Information and Networking Event
Horizon Europe 2023 Calls
Co-Funded by the Government of India (DBT)

HORIZON-HLTH-2024-DISEASE-08-20: Pandemic preparedness and response: Host-pathogen interactions of infectious diseases with epidemic potential

Friday, 13 October 2023

- TITLE of talk: Host-targeted therapeutics for infectious diseases with epidemic potential.
- Name of Presenter: Prof. Amit Awasthi
- Name of contributors: Dr. Supratik Das, Dr. Zaigham Abbas Rizvi, Dr. Tanvi Agarwal
- Name of Organisation: Translational Health Science & Technology Institute (THSTI)
- Country: India
- Your contact details: Email: aawasthi@thsti.res.in
- Your web url: https://thsti.res.in/en/faculty-profile/Amit-Awasthi

Project Overall

Title: Host-targeted therapeutics for infectious diseases with epidemic potential.

Objectives:

1. Characterization of host-factor driving the entry, replication and pathogenesis of DENV and CHIKV infection.
2. Integrated approaches for improved host-directed therapy and adjuvants.
3. Advanced pre-clinical platform for *in-vitro* and *in-vivo* validation.

Project Coordinator: Prof. Amit Awasthi

PI: Prof. Amit Awasthi, Dr. Supratik Das, Dr. Zaigham Abbas Rizvi, Dr. Tanvi Agarwal

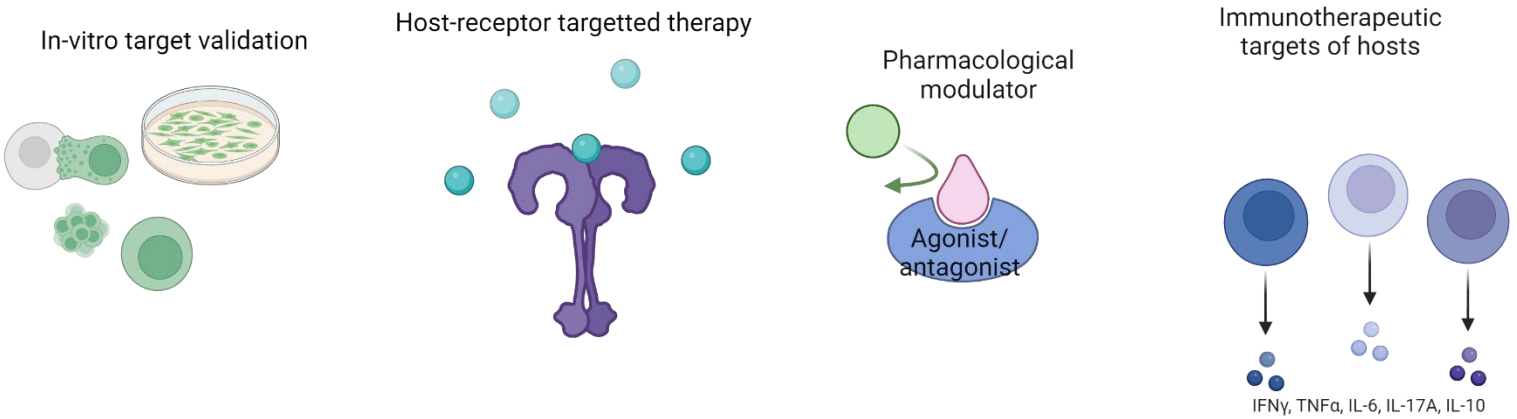
Project 1

Title: Development and validation of novel host-directed therapy.

