



# MOLDEMORT

A Genetically Engineered Chimeric Antifungal  
against Invasive Fungal Infections (IFIs)





## Beginning iGEM at IISER TVM



## Observing the Problem



Collection of various fungal samples present on damp walls

Culturing fungi on slant PDA (Potato Dextrose Agar) and sequencing them to identify their genera

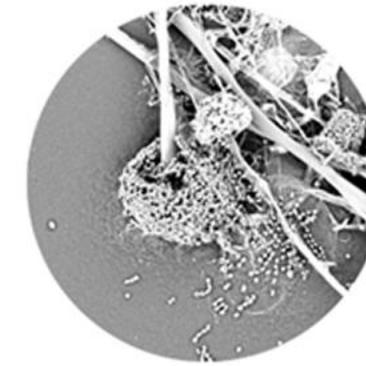




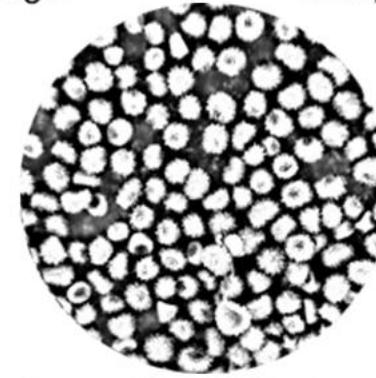
## Fungal identification within campus



*Aspergillus niger*

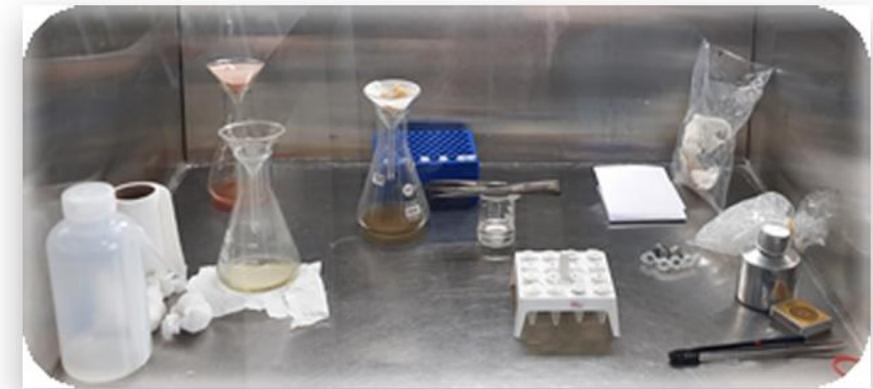
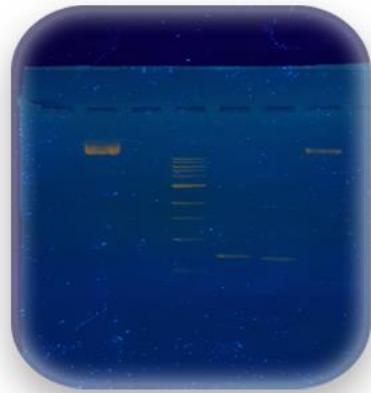
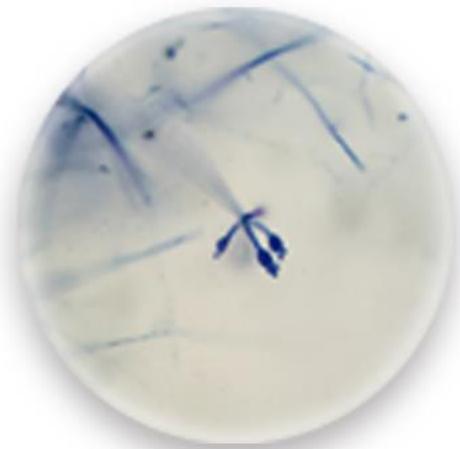


*Rhizopus oryzae*



*Aspergillus versicolor*





# Fungal Infestation in Various Settings

- Fungal infestation in various settings exposes the residents to various **harmful toxins** and **spores**.
- The **unregulated use of fungicides** can jeopardise public health and environment causing biomagnification.



