Bolstering local innovative drug discovery capabilities for pandemic preparedness: The Holistic Drug Discovery and Development(H3D) Centre in South Africa

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H3D

Founded in 2010 as an accredited research centre within the University of Cape Town

Vision: To be a leading organisation for integrated drug discovery and development

Mission

- Discover and develop innovative, life saving medicines for infectious diseases
- Building Africa-specific models to contribute to improving treatment outcomes in African patients
- Developing drug discovery platform technologies
- Training African scientists in drug discovery-related sciences

J&J Satellite Center for Global Health Discovery @H3D

Provides scientific & translational expertise and seed investment

Provides access to world class scientific talent, infrastructure & research ecosystem

Other Contributors

e.g. academic partners, government bodies, funding agencies, etc.

Focus Area: Antimicrobial Resistance, aiming to develop first in class MDR Gram-Negative therapeutics

J&J Centers for Global Health Discovery

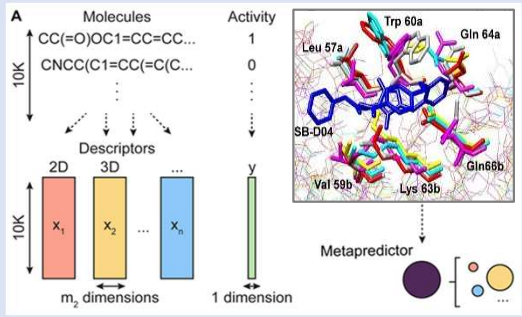
H3D Centre technology platforms

H3D
PIONEERING WORLD-CLASS DRUG DISCOVERY IN AFRICA

Faculty of Science	Faculty of Health Sciences

Medicinal chemistry

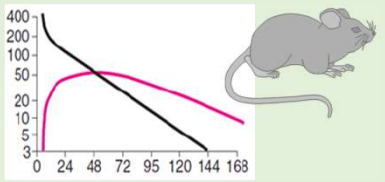
CADD, AI and ML



DMPK

In vitro ADME
Physicochemical, metabolism and binding assays

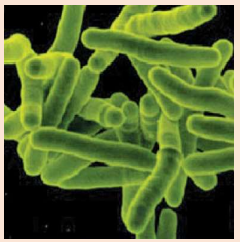
In vivo PK



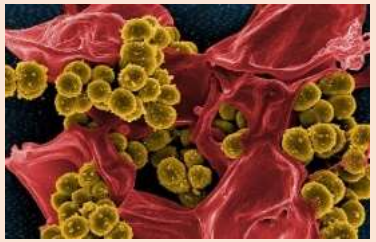
Biology

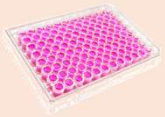
Malaria biology
(*in vitro* and *in vivo*)

TB biology



AMR screening





Cytotoxicity cross-screening

Enzymology

Data storage and sample management

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H3D Funding Partnerships & Scientific Programmes: 2022

Funders

Bill & Melinda Gates foundation; MMV Medicines for Malaria Venture; NIH; technology innovation agency; saMRC advancinglife; Neville Isdell; Merck; Johnson & Johnson; Newton Fund; science & innovation Department: Science and Innovation Republic of South Africa; NRF National Research Foundation

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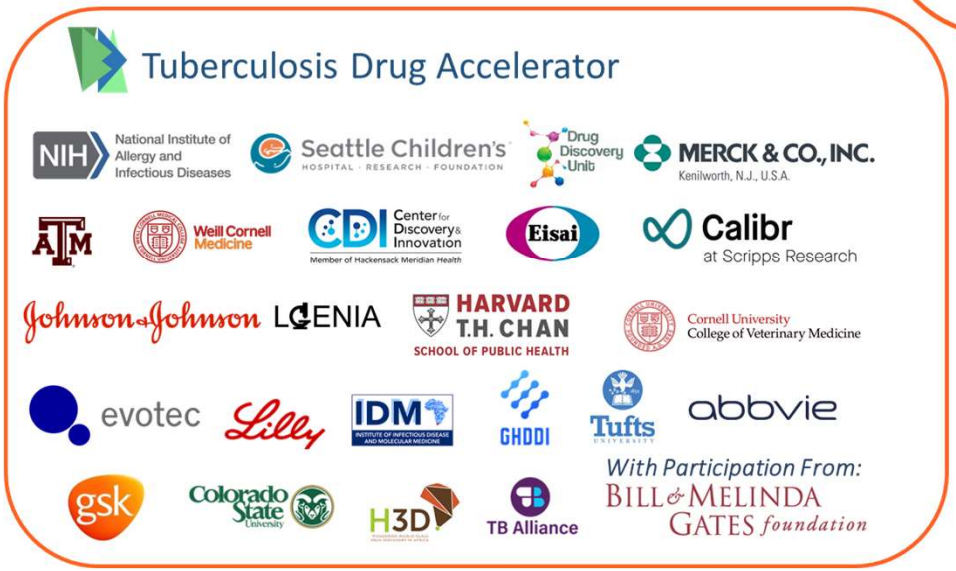
KC

