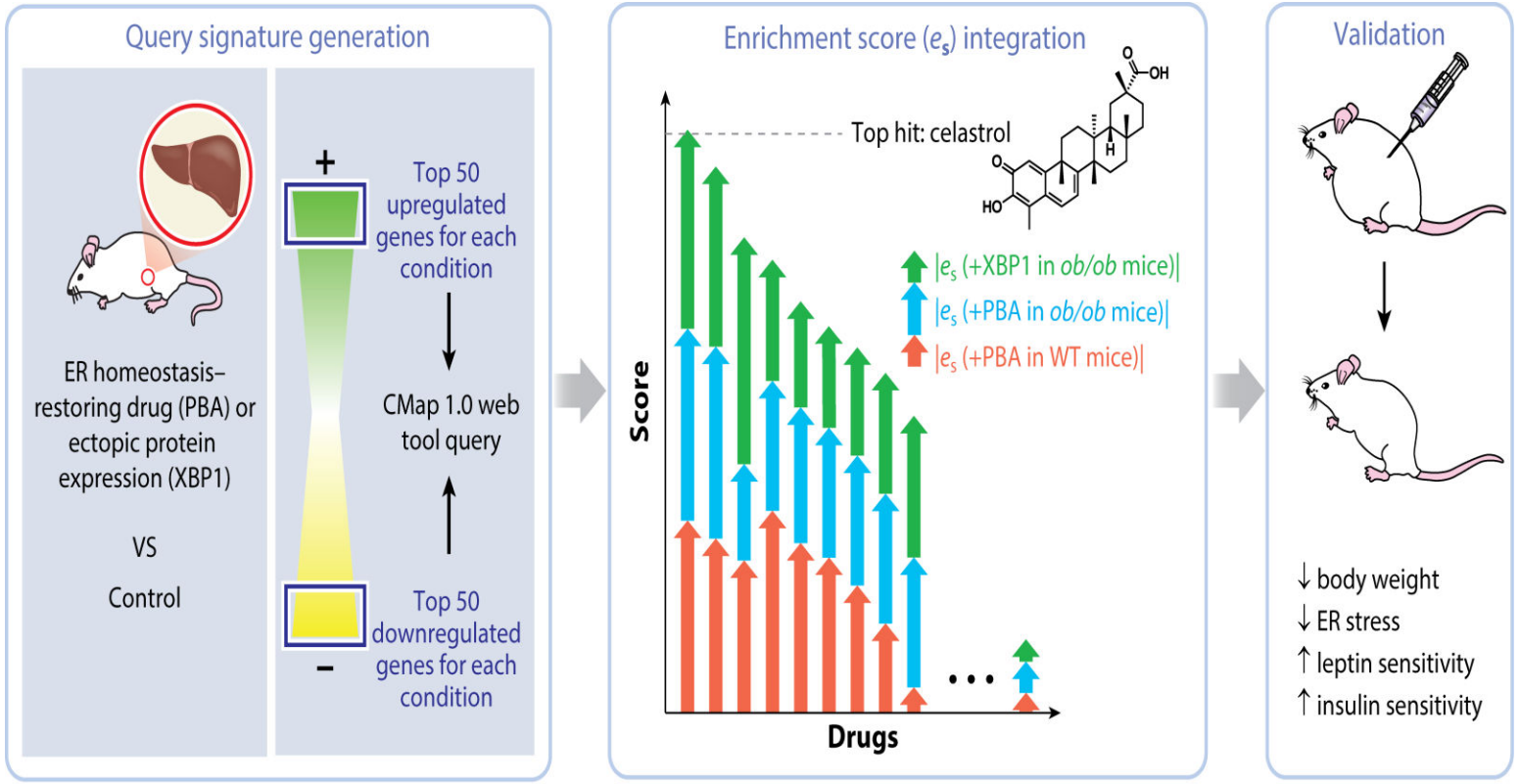
- Broad institute, Boston, USA – gene expression profiling Exscientia, Dundee, UK – AI: polypharmacology and phenotypic screening, NovaLead, Pune, INDIA: repurposing generic drugs

The process of drug discovery and development, and the failure rate



https://doi.org/10.1016/j.apsb.2022.02.002

An illustrative example of the use of connectivity mapping

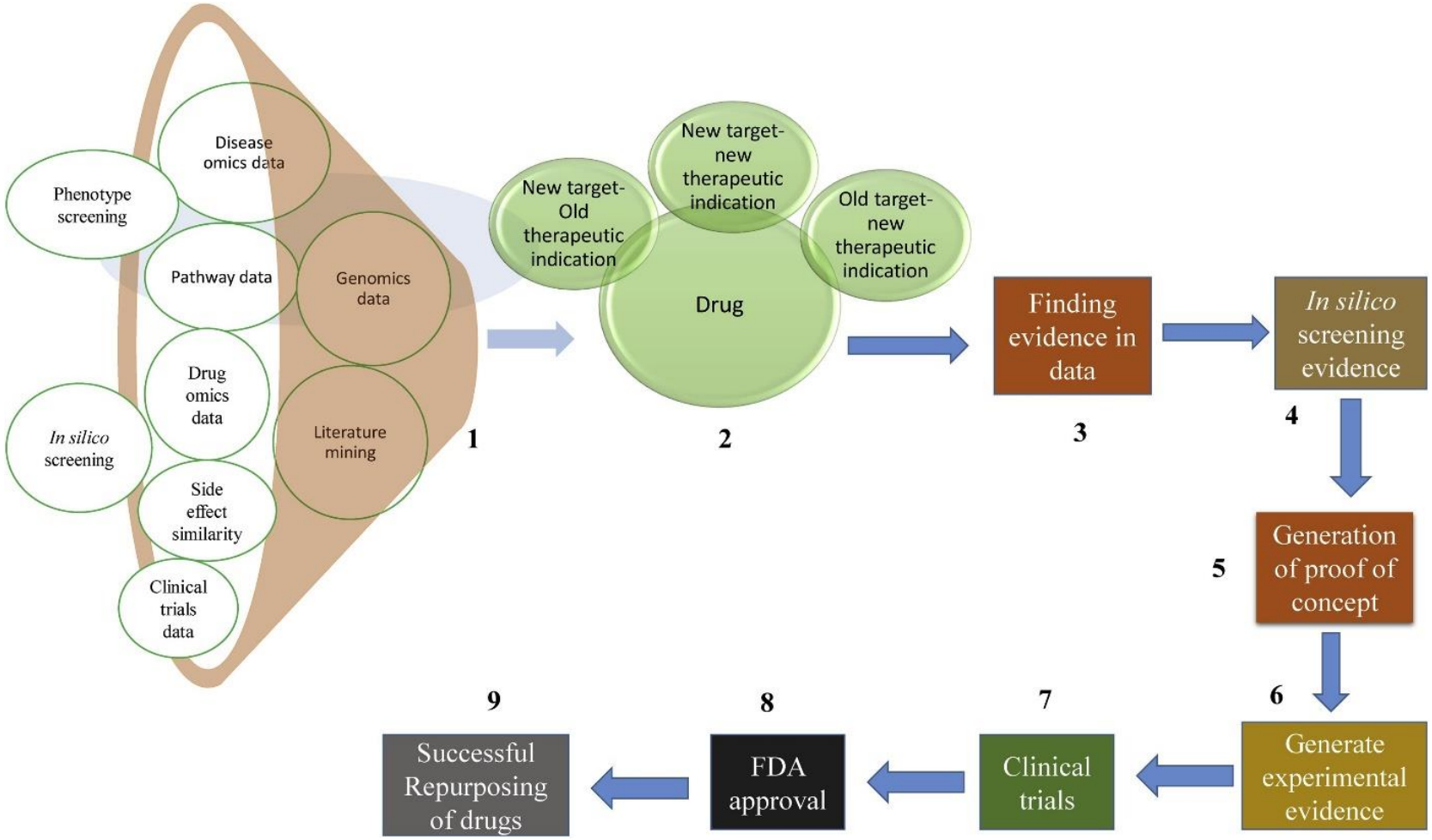


Gene expression signatures from mouse liver and hypothalamus were obtained under several experimental conditions designed to reflect pathways that restore ER homeostasis. The top 50 up and down differentially expressed genes from each signature were chosen to query the Connectivity Map.