Hospitals



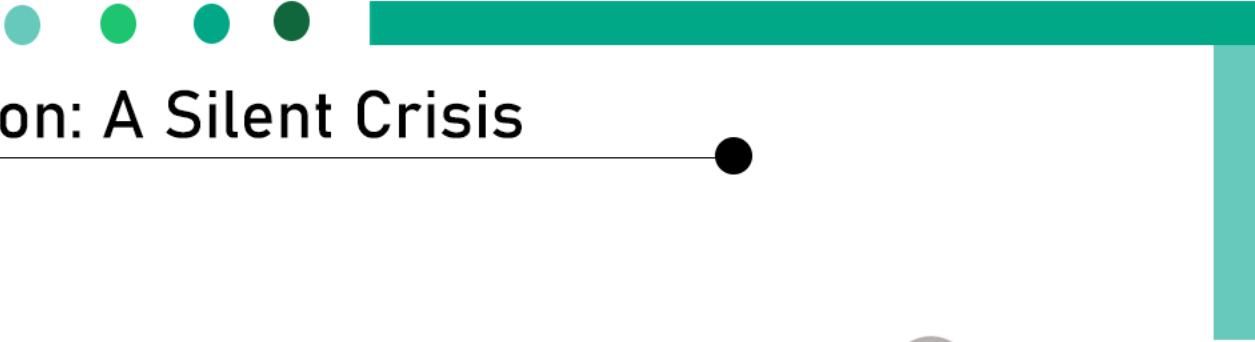
Industry



Homes



Agriculture



# Fungal Infection: A Silent Crisis



150 M cases reported annually



1.7 M deaths reported annually

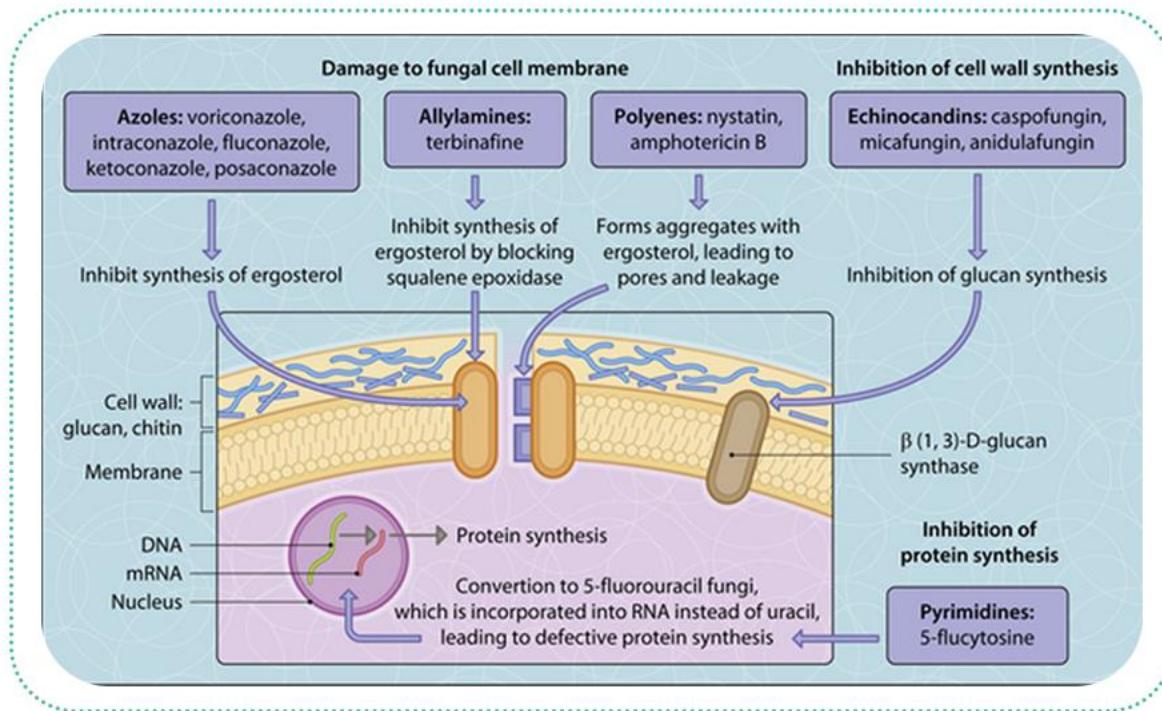
3 M cases of chronic  
pulmonary  
Aspergillosis

223,000 cases  
of  
cryptococcal  
menangitis

700,000 cases of  
invasive  
candidiasis

500,000 cases of  
*Pneumocystis*  
*jirovecii*  
pneumonia

# Current Antifungal Treatments



Emergence of (multi)drug-resistant fungi

Side effects of current antifungals (nephrotoxicity)