Malaria Programme	TB Programme	AMR Programme	COVID Programme	Technology Platforms	KC Academic Group
H3D **Malaria** project portfolio consisting of hit-to-lead, lead optimization, late lead optimization, preclinical, clinical and formulation projects	H3D **Tuberculosis** (TB) project portfolio consisting of hit-to-lead and lead optimization projects	H3D **Antimicrobial Resistance** (AMR) portfolio consisting of hit-validation and hit-to-lead optimization projects	H3D **COVID** programme is a target based programme at the hit validation stage and is supported with machine learning models	H3D **Technology Platforms** including DMPK and biology platforms	**Kelly Chibale (KC) Academic Group** focusses on drug discovery (use)-inspired basic science research

H3D Research Partners: 2022

- H3D has active collaborations with industry, product development partners and academia
- H3D is a full member of the BMGF supported Tuberculosis Drug Accelerator (TBDA) and the Malaria Drug Accelerator (MalDA)



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DRUG DISCOVERY IN AFRICA

Antiviral drug discovery & South-South Collaborations

BRICS STI Framework Programme 2020

COVID-AI

In silico assays

FDA-approved drugs and NIH clinical collection

Libraries of synthetic compounds and natural products

University of Cape Town, South Africa

Virtual screening **2**

1 Machine learning models (SARS-Cov-2 phenotypic, DHODH, proteases, ADME/Tox)

Bioassay data (literature)

Selected virtual hits

3 **Target-based assays**

Human DHODH

Proteases

Spike

Protein cloning, expression, purification and assay development

1 Shape-based models and molecular docking with spike-ACE2, proteases Mpro, PLpro, and human DHODH

Drug discovery and Repurposing

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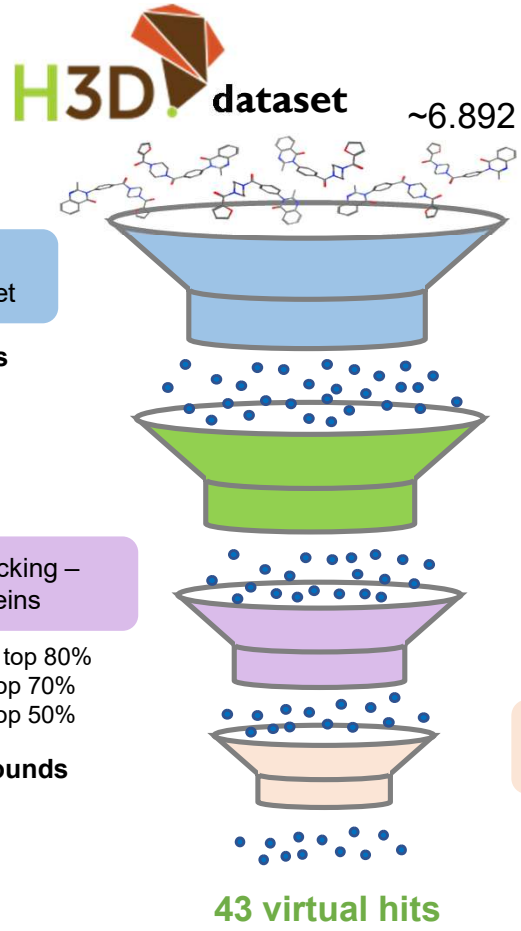
Virtual Screening: SARS-CoV-2 Mpro



- Mpro virtual hits:
  - 37 of the 43 compounds were available, covering 16 of the 18 identified clusters

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Bill & Melinda Gates foundation
Merck
The Royal Society
technology innovation agency
MMV Medicines for Malaria Venture
Novartis
GCRF Global Challenges Research Fund
saMRC advancinglife
Newton Fund
Celgene
The Wolfson Foundation
NRF National Research Foundation
NIH National Institutes of Health
Merck & Co., Inc. Kenilworth, N.J., U.S.A.
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Neville Isdell
Johnson & Johnson
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