Keenan AB, et al. 2019. *Annu. Rev. Biomed. Data Sci.* 2:69–92

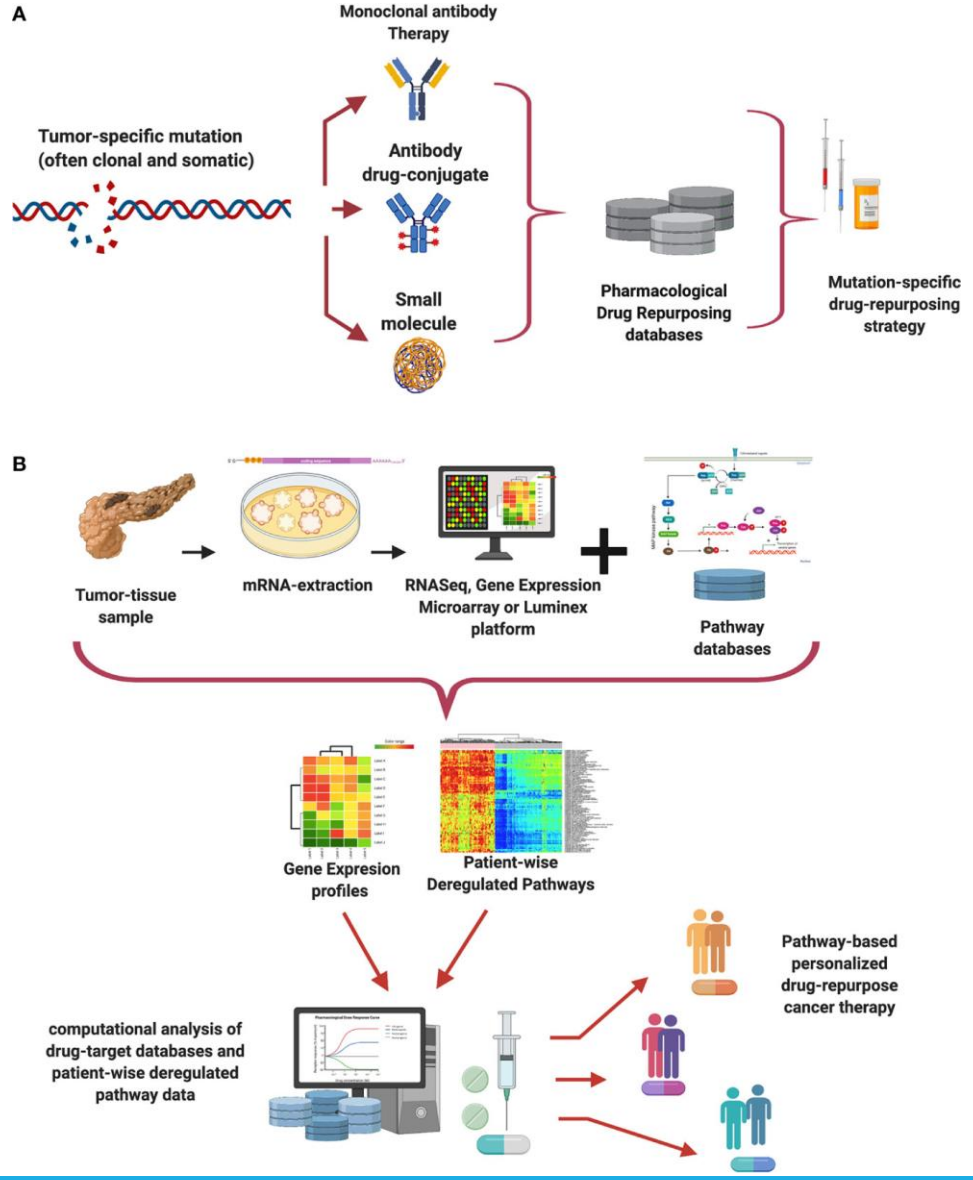
https://doi.org/10.1146/annurev-biodatasci-072018-021211

Route map for drug repurposing



Biomedicine & Pharmacotherapy,Volume 110, 2019, Pages 700-716, ISSN 0753-3322,

Mutation-specific and pathway-centric approaches to drug re-purposing



PANEL A: A simplified workflow for drug repurposing based on tumor mutation profiling, Panel (B) shows one possible pipeline for drug repurposing based on pathway activities as proxied by gene expression analysis.

https://doi.org/10.3389/fonc.2020.605680

OSPF's Initiatives in Repurposing

SOLUTION: AI-POWERED KNOWLEDGE GRAPH – A “GOOGLE MAPS” FOR TB DRUG DISCOVERY

Benefits to Drug Discovery Researcher

- **Faster:** do in hours what took months
- **Wider:** combines tens of thousands of otherwise siloed sources
- **More Current:** AI scrapes the world daily
- **Novel Insights:** better Ideas, via showing connections

KNOWLEDGE BASE AND KNOWLEDGE GRAPH

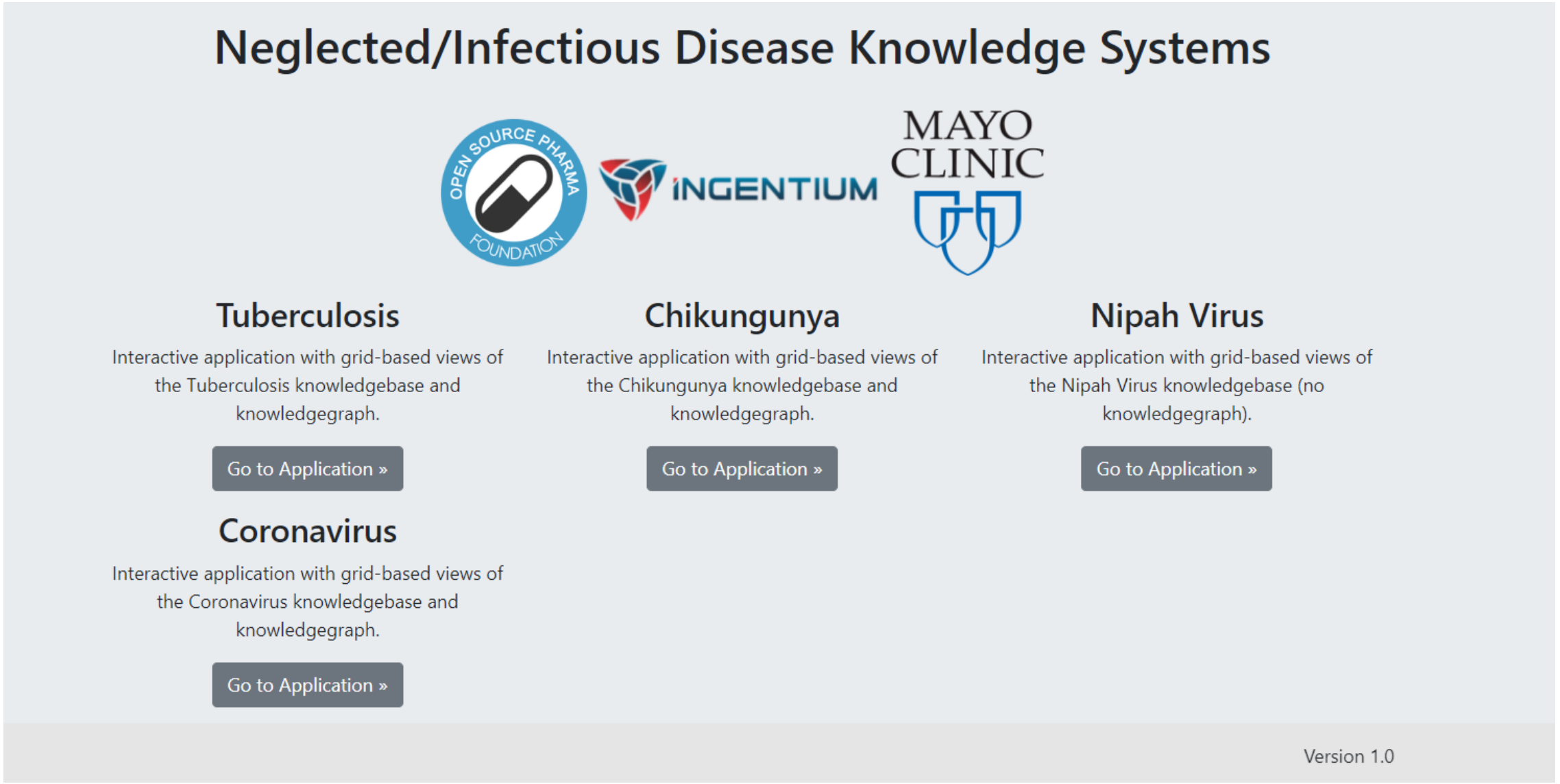
Dynamic, Machine-curated Knowledge Bases for Pathogens

- Knowledge bases focused on specific disease
  - TB, Covid-19, Nipah Virus, Chikungunya Virus, etc.
- AI System is trained to curate by subject matter experts using semantic Machine Learning models
- Includes patents, references, books, podcasts, reports, etc.
- 'Learns' rules for curation, 2x or more daily updates plus historical content from 20 years or more
- Newly identified content is pushed via 'news', 'alerts', 'journals and social media

Contextualized Biological Knowledge Graph

- Knowledge graphs based on specific biological context
  - e.g., Tuberculosis, Chikungunya, Covid-19, Cancer etc.
- Graphs are populated with semantically curated content from disease focused Knowledge base(s)
- NLP and Predication are used to 'read' articles, and incorporate new content into the graph
- New knowledge can be viewed on an integrated graph
- Multiple data resources are linked in knowledge graph
  - Compound libraries, screening data, etc.