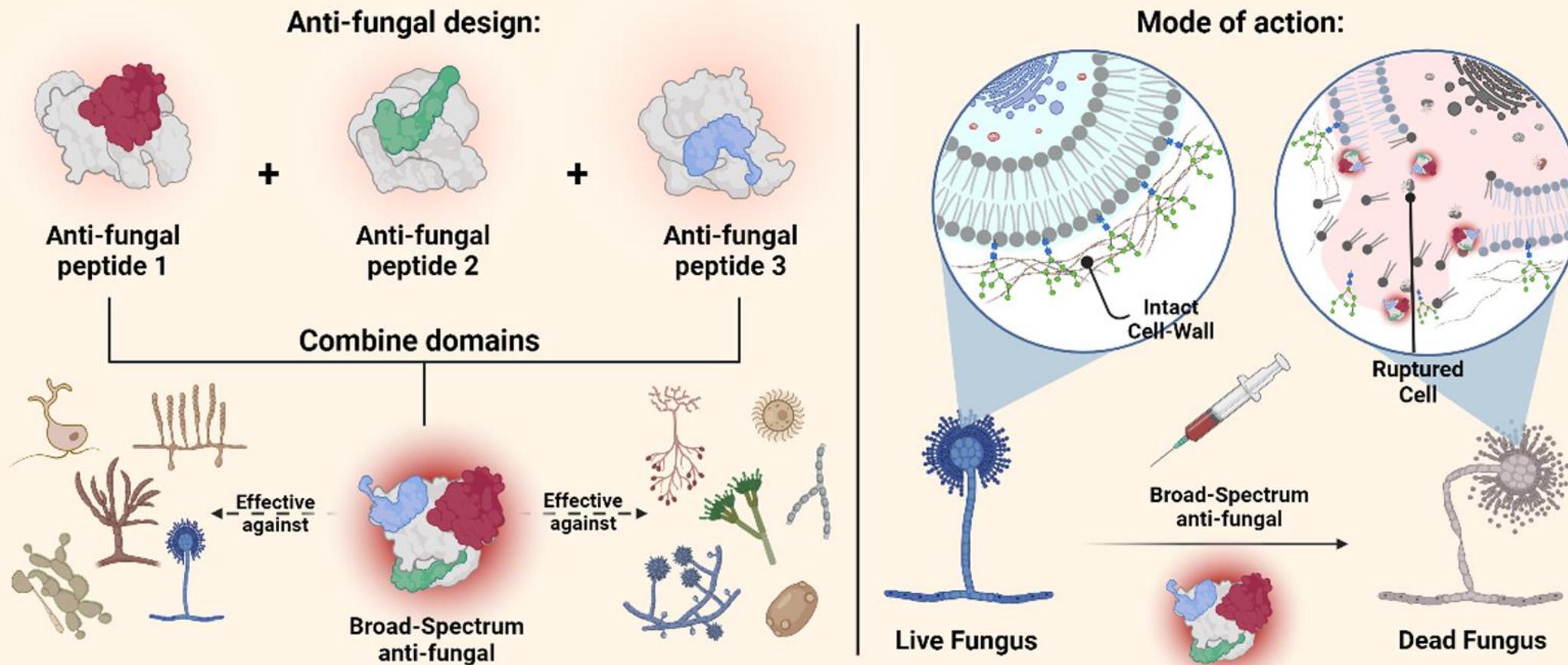
Limited repertoire of antifungals

Sold at high prices

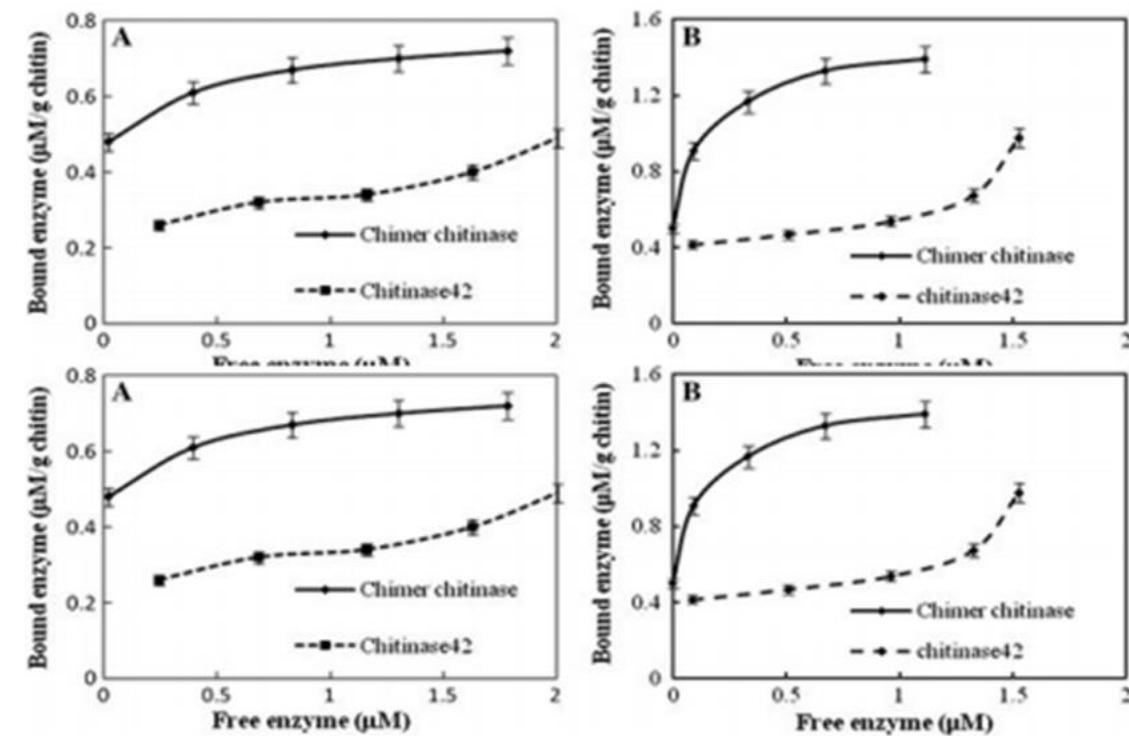
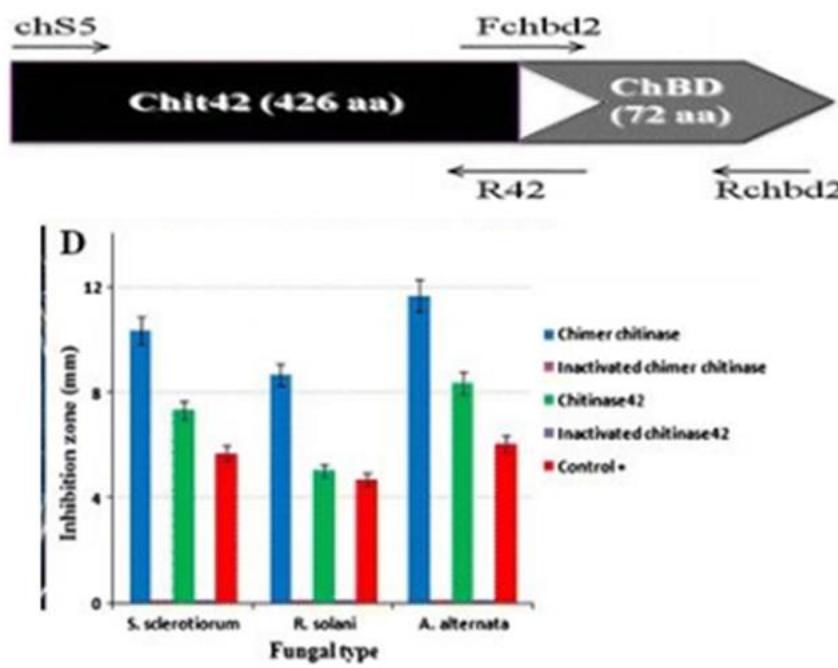
Most of the common antifungals work towards binding/inhibiting ergosterol formation

# Our Solution : Chitinases !

## Development of a broad spectrum anti-fungal against Invasive Fungal Infections(IFI)



# Chimeric Chitinase exhibit higher chitinase activity





## Designing Our Chimeric Chitinases



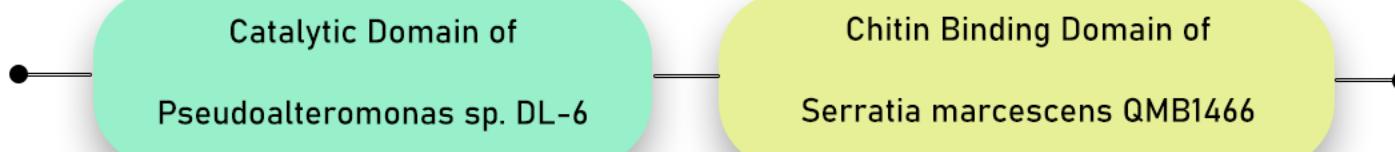


# Putative Broad Spectrum Chitinases



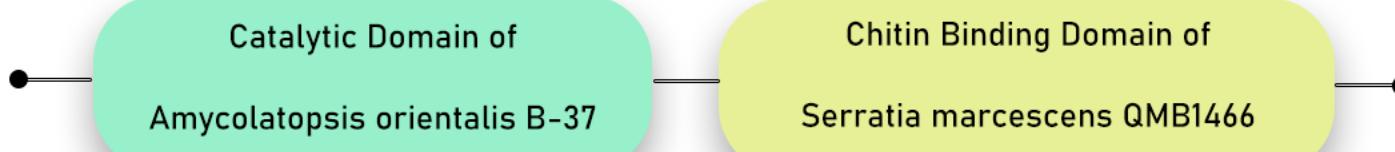
Bacterial combo I

(54.44 kDa)

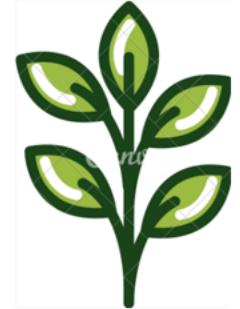


Bacterial Combo II

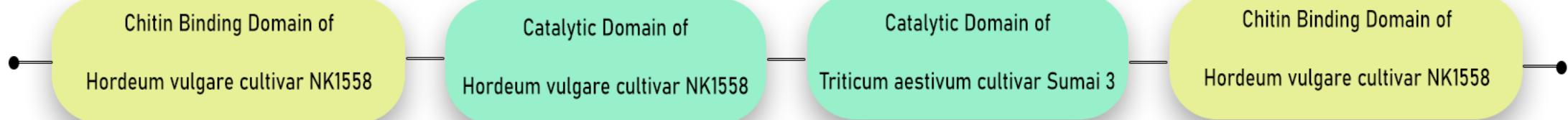
(39.72 kDa)