Objectives:

1. Screening, identification and characterization of novel host-directed therapy for CHIKV and DENV infection.

2. Next-gen adjuvants for existing vaccine candidates.



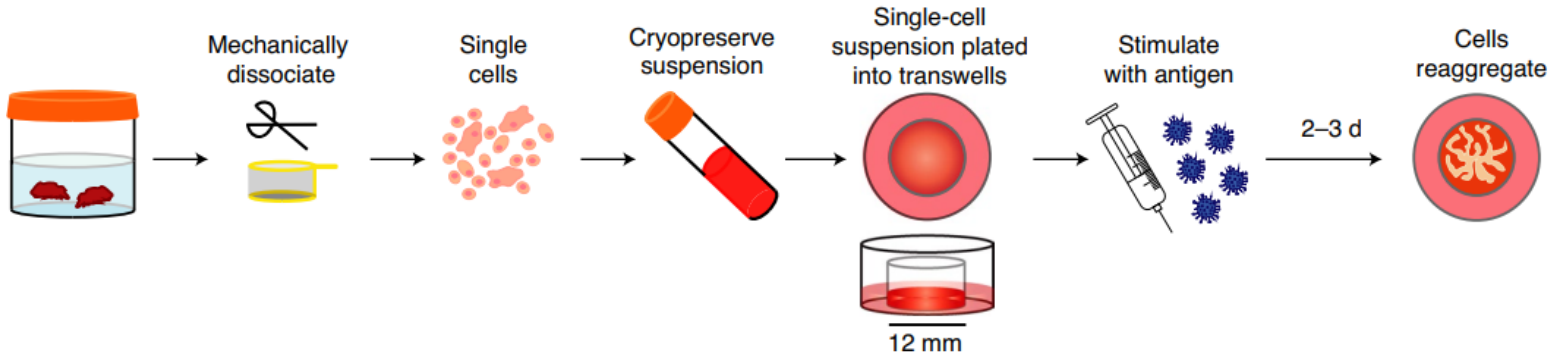
Project 2

Title: Establishment of advanced pre-clinical animal platform for CHIKV and DENV infection for translational research.

Objectives:

a. Humanized mice model for host-pathogen interaction.

b. Development and harmonization of human Immune organoid system.

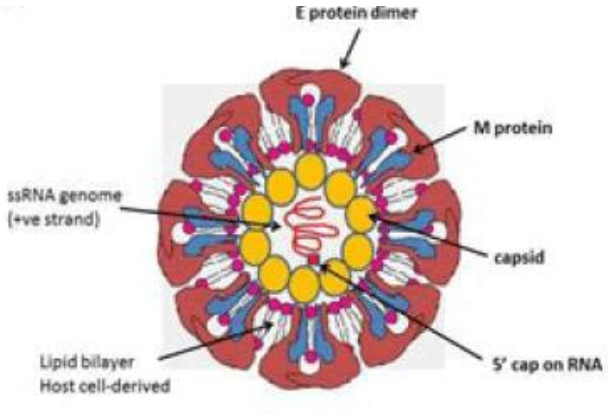


Vaccine Candidates and Host-Pathogen Interaction in DENV/CHIKV

A) To provide protein-based platform for subunit vaccine immunogen design for infectious diseases.

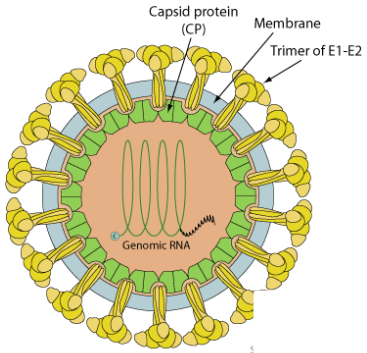
B) Understand host-pathogen interaction in order to identify drug targets.

