Indian Institute of Technology Delhi

School of Interdisciplinary Research (SIRe)

SIRe Project Number

2022-01-43

(will be assigned by SIRe)

PhD Project

Project Details	
Project Title	Probing dynamical control of the pathogen-responsive immune signaling network
Project Summary	Upon sensing microbial substances, mammalian cells activate the canonical RelA/NF-κB signaling module as well as the IRF3 pathway. Independently or in collaboration, RelA and IRF3 then mediate the expression of dozens of immune response genes. Stringent control mechanism hardwired within the pathogen-responsive signaling network ensures the rapid activation of these pathways and their dynamically regulated post-induction attenuation. On the other hand, immune-differentiating cues engage a "seemingly" separate noncanonical NF-κB module, which promotes nuclear translocation of RelB NF-κB factors. In a collaborative program between the National Institute of Immunology (NII) and IIT Delhi (IIT-D), we have previously uncovered signaling crosstalk between the canonical and the noncanonical NF-κB modules. Recent biochemical studies suggested that the noncanonical NF-κB pathway is also linked to the IRF3 signaling axis. However, a comprehensive computational model that describes both the NF-κB modules as well as the IRF3 signaling axis is lacking. Here we propose to combine quantitative experimental analyses and mathematical studies to arrive at an advanced computational model, which will recapitulate experimentally observed signaling dynamics of the individual canonical and noncanonical NF-κB modules as well as the IRF3 pathway. Simulation studies involving this advanced model version will provide insight into the dynamical regulation of the integrated pathogen-responsive immune signaling network. Experimental analyses will allow testing the computational predictions in cell culture settings in mouse embryonic fibroblasts and dendritic cells. We hope that the program will not only illuminate emerging properties of the interlinked signaling network but also establish relevance of such crossregulatory mechanisms in modulating immune responses.

PhD Supervisors

Role	**Faculty**	**Academic Unit in IITD**	**Email ID**
Supervisor 1	James Gomes	Kusuma School of Biological Sciences, IIT-D;	jgomes@bioschool.iitd.ac.in
Supervisor 2	Soumen Basak	Systems Immunology Laboratory, NII;	sobasak@nii.ac.in

Project requirements (Student qualification, experience required, etc)

- The student must have M.Sc. or M. Tech. degree in life sciences, biochemical/chemical engineering or other engineering stream with relevant biology background
- 65% marks or 6.5 CGPA on a 10-point scale; GATE score >550 OR

Valid JRF from CSIR/UGC/DBT/ICMR/DST of equivalent

- The student must have interest in computational biology and some experience in C++, R and/or MATLAB platforms.

Source of funding (IRD/FITT Project details, if any)

Dr. Basak and Dr. Gomes have already jointly supervised a Ph.D. student registered at IIT-D. Candidates with valid fellowships from CSIR/UGC/DBT/ICMR/DST of equivalent will be given preference. The PIs will be submitting al research grant for extramural funding as soon as critical preliminary data is obtained.

Role of Faculty Members involved:

Soumen Basak, NII: The PI will act as the co-supervisor. In collaboration with IIT-D, Dr. Basak previously constructed a computational model, which depicted the canonical and the noncanonical NF-κB pathways. Dr. Basak will mentor the student, who will expand the scope of the model to include the description of the IRF pathway. Dr. Basak will supervise experimental analyses that will generate quantitative data on IRF signaling. These data will be used for parameterizing the refined model at NII. Model simulations will generate experimentally testable hypothesis on dynamical network behaviors that will be examined in cell culture settings.
James Gomes, IIT-D: The PI will act as the supervisor. Dr. Gomes will supervise advanced model analyses, which include multiparametric sensitivity analyses and model reduction approaches. He will also mentor simulation studies to be carried out at the high performance computing cluster at IIT-D.