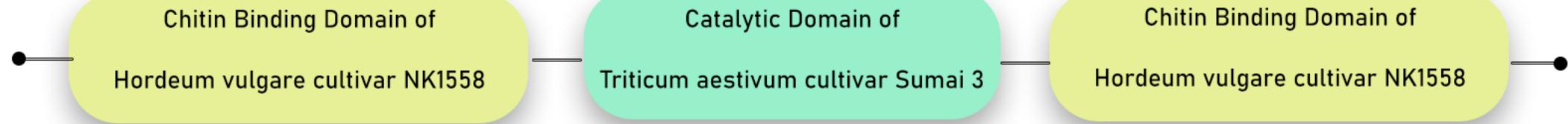
# Putative Broad Spectrum Chitinases



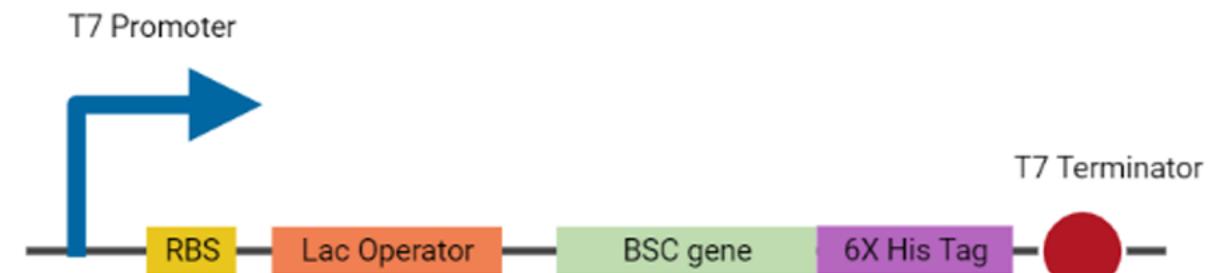
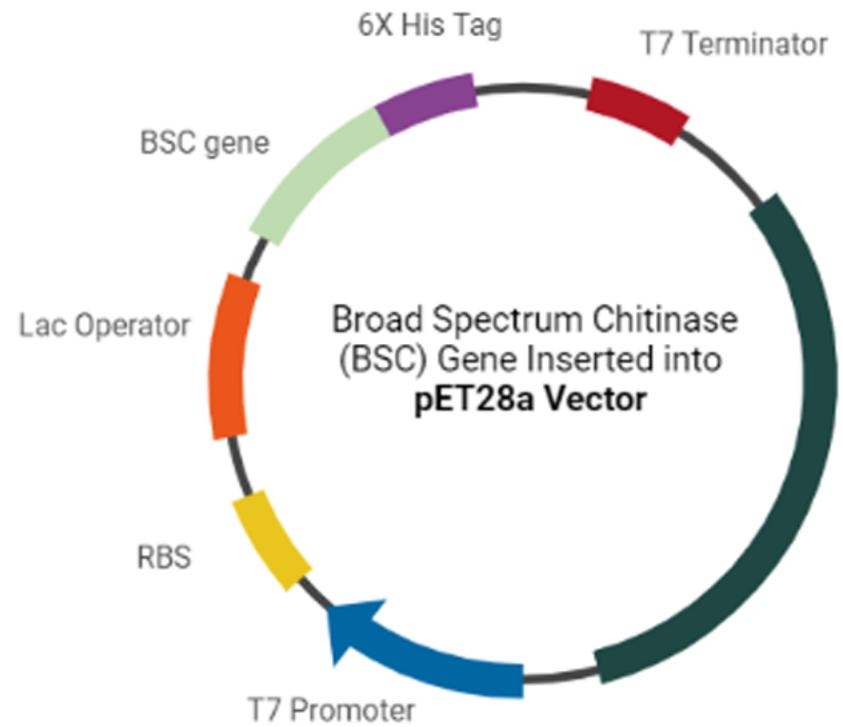
Plant combo I  
(69.63 kDa)



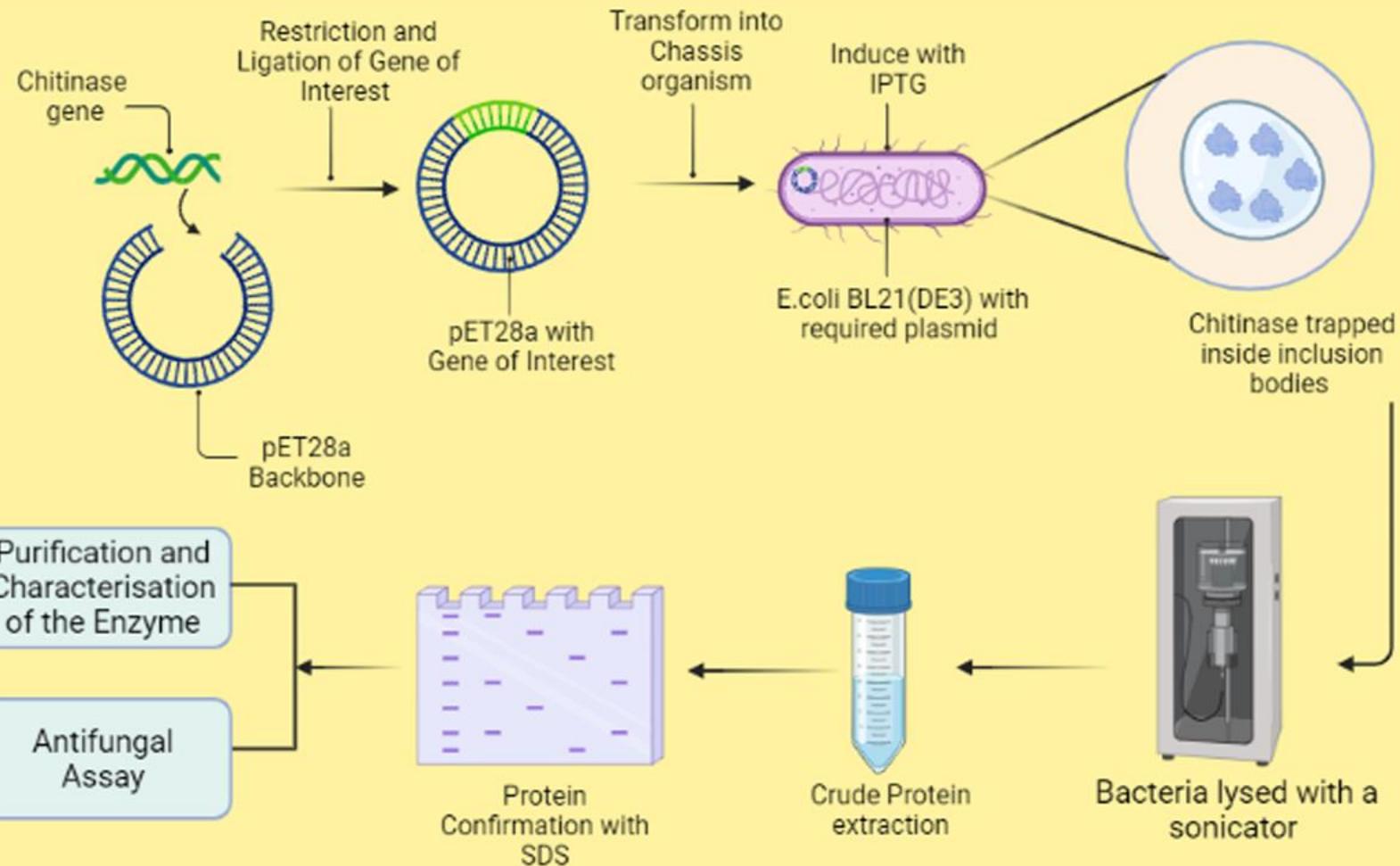
Plant combo II  
(32.38 kDa)