A



Dengue

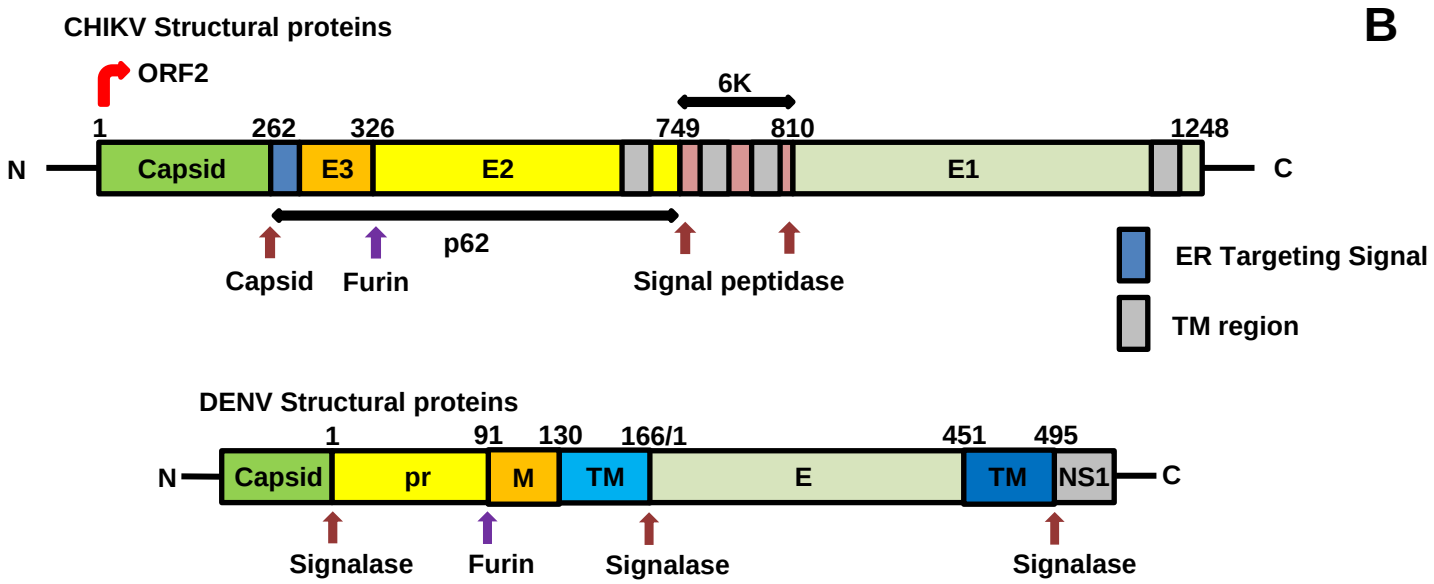
B



CHIKV

Generation of Vaccine Candidate Against Chikungunya Virus (CHIKV) and Dengue virus (DENV)

Background: CHIKV and DENV envelope protein spike is the sole target of desirable neutralizing antibodies.



Aim: To prepare CHIKV-sE1-sE2-E3 protein trimer and DENV1-4 sE dimer for use as a vaccine candidate.

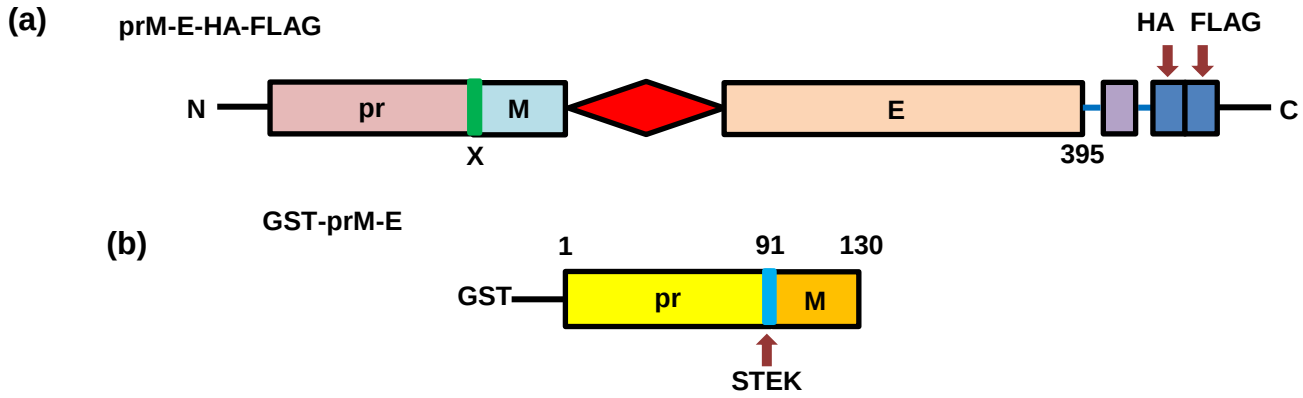
Results:

- Purified CHIKV sE1-sE2-E3 protein trimer to apparent homogeneity.
- Purified DENV3, DENV4 sE dimers to apparent homogeneity.
- Biochemical and antigenic characterization of CHIKV trimer and DENV3, DENV4 dimers completed.
- Structural characterization ongoing.
- Immunogenicity studies of CHIKV sE1-sE2-E3 timer in mice completed. Potent humoral and cell mediated immunity obtained.
- Purification and characterization of DENV1, DENV2 sE dimers ongoing.

Identifying Dengue virus (DENV) Structural Protein Interacting Host-Proteins

Background: DENV non-capsid structural protein interacting host proteins are not known. These interactions may be potent targets for therapeutic intervention.

Constructs used



Aim: To identify and characterize DENV non-capsid structural protein interacting host proteins.

Results:

- Initial constructs have been generated and characterized.

Identification and characterization of host receptors for Chikungunya virus for targeted drug designing

A) To identify and characterise host cell receptors interacting with envelope or capsid protein of Chikungunya virus.

B) To design and validate drug against identified host receptors.

Background:

Host receptors involved in entry of Chikungunya virus and not clearly defined. As no antiviral is available for Chikungunya identification and characterization of these receptors can serve as targets for designing better antiviral strategy.

Work Plan:

1. To identify and characterise host cell receptors interacting with envelope or capsid protein of Chikungunya virus.
   a) Identification of host receptors – Tagged construct of structural proteins will be used to pull interacting proteins which are identified by Mass Spectrometry.
   b) Identified receptors will be characterised across a repertoire of cells through either loss of function or blockage of receptors.

2 To design and validate drug(s) against identified host receptors both *in vivo* and *in vitro*.

Tanvi Agarwal

Available Infrastructure/Facility

Small Animal Facility

Established in 2013 at NCR-Biotech Science Cluster, CPSEA accredited (1685/GO/REBI/S/2013/CPCSEA)

Capacity

Mice
- 15 IVCs
- 2736 Cages
- 8000-13000 Mice

Rats
- 3 IVCs
- 390 Cages
- 1000-1500 Rats

3 Inbred mice strains
29 Mutant mice strains
1 Hybrid mice strain

Infectious Disease Research Facility

Established in 2018 at NCR-Biotech Science Cluster, RCGM accredited

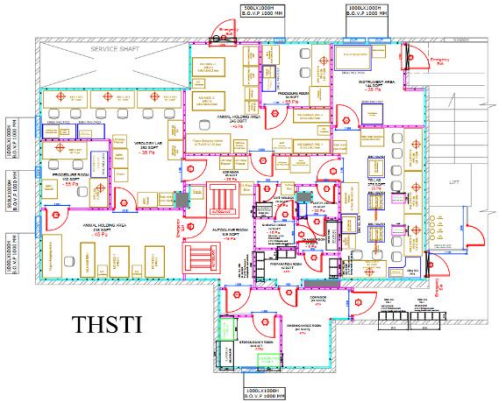
SARS-CoV2 in vitro and in vivo research
Mycobacterium tuberculosis research
HIV research