KNOWLEDGE SYSTEM



The Knowledge Graph

Scaffold of Known Biology and Chemistry

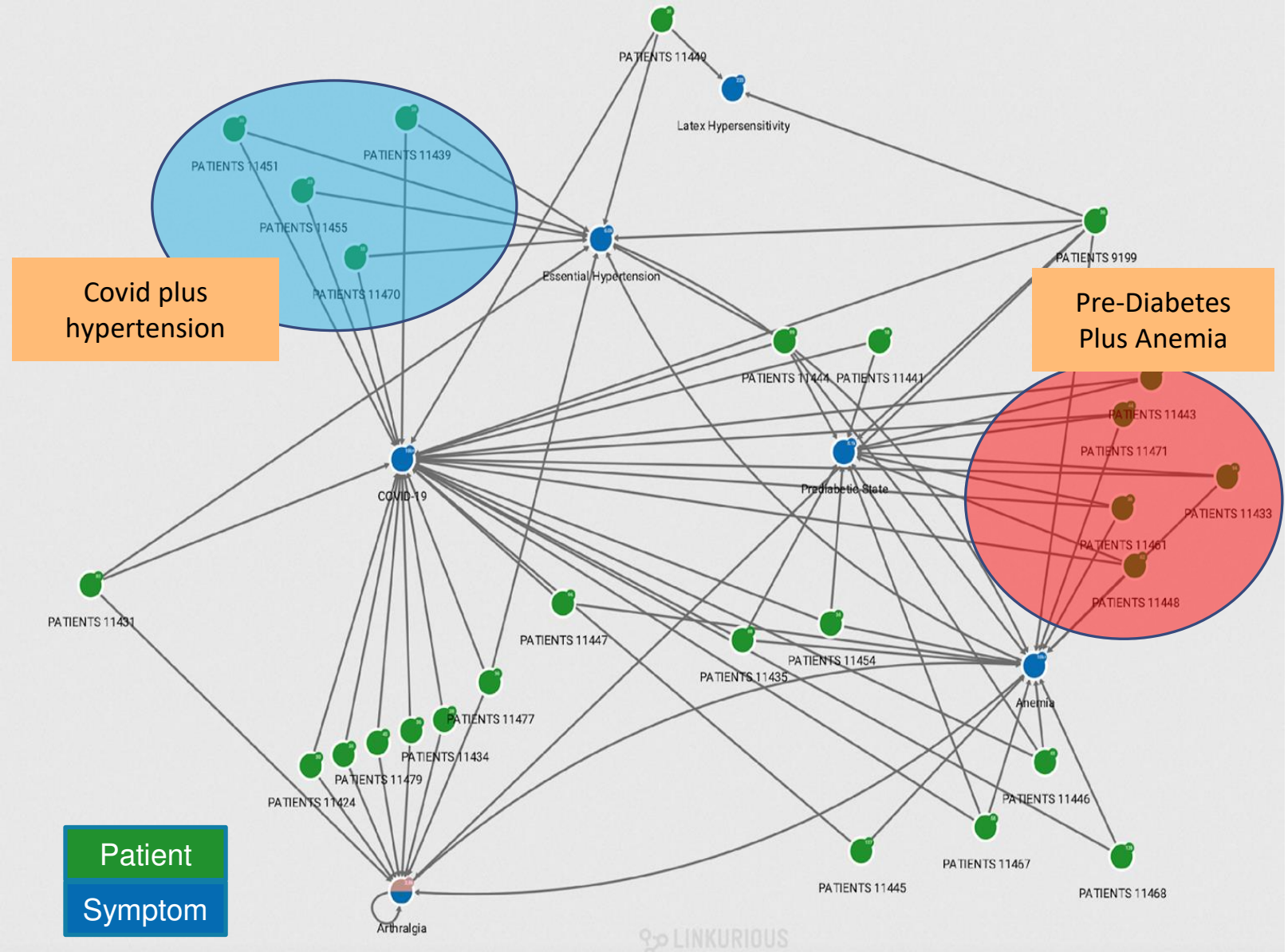
13.2M Nodes

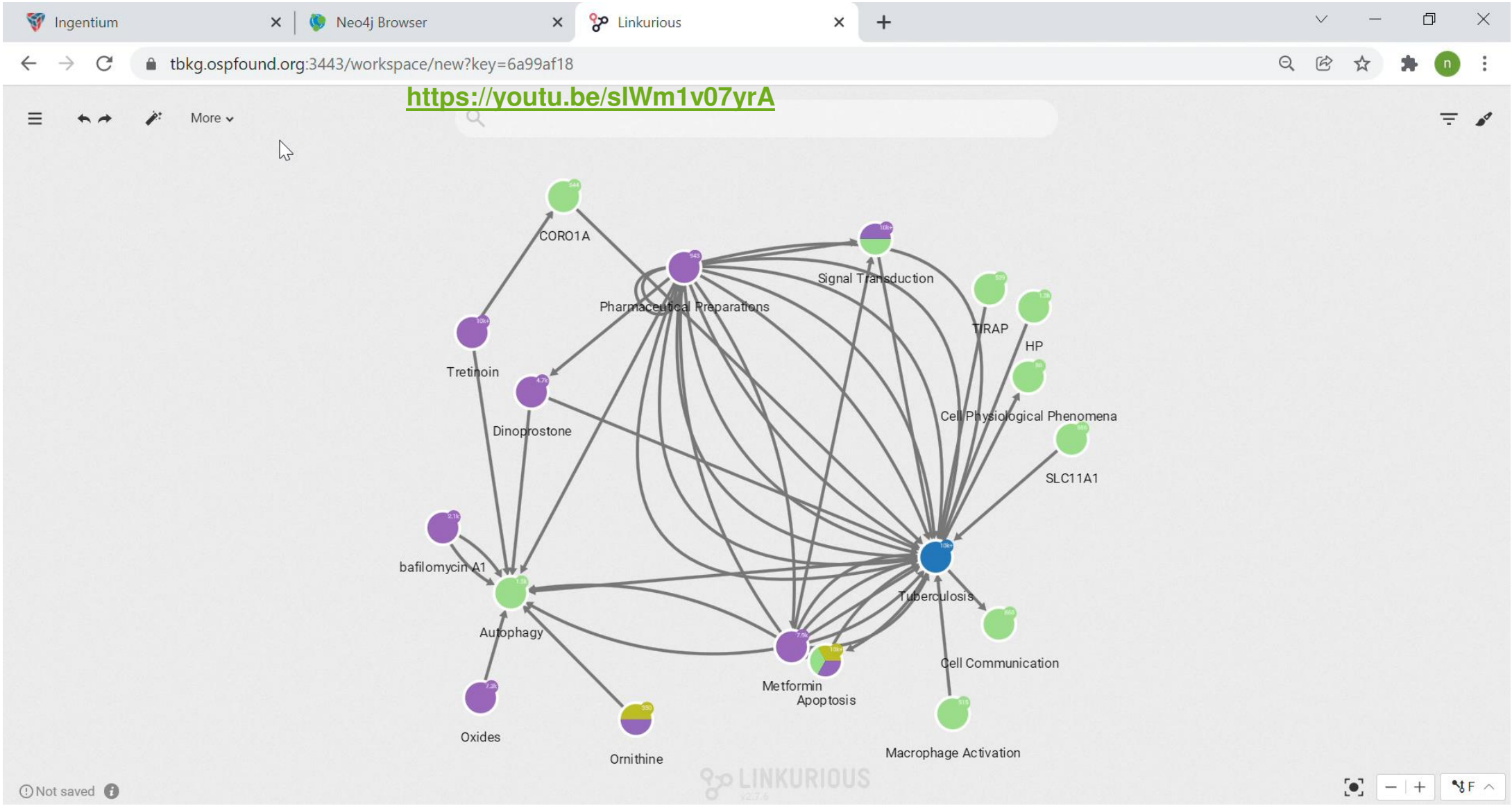
- Such as: protein, gene, drug, disease, symptom, clinical trial, pathway, images, etc.

48M Edges

- Such as: “treats”, “member of”, “NLP disease”, “NLP chemical”, etc.

Adding nodes and edges from content sources to the Disease focused scaffold




Ingentium
Neo4j Browser
Linkurious
tbkg.ospfound.org:3443/workspace/new?key=6a99af18
https://youtu.be/slWm1v07yrA
More
CORO1A
Pharmaceutical Preparations
Signal Transduction
TIRAP
HP
Tretinoin
Dinoprostone
Cell/Physiological Phenomena
SLC11A1
bafilomycin A1
Autophagy
Tuberculosis
Cell Communication
Metformin
Apoptosis
Oxides
Ornithine
Macrophage Activation
Not saved
LINKURIOUS

Randomized Trial of Metformin With Anti-Tuberculosis Drugs for Early Sputum Conversion in Adults With Pulmonary Tuberculosis

NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS

NIRT

Randomized Controlled Trial › Clin Infect Dis. 2022 Aug 31;75(3):425-434.

doi: 10.1093/cid/ciab964.

Randomized Trial of Metformin With Anti-Tuberculosis Drugs for Early Sputum Conversion in Adults With Pulmonary Tuberculosis

Chandrasekaran Padmapriydarsini [1], Megha Mamulwar [2], Anant Mohan [3], Prema Shanmugam [1], N S Gomathy [1], Aarti Mane [2], Urvashi B Singh [3], Nathella Pavankumar [1], Abhijeet Kadam [2], Hemanth Kumar [1], Chandra Suresh [1], Devaraju Reddy [1], Poornaganga Devi [1], P M Ramesh [4], Lakshmanan Sekar [1], Shaheed Jawahar [5], R K Shandil [5], Manjula Singh [6], Jaykumar Menon [5], Randeep Guleria [3]

Why repurpose Metformin for TB

- Innate immunity plays a key role in controlling TB
- ~90% infected humans contain TB without disease.
- Hence immunomodulators/HDT hold promise

Metformin is a biguanide used to treat diabetes mellitus

A significant preclinical evidence exist on Metformin in TB

An immunomodulator that enhances intracellular killing of TB via modulation of AMPK, ROS and Autophagy.