# Our Broad Spectrum Chitinase Construct



# Experimental Setup





## Project Modelling



# Growth Curve

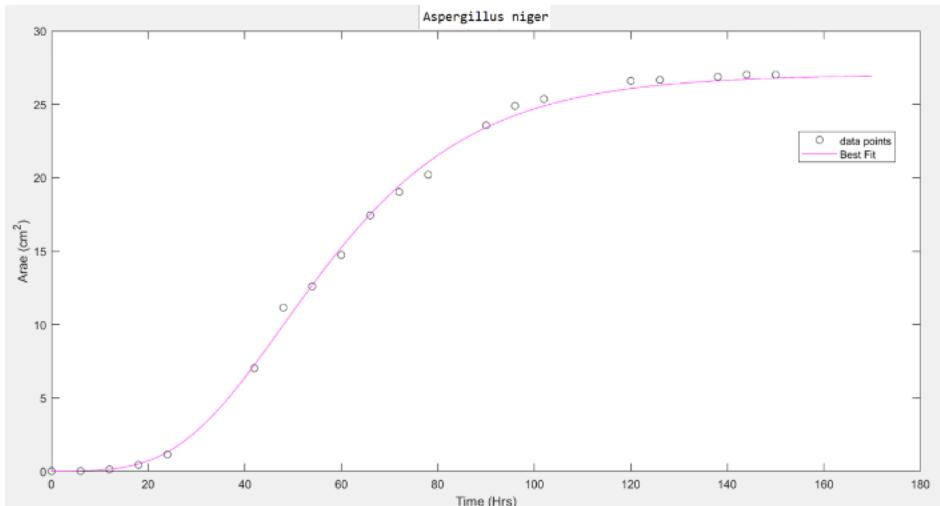


Fig.1: *Aspergillus niger*  
(Area vs Time)

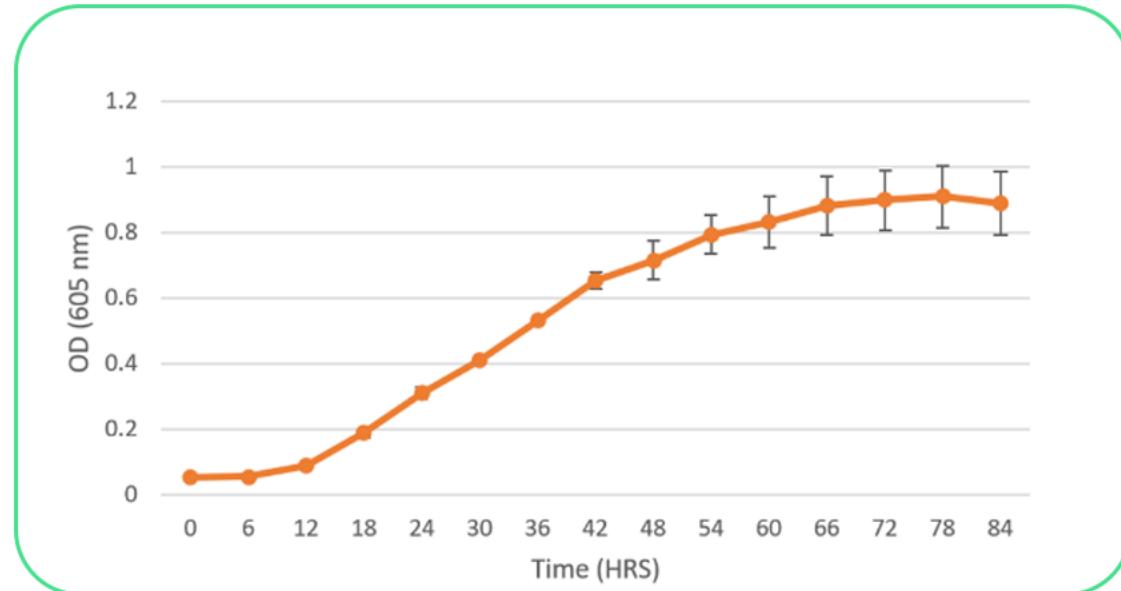


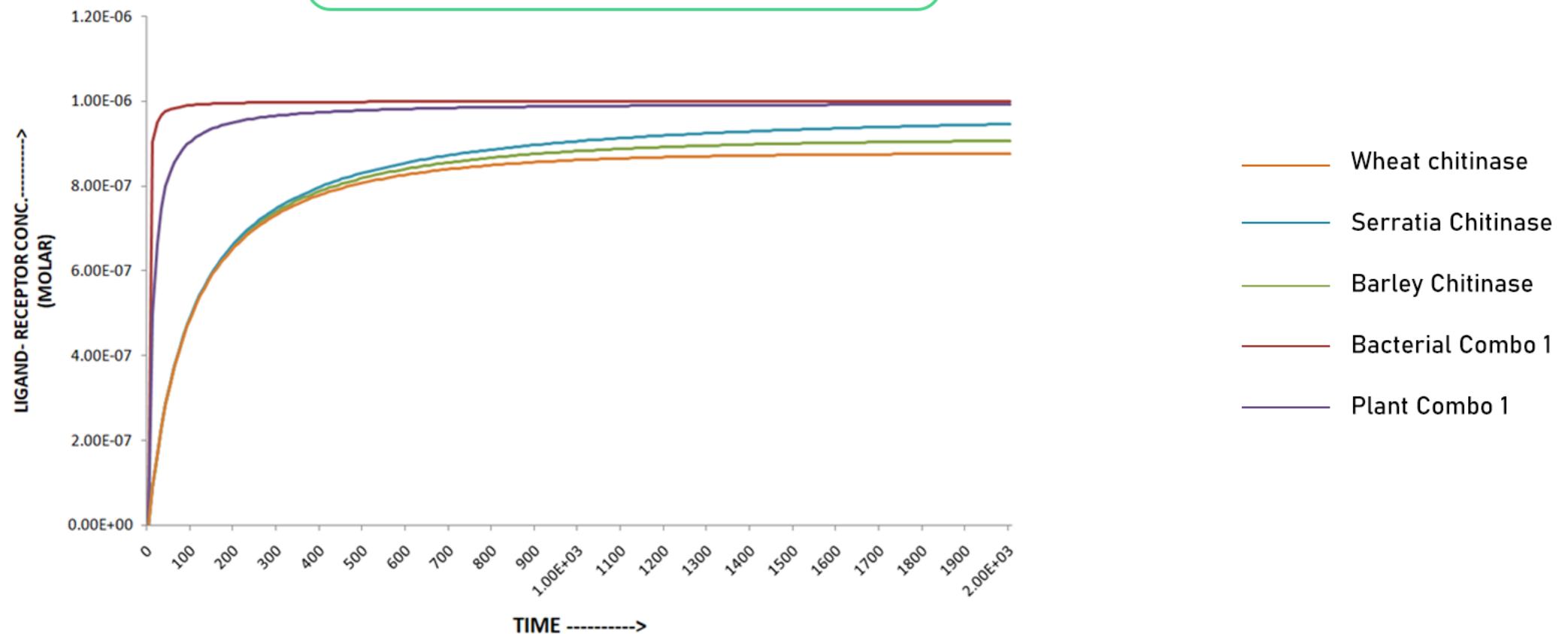
Fig.2: *Aspergillus versicolor*  
(OD vs Time)

