

An Indian-Australian research partnership

Project Title: **Elucidating the mechanism of functions of chromatin remodeler in *Candida albicans***

Project Number **IMURA0477**

Monash Main Supervisor

(Name, Email Id, Phone)

Prof. Dr. Ralf Schittenhelm

Full name, Email

Monash Co-supervisor(s)

(Name, Email Id, Phone)

Monash Department:

Department of Biochemistry & Molecular Biology

IITB Main Supervisor

(Name, Email Id, Phone)

Santanu K Ghosh

santanughosh@iitb.ac.in

Full name, Email

+91-022-2576-7766

IITB Co-supervisor(s)

(Name, Email Id, Phone)

IITB Department:

Department of Biosciences and Bioengineering

Research Academy Themes:

Highlight which of the Academy's Theme(s) this project will address?

(Feel free to nominate more than one. For more information, see www.iitbmonash.org)

6. Biotechnology and Stem Cell Research

The research problem

As a pathogen *C. albicans* exists in different morphological forms presumably to survive within various environments within the host. These morphological switchings appear to play crucial roles in host-pathogen interactions. The frequency with which this switching happens argues for an epigenetic rather a genetic control on these switching events where chromatin plays a pivotal role. Chromatin can be influenced by two kinds of enzymes viz. histone modifier and ATP-dependent chromatin remodeler. Several histone modifiers and SWI/SNF chromatin remodeling complex have been shown to have roles in morphological changes in *C. albicans*. We hypothesize the RSC complex which serves as a fungal specific chromatin remodeler should have profound role in morphogenesis in *C. albicans* given the role of RSC on chromosome segregation/cell cycle in the distant yeast *Saccharomyces cerevisiae*.

Project aims

Elucidation of function of chromatin remodeling in *Candida* biology.

Expected outcomes

Ways to resist *Candida* infestation include blockage in cell proliferation and morphological switching that argues for studies of chromatin proteins that regulate both these processes. Furthermore, unlike bacteria, indiscriminate development of drugs against *Candida* is not possible as this pathogen and its human host both are eukaryotes. Although drugs are available that mostly target *Candida* cell wall and the membrane, there is an increasing occurrence of resistance against these drugs. Consequently, there is a need to identify novel physiological target which can be fungal-specific against which a drug can work better without jeopardizing the fitness of the host. RSC complex, being a fungal specific chromatin protein, is therefore could be such a target and thus deciphering its mechanism of action will throw light to decide whether RSC or its essential interactors can be a potential target for development of anti-*Candida* drug in future.

The above mentioned outcomes will be achieved following these objectives:

Obj 1: To analyze the change in proteome and transcriptome of *Candida* upon loss of RSC (chromatin remodeler) function.

Obj 2: To identify the physical interactors of RSC using mass spectrometry analysis.

Obj 3: To analyse whole genome to identify the DNA loci where RSC binds.

Obj 4: Quantitative proteomic profiling of *Candida* white and opaque cells in presence and absence of RSC function

How will the project address the Goals of the above Themes?

If this study reveals that RSC complex mediated chromatin remodeling indeed has significant roles in *Candida* biology, this complex, being fungal specific, can be a potential target to develop anti-*Candida* drug in future studies. This will be a biotechnological achievement given that *Candida* is the most prevalent human fungal pathogen with immense importance in medical mycology.

Capabilities and Degrees Required

Eligibility :

- 1) B.Tech, M.Tech or MSc in Biotechnology or MSc in Microbiology or Biochemistry (Master's degree is preferred)
- 2) Should have Biology in 10+2 standard
- 3) Should be sound in English (speaking and writing)
- 4) Should have passed at least any one national level test like GATE, CSIR NET, UGC NET, DBT BET
- 5) Should be physically fit

Potential Collaborators

1. Dr. Oded Kleifeld
Scientific Director, Monash Biomedical Proteomic Facility
Research Fellow
Department of Biochemistry & Molecular Biology
Building 77, Monash University
2. Dr. Vivien Vasic
Sequence centre manager
Medical Genomics Facility

Additional costs and equipment

This project requires 7 lakhs INR per year consumables.

Out of the total budget there should be at least 15000 AUD.

Please provide a few key words relating to this project to make it easier for the students to apply.

Candida, fungal pathogen, chromatin remodelling, proteomics

Detailed justification - Additional costs and equipment

Please justify why is this level funding is required?

This project requires i) fine chemicals ii) oligo-nucleotides iii) antibodies iv) reagents for proteomics v) reagents for ChIP seq and RNA seq.
All these are very expensive consumables and since these experiments will be performed for several times for standardization, for different controls, a large amounts of these costly reagents are required throughout the project. Therefore, 12 lakhs INR per year consumables is justified.

Please note that out of the total budget, 15000 AUD will be needed for sequencing as well as reagents and analysis cost for running mass spectrometry.

	INR	
What is the total funding required for the entire project?	28,00,000 (Out of this, 15000 AUD)	(X)
How much bare minimum seed funding will be required to kick off the collaboration?	10,00,000	(Y)
What are the additional funds that will need to be sourced?	18,00,000	(X-Y)

How will the additional funds (X-Y) be sourced?

Once some preliminary results are available, a proposal will be submitted to Indian funding agencies to get the additional funds

What happens if the PIs are unsuccessful in sourcing (X-Y) and we have a student selected?

Student can continue work using funds granted to other running projects in the laboratory. However, pace of work may slow down due to lack of enough funds

Is there any industrial partner that might fund this project that we might approach?

Do not know

Please also fill up the Project Consumables Budget Excel spreadsheet template(available from The Academy) which is required for any budget request which is in excess of INR 3 lakhs OR \$6000.