Enhances in vivo efficacy of anti-TB drugs

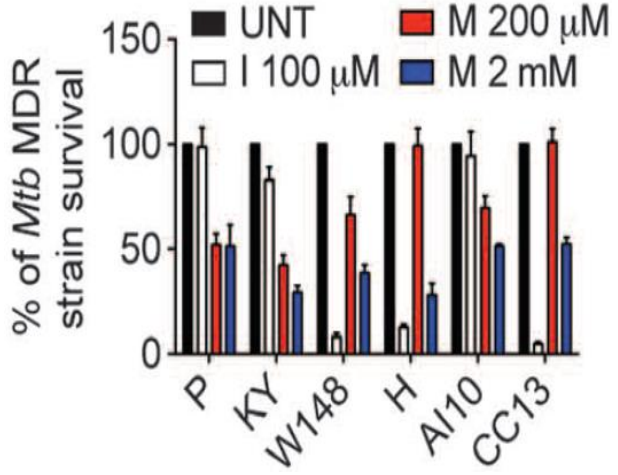
Reduces TB-induced lung pathology

Singhal et.al. ScienceTranslationalMedicine.org, 2014: 6 Issue 263 263ra159

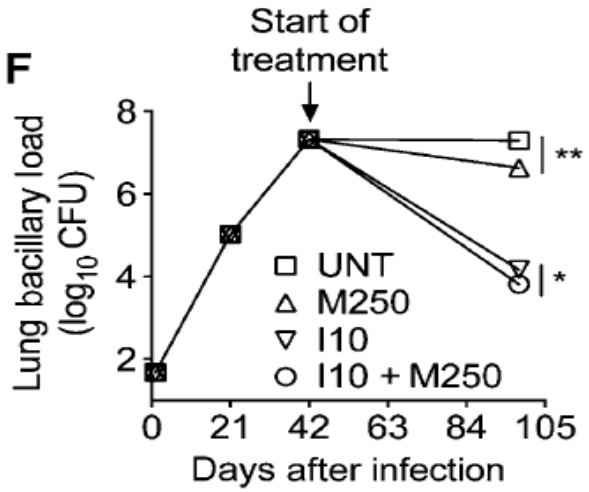
Few retrospective human studies also suggest role of Metformin in TB and disease control

Metformin Adjunct therapy in Mac, Mice and TB patients

THP1 Macrophages



Mouse model



Retrospective data: TB-Diabetes patients

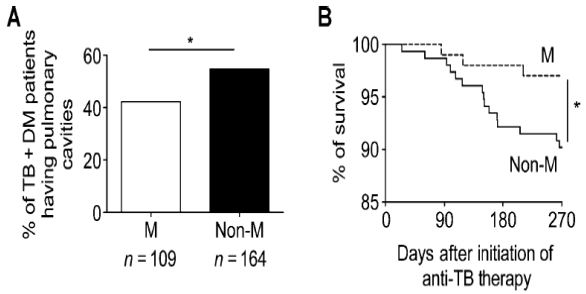


Fig. 5. Effect of MET in TB patients with DM as comorbidity. (**A**) Percent-

- **Metformin-Adjunct studies in mice and TB patients are encouraging**
- **This is basis of new TB clinical trials of metformin for Rx of TB**

Singhal et. al. 2014, Science Trans. Med. 6: 263 ra159

Objectives

Primary Objective:

- To evaluate the anti-bacterial activity of Metformin, when given for 8-weeks with standard anti-TB treatment

by measuring the time to sputum culture conversion

Secondary Objectives:

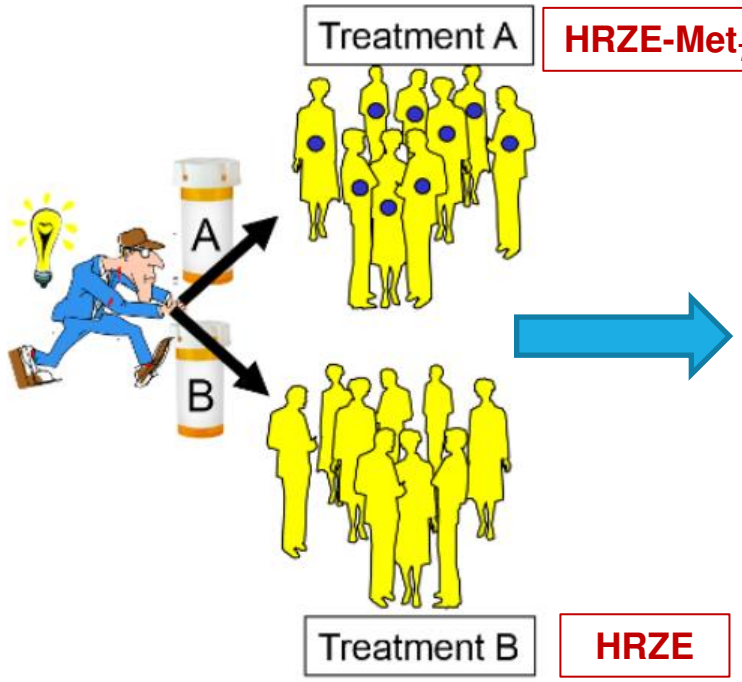
- To evaluate the time to detection in culture
- To determine % of patients with sputum culture conversion
- To study the pharmacokinetics of Metformin and other drugs
- To assess the safety and tolerability of Metformin combination
- To study the immune responses in the study subjects

Current status of Metformin clinical trial

Current Status - ~100% Completed

- Enrollment completed ahead of schedule (324 TB patients)
- 6month follow up after Rx -Completed
- Lab results: Sputum bacteriology, PK, Pharmacogenomics, Immunology (Autophagy, Cytokines and ROS) being analyzed
- PFT sub-study: Pulmonary function test to quantify improvements in lung function after MET treatment completed

Randomized, open-label, parallel arm controlled clinical trial



Months Rx	1	2	3	4	5	6
Test Regimen	HRZE-Met$_7$	HRZE-Met$_7$	HRE$_7$	HRE$_7$	HRE$_7$	HRE$_7$
Control Arm	HRZE$_7$	HRZE$_7$	HRE$_7$	HRE$_7$	HRE$_7$	HRE$_7$

Primary end point: Bacteriology
- Time to sputum culture conversion at 8 wk Rx

Secondary endpoints:
- **P**harmacokinetics & Pharmacogenomics
- Drug–drug interactions
- Safety and tolerability of combinations
- Measurement of autophagy and immune responses

Baseline and 8 weeks of anti-tuberculosis treatment (ATT) plasma levels of acute phase proteins in pulmonary tuberculosis (PTB) patients in the METRIF arm and control arm

Figure 4a

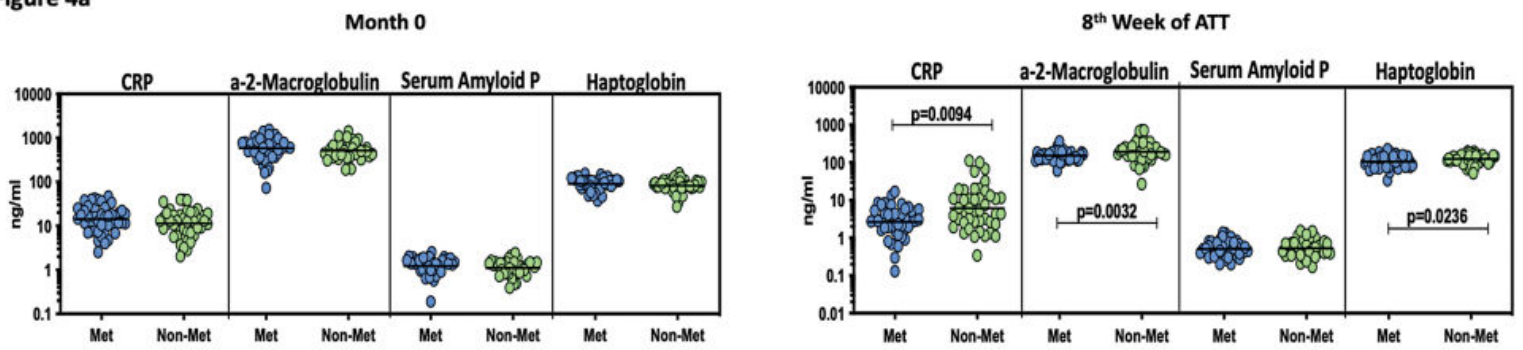
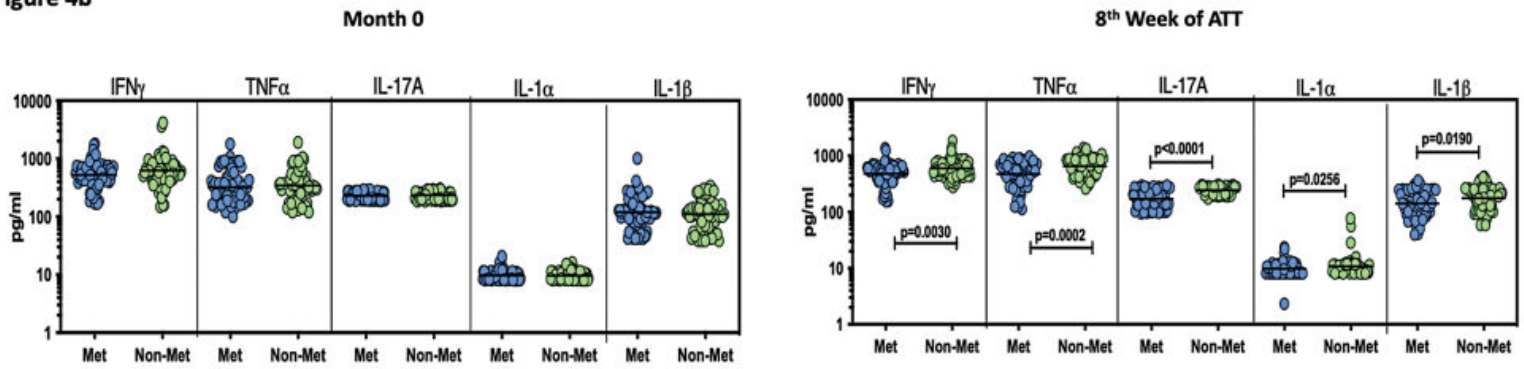


Figure 4b



Acute Phase Proteins and Inflammatory Cytokines Plasma levels of acute-phase proteins CRP, a2M, SAP, and Hp were similar in both arms at baseline At the eighth week of ATT, patients in the METRIF arm exhibited significantly diminished circulating levels of these acute phase proteins compared with the control arm:

Padmapriydarsini C, etal. Clin Infect Dis. 2022 Aug 31;75(3):425-434. doi: 10.1093/cid/ciab964.
PMID: 34849651; PMCID: PMC9427151.

Radiological Improvement

Chest X-ray results were compared at baseline and at 8 weeks of treatment. Two readers read the X-rays independently, and any discrepancies were resolved by an umpire reader.