Immunology Core

Established in 2020 at THSTI

Infectious disease research
SARS-CoV2 pre-clinical and clinical trials

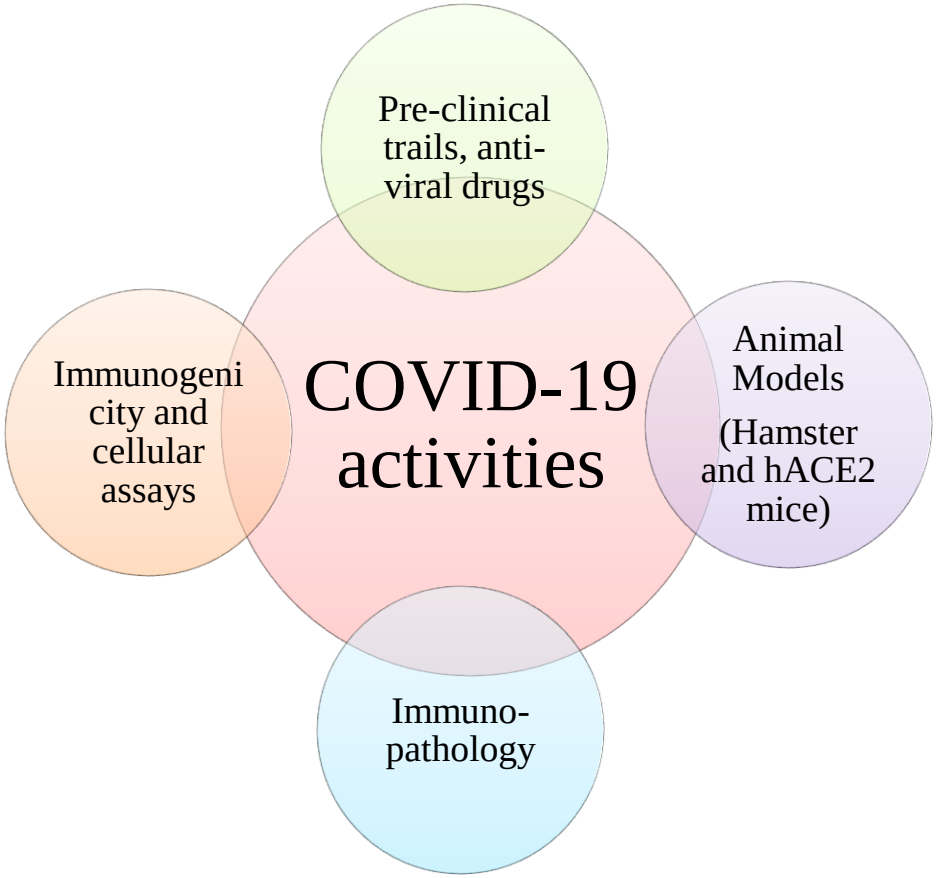
New Bsl3 facility has been commissioned and functional.



THSTI

Capacity in Vaccine Research

- Support to vaccine development
- Indigenous vaccine development
- Training and capacity building



Sub-unit vaccine candidate

Worlds first COVID-19 DNA-vaccine candidate developed by Zydus Cadila

WARM COVID-19 vaccine developed by Mynvax

Developed by Bharat Biotech

Reliance Life Sciences, Permas Biotech

USD 12.5 million Grant

CEPI, THSTI and Panacea Biotec partner to develop broadly protective Betacoronavirus vaccines

thsti

INFLUENZA VIRUS REASERCH

MANDATE

A translational research platform to accelerate the development of broadly effective and low-cost Influenza vaccines and therapeutics

Four major thematic areas

Well characterized virus repository and reagents

Influenza A and B viruses, soluble antigens, inactivated virus,

Next generation vaccine development

Indigenous Influenza M2e and HA monomer based vaccine development in mammalian culture

Pre-clinical animal model

INDIA's first ferret facility to facilitate next generation vaccine development

Virus pathogenesis and Immunobiology

Reverse genetics system to study mutational landscape, host-immune response

Horizon 2020 (DBT-EU program)
Initiated on: Jan 2021

EndFlu

INDIGO
Affordable Flu Vaccines

INCENTIVE

What we are looking for in collaborators.

a) We are looking for collaborators who have existing or are developing or are interested in developing non-mice animal models (including non-human primates) which can be used to test CHIKV and DENV vaccine candidates.

b) We are looking for collaborators who are interested in dynamics of host receptor – ligand interaction.

c) Potential collaborators to take PoC drug and vaccine targets for NHP trials.

d) Potential collaborators who are interested in pre-clinical trials of putative drug candidates.

Golden Syrian Hamster

Ferret

Industrial Partner

SII
SERUM INSTITUTE OF INDIA

Rhesus Macaque