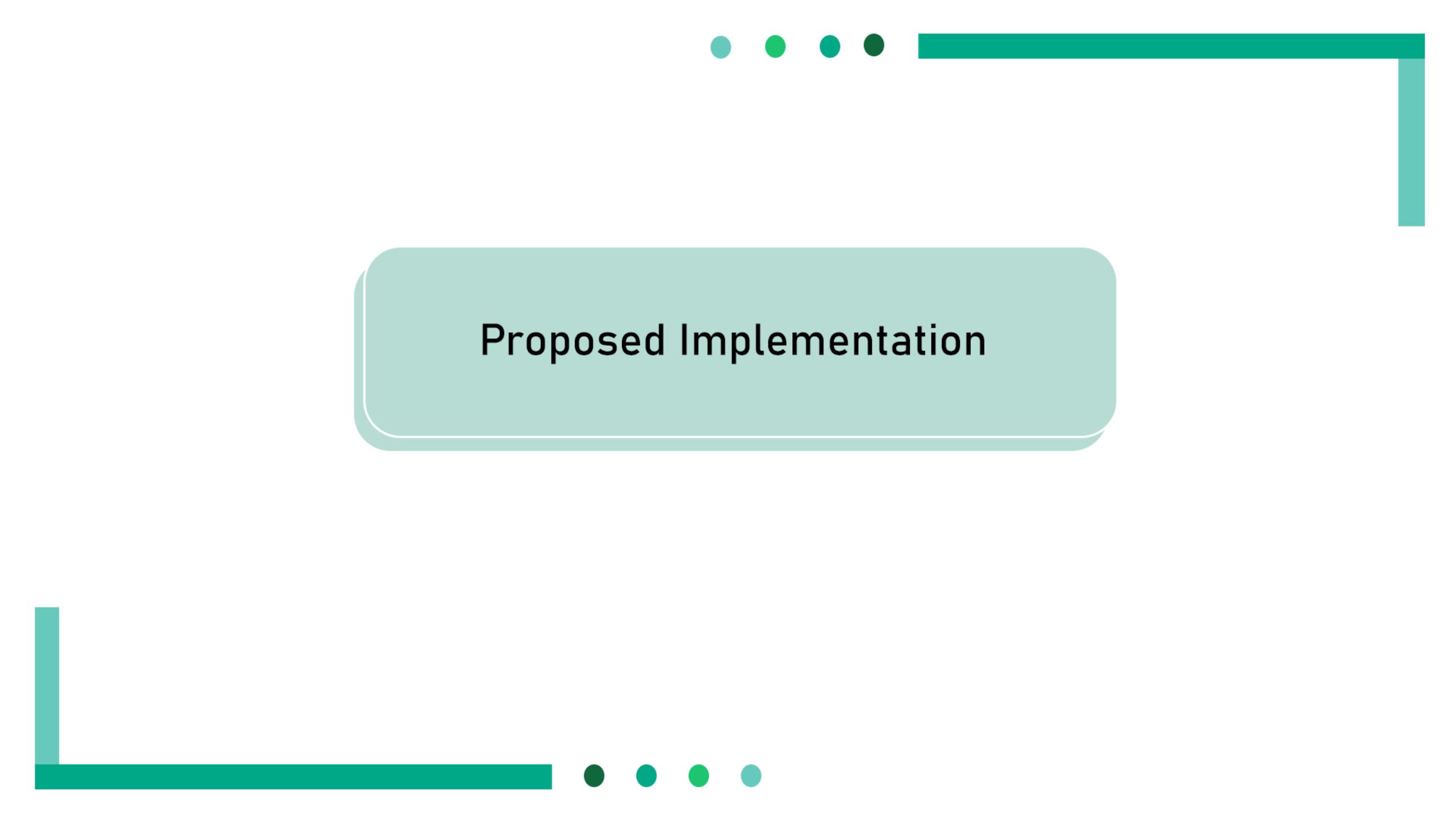
$$y = y_0 + C(e^{(-e^{(\mu e(\lambda-t)/C+1)})})$$

Gompertz Equation

# Recombinant Chitinase Show Higher Chitin Binding Efficiency as Compared to Wild type Chitinases

$$\frac{d[L-R]}{dt} = k_1 \cdot ([L]_T - [L-R]) \cdot ([R]_T - [L-R]) - k_2 [L-R]$$