Time point	Cough n (%)		Expectoration n (%)		Loss of appetite n (%)		Breathlessness n (%)		Chest pain n (%)	
	METRIF	Control	METRIF	Control	METRIF	Control	METRIF	Control	METRIF	Control
Baseline	155 (96.9)	161 (99.4)	135 (84.4)	144 (88.9)	104 (64.2)	113 (70.6)	73 (45.6)	79 (48.8)	58 (36.3)	50 (30.9)
1st week	120 (75.9)	124 (76.5)	98 (73.7)	101 (70.1)	42 (40.8)	46 (40.7)	21 (28.8)	21 (26.6)	11 (19.3)	11 (22.0)
2nd week	84 (54.5)	94 (59.1)	59 (45.7)	70 (49.6)	32 (31.4)	23 (20.9)	7 (9.7)	13 (16.7)	5 (8.9)	6 (12.0)
3rd week	67 (44.1)	85 (54.5)	48 (37.5)	48 (34.8)	16 (16.3)	16 (15.0)	6 (8.7)	13 (17.1)	6 (11.1)	5 (10.2)
4th week	50 (34.2)	61 (40.4)	30 (24.6)	34 (25.6)	14 (14.4)	17 (16.0)	6 (9.1)	16 (21.6)	5 (9.8)	6 (12.2)
5th week	38 (27.0)	48 (31.8)	28 (23.5)	30 (22.6)	12 (12.5)	16 (15.1)	6 (9.2)	10 (13.2)	5 (10.2)	4 (8.3)
6th week	32 (22.7)	42 (28.0)	22 (18.6)	27 (20.3)	8 (8.4)	12 (11.2)	7 (10.8)	6 (8.0)	6 (12.8)	3 (6.1)
7th week	30 (21.1)	36 (24.7)	15 (12.6)	20 (15.5)	6 (6.4)	9 (8.5)	3 (4.7)	4 (5.3)	2 (4.2)	1 (2.0)
8th week	24 (16.6)	32 (21.3)	14 (11.5)	13 (9.8)	13 (13.4)	12 (11.2)	6 (9.0)	6 (7.9)	6 (12.0)	4 (8.2)

At baseline, cavity on chest X-ray was in an equal proportion of patients in the study arms, that is, 27 (19%) patients in the METRIF arm and 27 (18%) in the control arm. By the eighth week, cavity on chest X-ray was noticed in 7 (5.3%) patients in the METRIF arm and 18 (13%) patients in the control arm. The relative risk was 0.42 (95% CI, .18–.96), showing a statistically significant difference between the 2 arms (P = .041). Clinically, a higher proportion of patients in the control arm continued to be symptomatic (especially cough) at the fourth week and the eighth week compared with the METRIF arm. However, this was not statistically significant.

Summary and Implications

- Metformin addition was associated with faster resolution of the cavity on chest X-ray and reduction in the level of circulating plasma proinflammatory cytokines after 8 weeks of treatment in patients with PTB.

- This suggests that a metformin-containing 5-drug regimen may reduce the infectiousness and transmissibility in patients with the cavitary disease. It may also play a role in reducing the post-TB lung sequelae, such as fibrosis or structural damage, by a faster decline in the proinflammatory cytokines.

- However, it did not affect the 2-month culture conversion rate at the dose used in this study and hence cannot suggest shortening the duration of treatment.

- The findings suggest exploration of a higher dose or extended use of metformin in culture conversion in addition to its anti inflammatory property.

Repurposing Vaccines

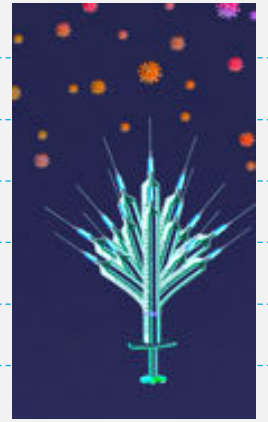
TRANSFORMATIVE PROJECT EXAMPLE: UNIVERSAL INNATE IMMUNITY VACCINES

A NEW SCIENTIFIC AND A NEW LEGAL ECONOMIC PARADIGM, TO CURB PANDEMICS AND OTHER DISEASES FAR EARLIER, FOR ALL PEOPLE.
HOW? VIA REPURPOSING CERTAIN EXISTING WIDELY AVAILABLE AND TRUSTED VACCINES THAT ACTIVATE INNATE IMMUNITY (BCG, MEASLES, OPV, FLU) AND VIA CREATING NOVEL ONES

Current COVID-19 Vaccines

- Narrow (vs One Bug or Variant)
- Adaptive Immunity-Focused
- COVID-19 only
- Proprietary
- Expensive
- Inaccessible to Most, for Years
- Later (1+ years into pandemic)
- Slow-Acting (1-2 weeks)
- Trust Issues
- Limited Duration, Variant Evasion

Innate Immunity (at Phase 3 clinical trials)



- Universal (vs Many Bugs, All Variants)
- Innate Immunity-Focused
- Future Pandemics/Disease X, Other Diseases
- Open Source / Open IP
- Cheap, at little as 1-10 cents a dose
- Accessible to Almost All
- Sooner (day 1 of a pandemic, or before)
- Possibly Faster Acting (1 hour)
- Long Safety Track Record
- Could Reduce Evasion and Severity

"Imagine if we could use existing vaccines to curb pandemics - that would change world history"(1)
The New York Times, quoting team member

Small phase 3 trials complete, large-scale manufacturing in place

The New York Times | Newsweek cover story | The New Yorker | Newsweek | Cell | The New England Journal of Medicine | PNAS | Cell | BMJ | World Health Organization | Strategic Advisory Group of Experts on Immunization (SAGE)

Sources: Click logos for articles. **Note that WHO (at p. 12) calls specifically for the trials proposed here.**
OSPF Scientific Advisory Committee includes scientific legends Tachi Yamada (in memoriam), Robert Gallo, Mihai Netea.
WHO Chief Scientist Soumya Swaminathan is an Observer

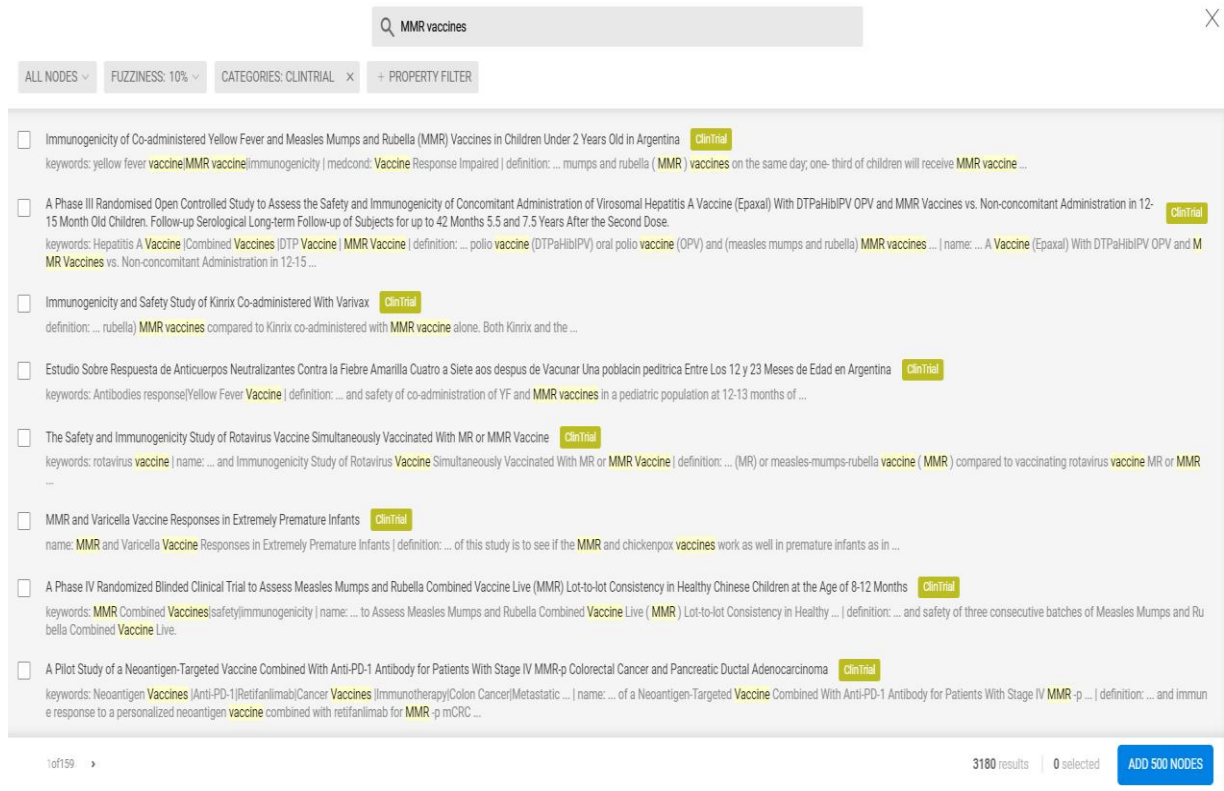
OPEN SOURCE PHARMA FOUNDATION

List of childhood vaccines that have heterologous or nonspecific protective effect against various pathogens or diseases

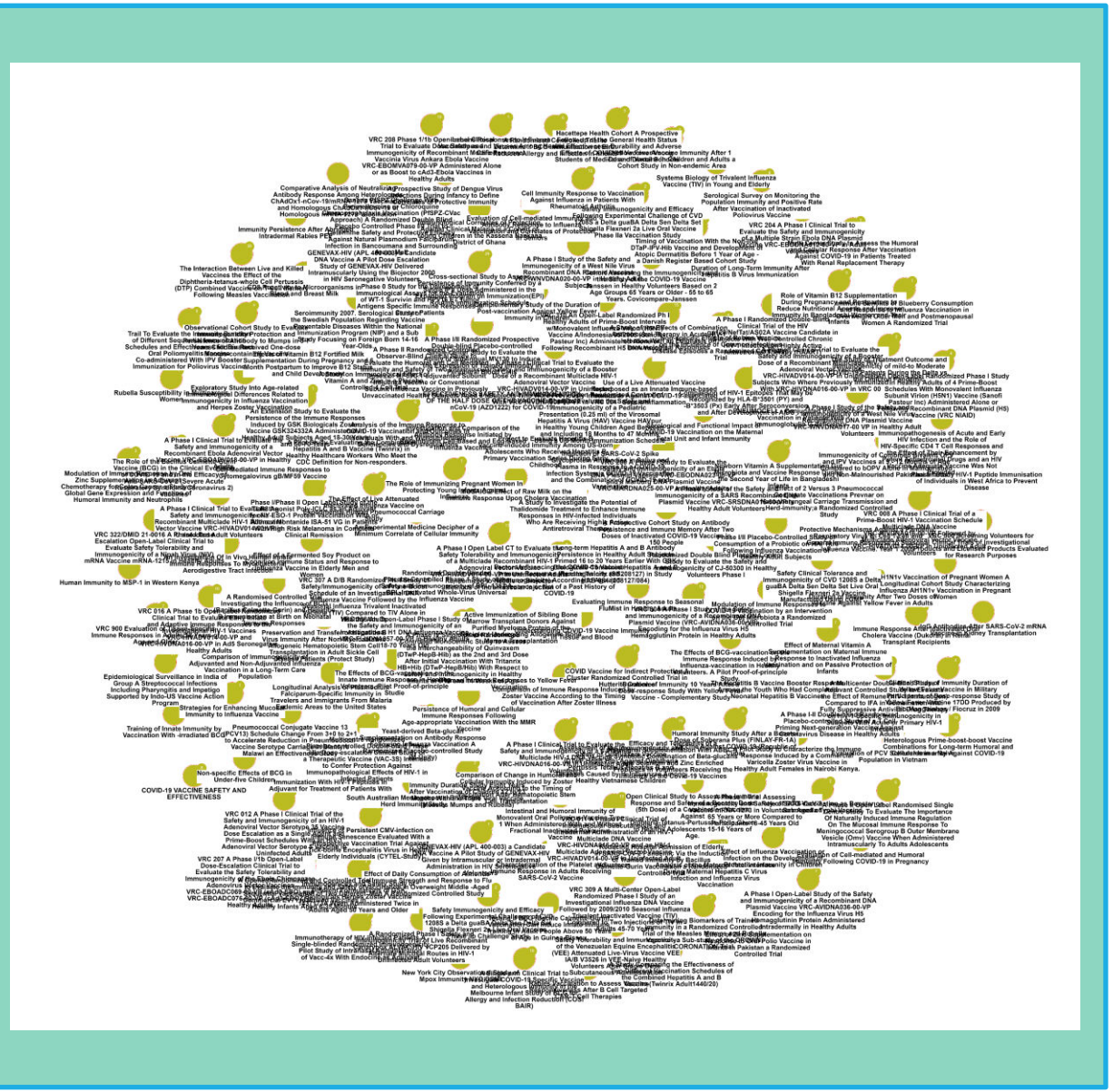
Vaccines	Types of vaccines	Pathogen-specific intended use	Heterologous or nonspecific protective effect against the pathogens or Diseases	Possible mechanisms
Bacille Calmette-Guerin (BCG) vaccine	Live-attenuated	M.tuberculosis M.leprae and Buruli Ulcers	Bladder cancer All-cause of infectious diseases, COVID-19	Trained Immunity, Immune-modulation Cross-reactivity
Measles vaccine	Live-attenuated	Measles virus	H. influenzae S. pneumonia, COVID-19	Trained Immunity, Immune-modulation Cross-reactivity
Measles, Mumps, Rubella (MMR) Vaccine	Live-attenuated	Measles, Mumps, and Rubella viruses	Respiratory infections, COVID-19	Trained Immunity, Immune-modulation Cross-reactivity
Yellow fever vaccine	Live-attenuated	Yellow fever virus	H. influenzae S. pneumoniae	Trained Immunity, Immune-modulation Cross-reactivity
Smallpox vaccine or Vaccinia vaccine	Live-attenuated	Smallpox virus	All-cause of infectious diseases, Malignant Melanoma	Trained Immunity, Immune-modulation Cross-reactivity
Oral polio vaccine	Live-attenuated	Poliovirus	All-cause of infectious diseases, Diarrhea, COVID-19	Trained Immunity, Immune-modulation Cross-reactivity
Diphtheria–Tetanus–Pertussis (DTaP) vaccine	A mixture of toxoids (Diphtheria & Tetanus) and killed bacteriaor pertussis antigens	Diphtheria–Tetanus–Pertussis	All-cause of infectious diseases	Trained Immunity, Immune-modulation Cross-reactivity

Sharma D. (2021). Repurposing of the childhood vaccines: could we train the immune system against the SARS-CoV-2. *Expert review of vaccines*, *20*(9), 1051–1057. https://doi.org/10.1080/14760584.2021.1960161

BCG Vaccines



BCG Vaccines and Innate Immunity



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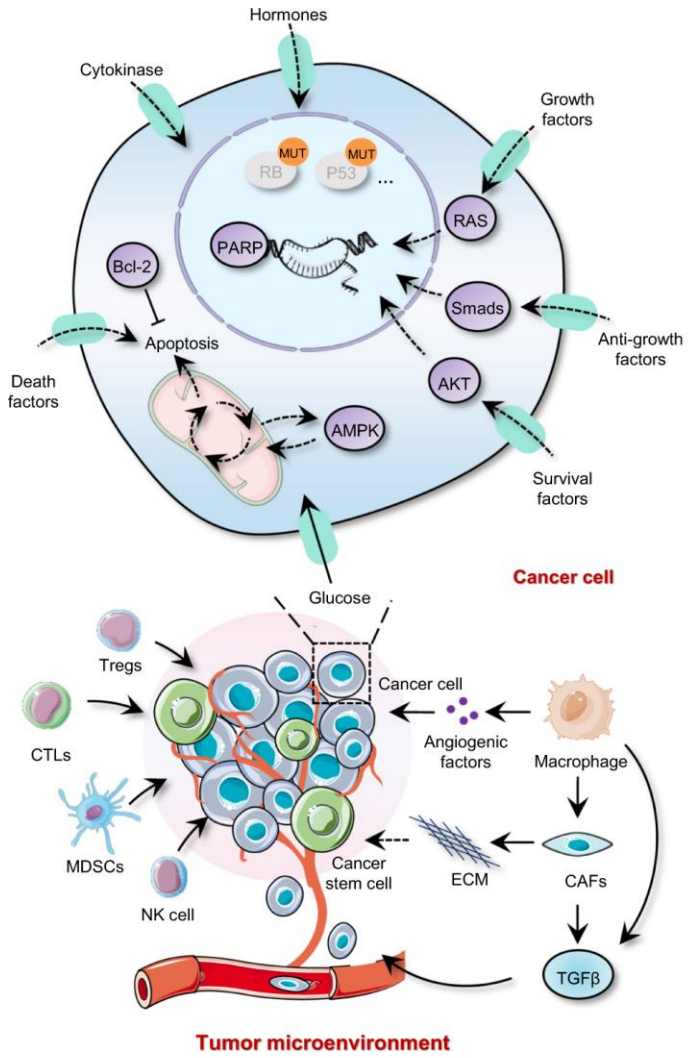
2	3739131	Radboud			Interventi	CTGOV:NC	CTGOV	Trained in		NCT02259	https://cli	scaffold	Trai	Rationale The live atten	Innate Imr	Completed	
3	4166042	London Sc			Interventi	CTGOV:NC	CTGOV	Immunity		NCT02710	https://cli	scaffold	The	The purpose of this stud	Non-targe	Completed	
4	3812354	InnaVirVa		Phase 1/P	Interventi	CTGOV:NC	CTGOV	HIV-1 HIV		NCT01549	https://cli	scaffold	Mul	The purpose of this trial	HIV-1 Infe	Completed	
5	3808578	Louisiana		Phase 3	Interventi	CTGOV:NC	CTGOV	MMR vacc		NCT04475	https://cli	scaffold	Use	The objective of this ran	Sepsis Syn	Recruiting	
6	4159996	Emory Uni			Interventi	CTGOV:NC	CTGOV	Innate imr		NCT01232	https://cli	scaffold	Syst	Vaccination is the most	Influenza	Completed	
7	4014843	Inmunotel		Phase 1/P	Interventi	CTGOV:NC	CTGOV	Trained in		NCT05208	https://cli	scaffold	A Ph	A mechanistic clinical tri	Immune R	Not yet recruiting	
8	4101854	St George			Interventi	CTGOV:NC	CTGOV	innate imr		NCT01074	https://cli	scaffold	An I	The approach we will us	Bacterial I	Completed	
9																	