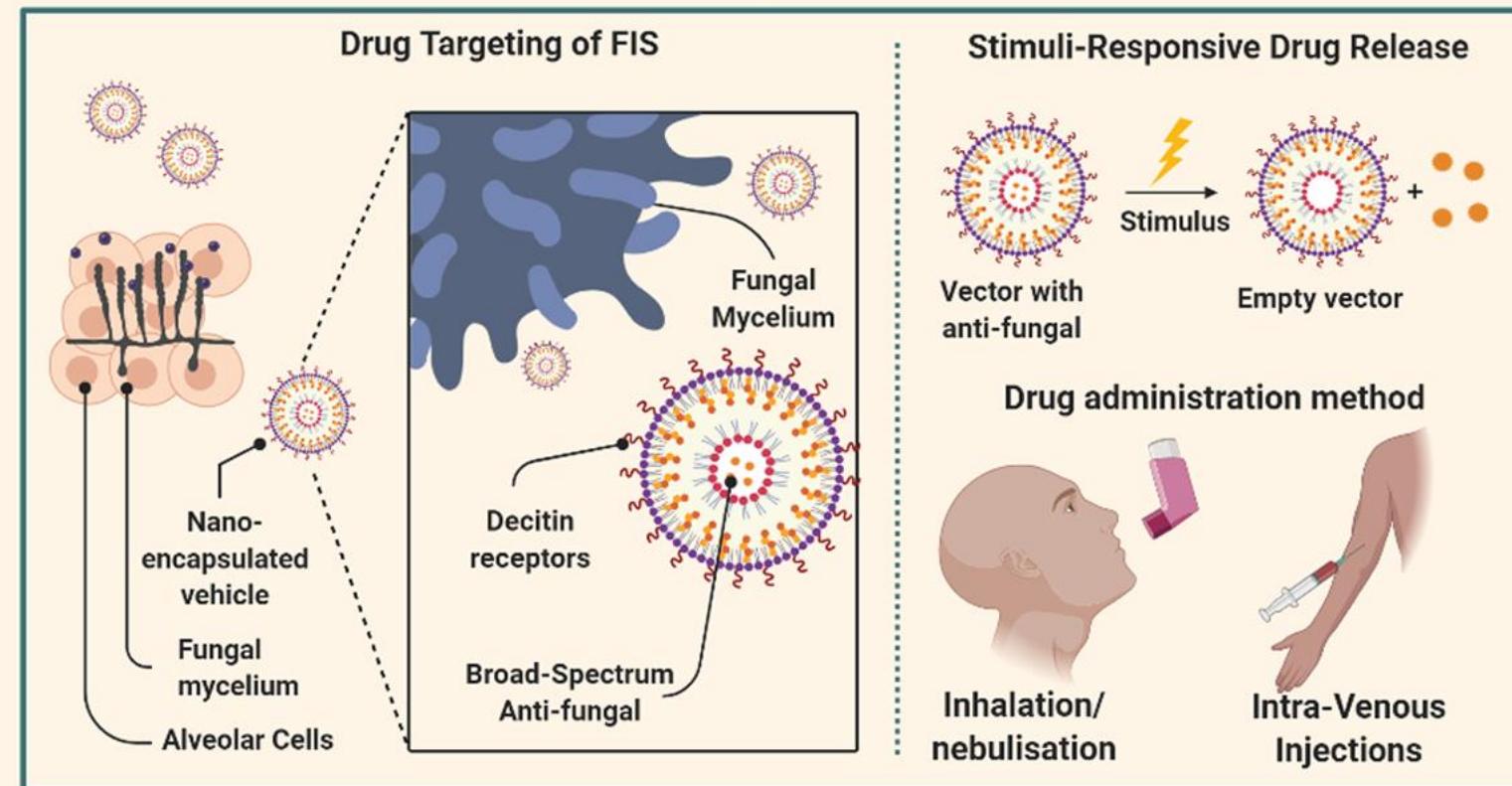
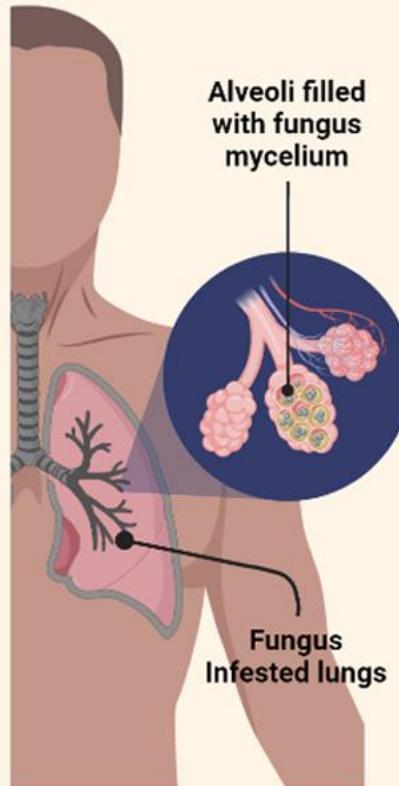


## Proposed Implementation

# Delivery system

## Nano-encapsulated drug delivery to Fungal Infection Sites (FIS)

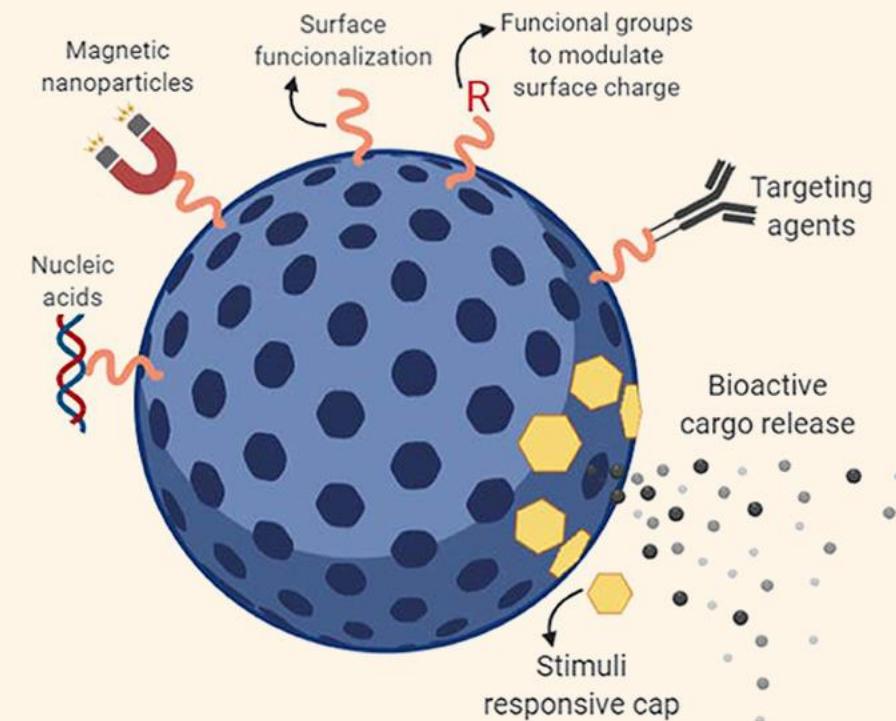
### Delivery Mechanism:





## Why nanoparticles?

- 01 Protect drug from degradation
- 02 Improve drug targeting
- 03 Delivery of hydrophobic or partially soluble drugs
- 04 Biocompatible and biodegradable