Reusing strategies in the context of cancer treatment

Drug Candidates for Cancer



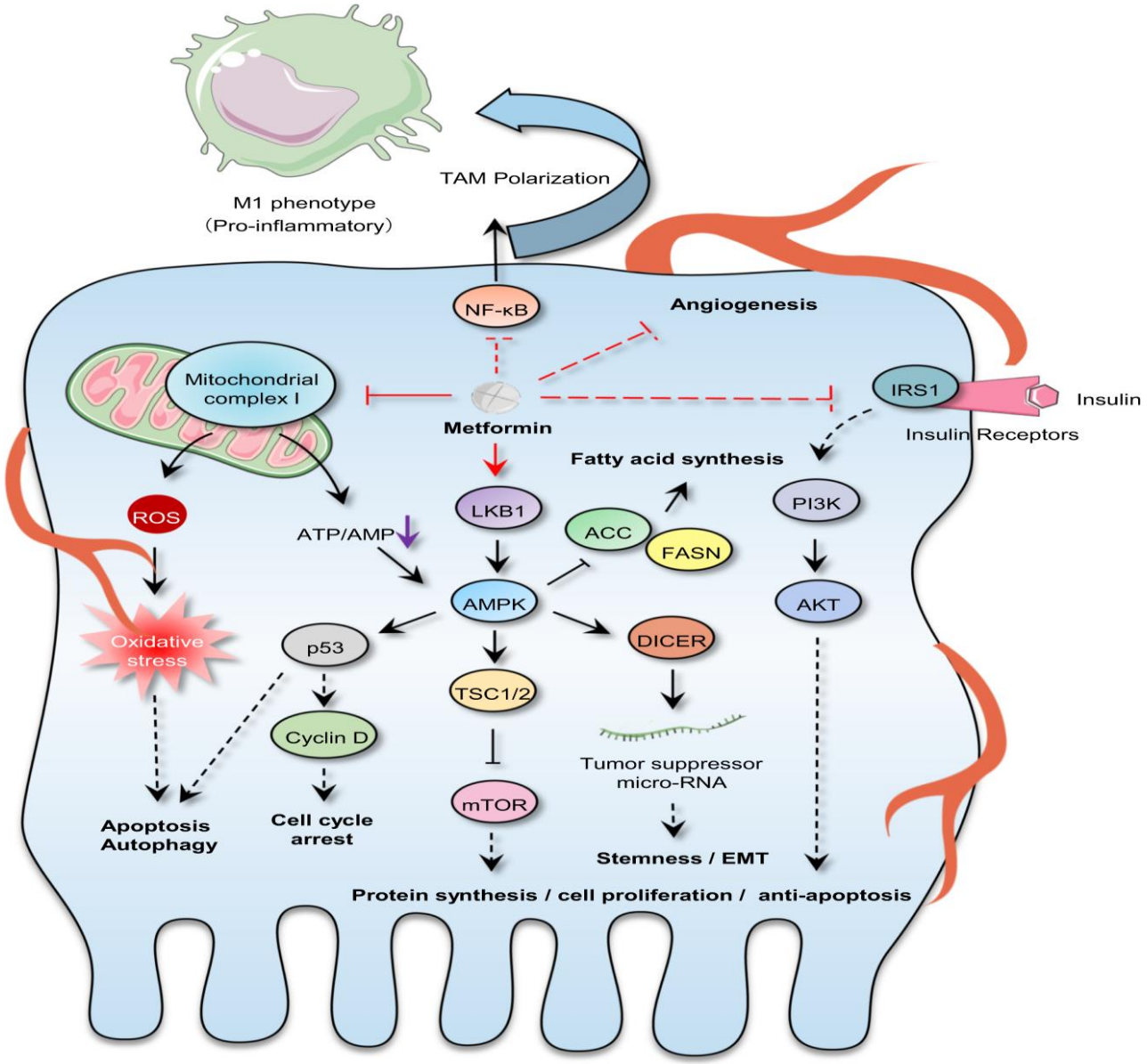
Cancer Hallmarks

- **Sustaining Proliferative Signaling (Monotherapy)**
  Rapamycin Prazosin Indomethacin
- **Evading Growth Suppressors (Combinatorial therapy)**
  Quinacrine Ritonavir
- **Resisting Cell Death (Monotherapy)**
  Artemisinin Chloroquine
- **Enabling Replicative Immortality (Combinatorial therapy)**
  Curcumin Genistein
- **Genome Instability and Mutation (Combinatorial therapy)**
  Spironolactone Mebendazole
- **Reprogramming Energy Metabolism (Monotherapy)**
  Metformin Disulfiram
- **Inducing Angiogenesis (Combinatorial therapy)**
  Thalidomide Itraconazole
- **Activating Invasion and Metastasis (Combinatorial therapy)**
  Berberine Niclosamide
- **Tumor-Promoting Inflammation (Combinatorial therapy)**
  Aspirin Thiocolchicoside
- **Evading Immune Destruction (Monotherapy)**
  Infectious disease vaccines

Identification of drug candidates targeting the hallmarks of the cancer cell using drug repurposing enabled by recapitulative signaling networks. The complex signaling interactions contributing to the hallmarks of cancer cells can be orchestrated, rationalizing the complexities of neoplastic disease. Drug candidates interfering with cancer capabilities are shown. CAFs cancer-associated fibroblasts, CTLs cytotoxic T lymphocytes, ECM extracellular matrix, MDSCs myeloid-derived suppressor cells, NK cells natural killer cells, Tregs regulatory T cells

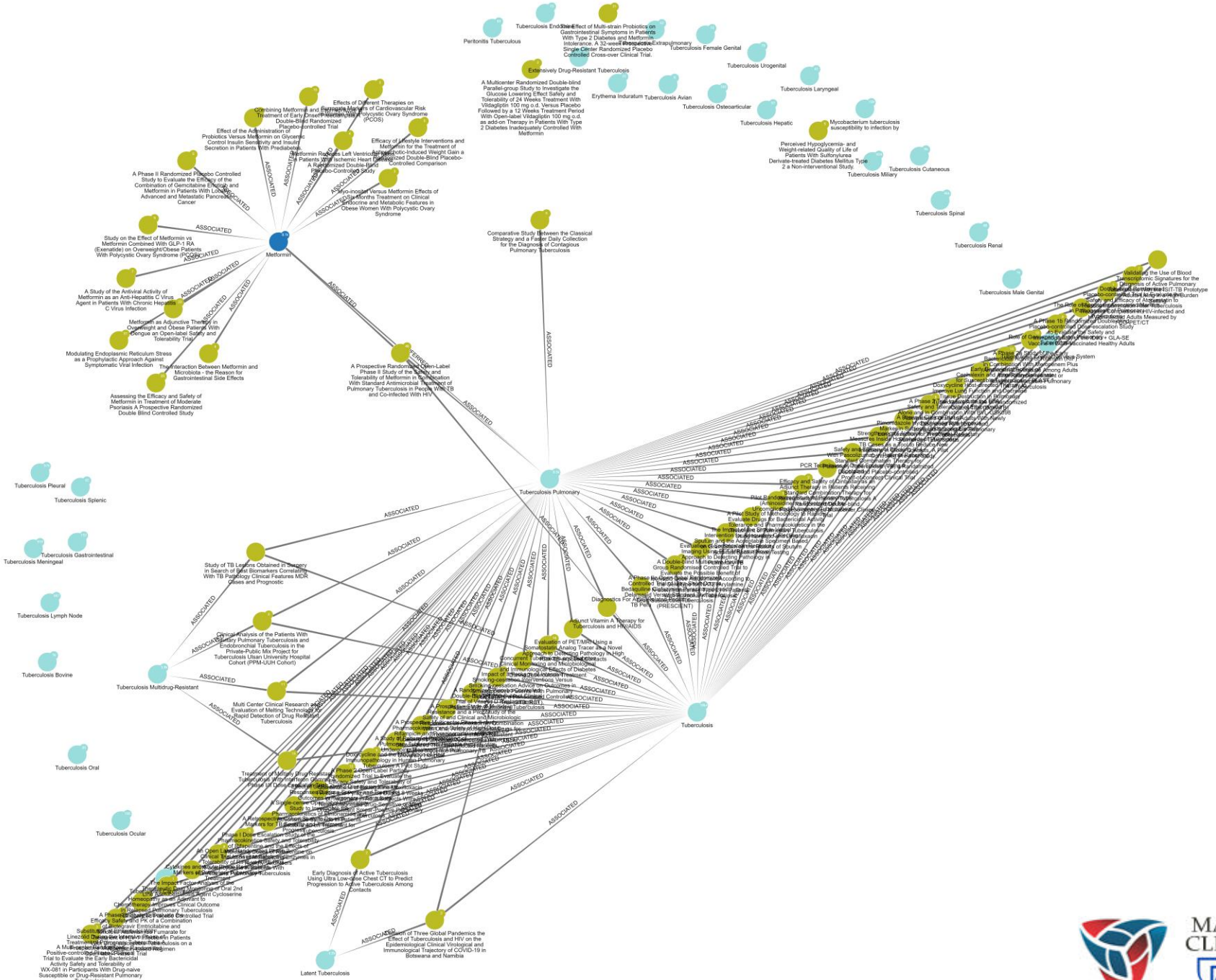
https://doi.org/10.1038/s41392-020-00213-8