Mesoporous silicon-based nano-carriers (MPSNPs)

Vega-Vásquez, Pablo, et al. (2020)

# Human Practices and Outreach



# Human Practices and Outreach Activities



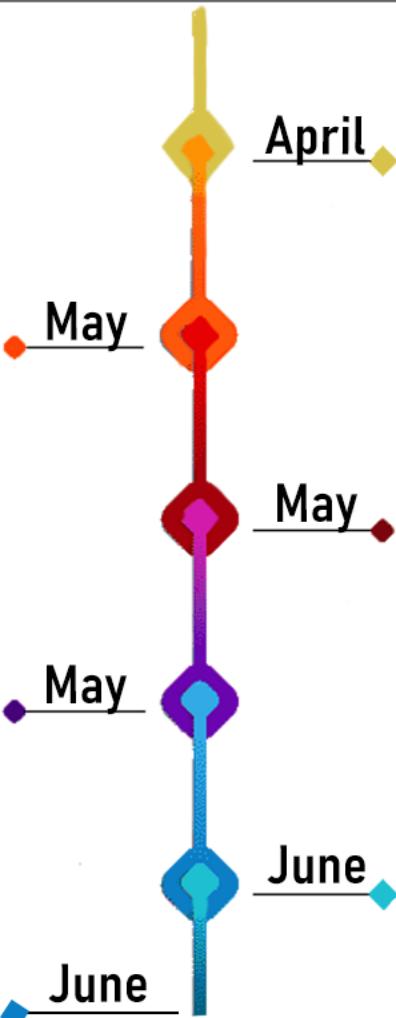
Interaction with  
Microbiologist  
**Dr. Binod Parameswaran**  
(NIIST)



Interaction with Medical Experts:  
**Dr. Rashmi Mary** (Dermatologist)  
**Dr. Sabu Stephen** (General Physician)  
**Dr. Kiran** (Pediatrician )  
**Dr. Shinu** (Pulmonologist)



Interaction with  
**Dr. Harilal Madhavan**  
(IISER TVM)  
(Biotech Handbook and Public  
Surveys )



Interaction  
with **Structural Biologists**  
**Prof. M.R.N. Murthy**  
**Prof H.S Savithri**  
(IISc)



Interaction with  
**Dr. Rachit Agarwal**  
(IISc)  
(Drug Delivery)



Interaction with  
**Dr. Chita Ranjan Sahoo**  
(SOA University):  
Pre-Clinical Trials of Drugs



# Collaborations and Other Activities



Handbook  
(IISER Tirupati)

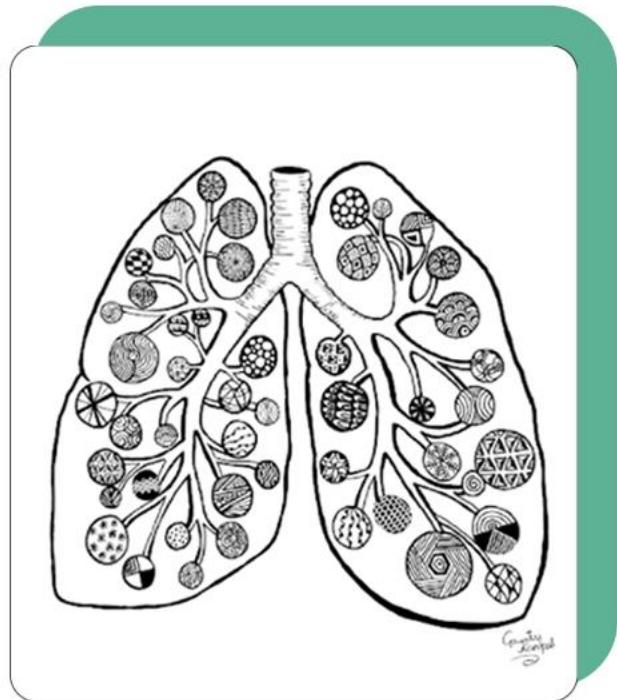


Reading  
Day Event

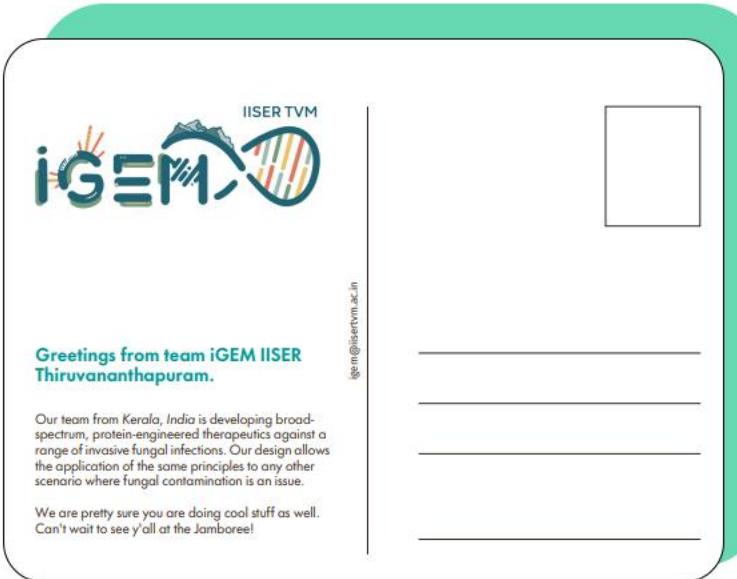


MycoExpo  
Fungal Exhibition

# Collaborations and Other Activities



BioDoodle  
(iBowu\_China)



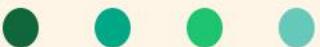
Post Card  
(Düsseldorf)



iJet  
(Darmstadt)



## Meet the TEAM !



# Meet the TEAM !



Dr. Ravi Maruthachalam

Principal Investigator (PI)



Dr. Mohammed Aiyaz

Advisor



Arun Sathyan

Advisor



Ankit Kumar Pradhan

Mentor



## Our Sponsors



**ThermoFisher**  
SCIENTIFIC



**Crompton**



**Crescent**  
Lab Equipments



Thank You !!



## Characteristics of Chitinase Combo

Combination	Mol Weight (kDa)	pI	Half life	Instability Index	Aliphatic index	Hydropathicity (GRAVY)	Net charge at pH 7
Bacterial Combo 1	65.40	4.93	30 hrs	28.26	70.12	-0.390	-24.503
Bacterial Combo 2	39.71	9.35	30 hrs	26.33	81.67	-0.058	+9.723
Plant Combo 1	64.40	6.96	30 hrs	36.04	50.55	-0.221	-4.364
Plant Combo 2	34.84	5.18	30 hrs	36.38	39.58	-0.280	-8.714