Signaling pathways mediated by metformin

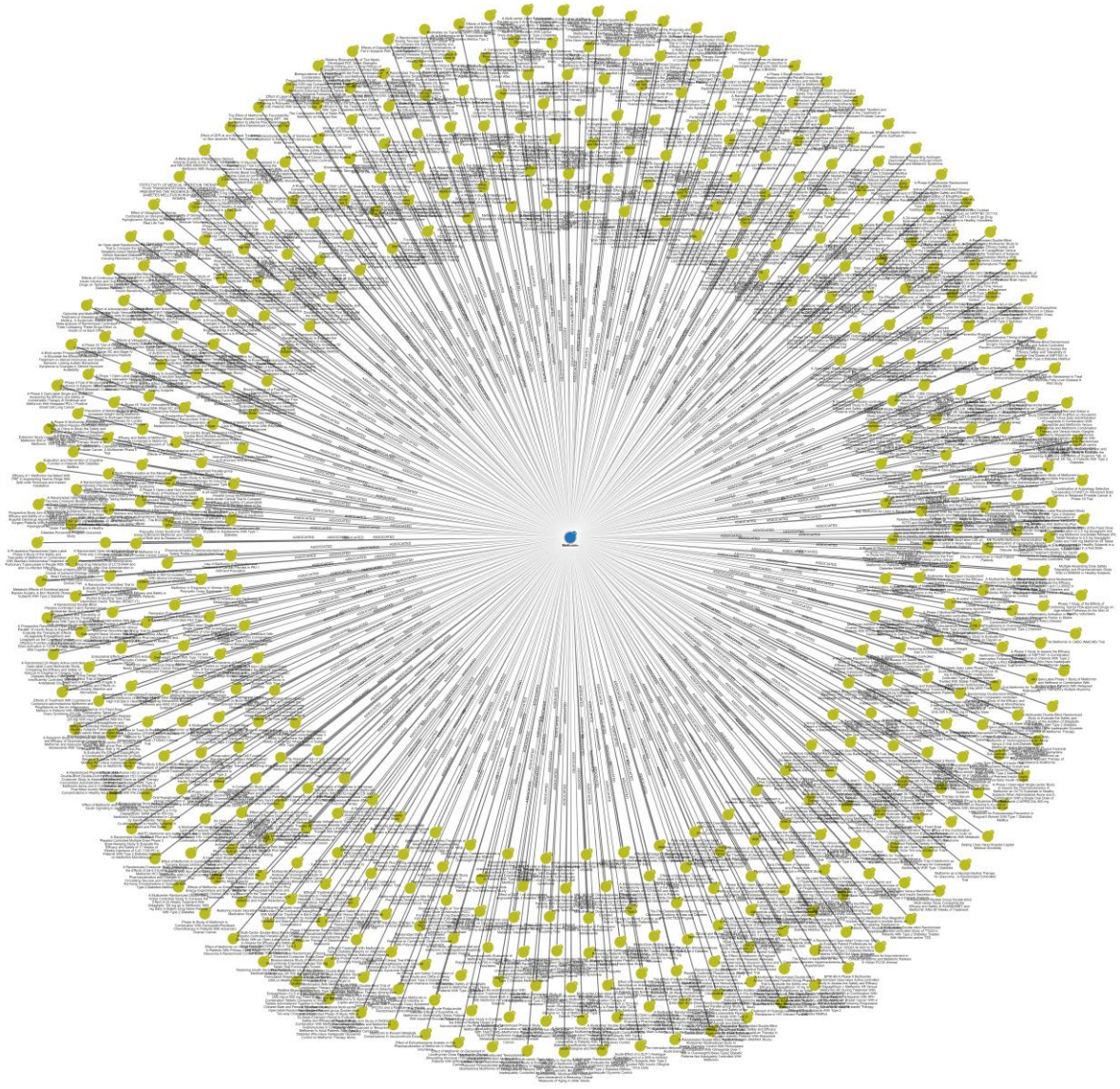


Direct or indirect protein targeting by Metformin is shown. These influences diverse hallmarks of cancer including regulating cell proliferation, self-renewal, cancer metastasis, angiogenesis and energy metabolism

Metformin as HDT



Metformin Trials



MAYO CLINIC

Metformin for Lung Cancer

4015503	University		Phase 2	Interventi	CTGOV:NC	CTGOV	Tumor Hy		NCT04170	https://cli	scaffold	Randomiz	Study the	Carcinoma	Terminated
3883816	Mayo Clin		Phase 2	Interventi	CTGOV:NC	CTGOV	Bronchosc		NCT01717	https://cli	scaffold	A Pilot Stu	The purpo	Lung Neop	Terminated
3988415	Tianjin Me		Phase 2	Interventi	CTGOV:NC	CTGOV	Sintilimab		NCT03874	https://cli	scaffold	An Open-L	Evaluate t	Non Small	Unknown status
3860799	NRG Onco		Phase 2	Interventi	CTGOV:NC	CTGOV			NCT02186	https://cli	scaffold	Randomiz	This randc	Adenosqu	Active not recruiting
3792577	M.D. Ande		Phase 2	Interventi	CTGOV:NC	CTGOV	Lung Canc		NCT02285	https://cli	scaffold	Tumor Mu	The goal o	Lung Canc	Terminated
3930591	Sidney Kin		Phase 2	Interventi	CTGOV:NC	CTGOV	Carcinoma		NCT01578	https://cli	scaffold	A Random	To determ	Carcinoma	Terminated
3852212	University		Phase 2	Interventi	CTGOV:NC	CTGOV	Lung Canc		NCT03086	https://cli	scaffold	Phase II St	This is a pl	Non Small	Completed
3930138	Ontario Cl		Phase 2	Interventi	CTGOV:NC	CTGOV	Metformir		NCT02115	https://cli	scaffold	A Phase II	ALMERA is	Lung Canc	Terminated
3936622	Beth Israe		Phase 2	Interventi	CTGOV:NC	CTGOV	non squar		NCT02019	https://cli	scaffold	Metformir	Metformir	Non-small	Terminated
4158650	National C		Phase 2	Interventi	CTGOV:NC	CTGOV			NCT04931	https://cli	scaffold	Metformir	This phase	Lung Carci	Recruiting
4057963	Fondazion		Phase 2	Interventi	CTGOV:NC	CTGOV	LKB1-inact		NCT03709	https://cli	scaffold	Exploiting	Lung aden	Advanced	Recruiting
3819855	Northwest		Phase 2	Interventi	CTGOV:NC	CTGOV			NCT03048	https://cli	scaffold	Parallel Pr	The purpo	Recurrent	Unknown status
4116728	Hunan Ca		Phase 2	Interventi	CTGOV:NC	CTGOV	immunoth		NCT03994	https://cli	scaffold	A Phase II	In this Sing	Small-cell	Unknown status
3910841	Instituto N		Phase 3	Interventi	CTGOV:NC	CTGOV			NCT05445	https://cli	scaffold	Effect of M	Lung canc	Non Small	Recruiting

Global open-source health research and development hub focused on medicinerepurposing.

Co-Founders

The US National Institute of Health's (NIH) National Center for Advancing Translational Sciences (NCATS)

The European Infrastructure for Translational Medicine (EATRIS)

Gov't of Brazil -The Oswaldo Cruz Foundation (FIOCRUZ)

Open Source Pharma Foundation (OSPF)

We aim to make it possible for anyone in the world to access our expertise and resources and enable drug repurposing efforts.

www.newfoundmed.org

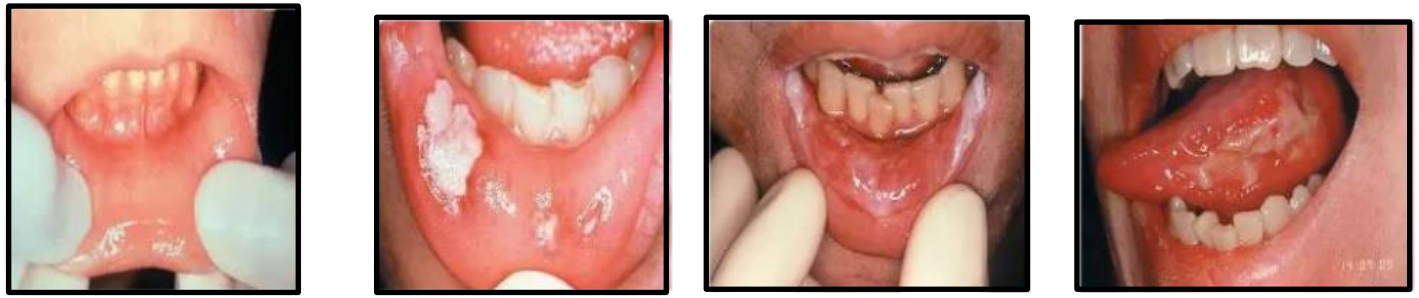
Supportive & Complementary therapies for management of adverse effects of Cancer treatment and improvement of quality of life

Challenges associated with OM

- Oral mucositis develops in 42% of the patients treated with high dose chemotherapy
- 90% of patients treated with head and neck irradiation
- Short-term and Long-Term Complications

WHO oral toxicity scale

Grade 1	Grade 2	Grade 3	Grade 4
Soreness ± erythema	Erythema, ulcers; patient can swallow solid food	Ulcers with extensive erythema; patient cannot swallow food	Mucositis to the extent that alimentation is not possible



Specific Local and Internal Treatments for Oral Mucositis

Gandoosha (Gargles)	sapthachadadi kashayam gandoosha	AHU 22/103
Ghritha (Ghee preparations)	panchatiktha ghritha shatavari ghrita	rasa Ratnakar sahasra yoga
Guggulu (resins)	saptavimshati guggulu triphala guggulu	AFI sharangdhar samhitha
Bhasma (Nano Hero-bo-minerals)	swarna makshika bhasma- sphatika bhasma -	rasa tarangini 21/19-20 ayurveda sara sangraha
Vati (Tablets)	pravala panchamrita- kamadugha mauktika-	bharat bhaishajya Ratnakar bhashajya ratnavali
Choornam (Powders)	Yastimadhu	Sushrutha samhitha

सप्तच्छदोशीरपटोलमुस्त-हरीतकीतिक्तकरोहिणीभिः|
यष्ट्याह्वराजद्रुमचन्दनैश्चक्काथं पिबेत्पाकहरं मुखस्||१०३||

AHU 22/103

Alsotnia scolaris

SUMMARY

Repurposing offers a potential solution to the challenges of availability and access of therapeutics in low and middle income countries.

By leveraging existing drugs and vaccines and their infrastructure, repurposing can expedite the availability of therapeutics and improve accessibility, potentially saving lives in resource-constrained settings.

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OpenVax: OSPF Scientific Advisory Committee

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Co-founder, Global Virus Network; Co-Discoverer, HIV; has been most widely referenced scientist in the world.

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Venture Partner, Frazier Health Care Partners
Former Chair of R&D, GlaxoSmithKline
Former President, Global Health, Bill and Melinda Gates Foundation (managed $9B budget)

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Bernard Munos, MBA
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Available
Accessible
Affordable

Thank You


Available
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