



# Centre for Biosystems Science and Engineering

## SEMINAR

at 11:30 AM on May 13, 2016  
Seminar Hall, MRDG, Biological Sciences

### Biophysical Insights into the Ras-Membrane Interactions & Small-molecule mediated modulation of signaling pathways

**Dr. Shobhna Kapoor**

Post Doctoral Research Associate, Max Planck  
Institute for Molecular Physiology, Dortmund, Germany

The talk will be conducted in two parts. The first part would deal with biophysical study of Ras protein-membrane interactions. Ras proteins existing as four isoforms, act as membrane-associated molecular switches in the early steps of signal transduction pathways associated with cell growth and differentiation. For their biological activity, these proteins need to be anchored to membranes, which is achieved by posttranslational lipidation. De-regulated isoform-specific Ras signaling accounts for 30% of all human tumors, thus placing them at the focal point of academic and pharmaceutical research. Despite their enormous potential as drug targets, pharmacological intervention of Ras driven cancers has not been realized till date and is dubbed as a “holy grail” in cancer therapy. Due to the common structures of Ras isoforms, most drugs often lead to undesirable off-target effects. Thus, a major hurdle in drugging Ras in a specific manner has been the lack of detailed molecular level characterization of these proteins in their cellular environments. Using various state-of-the-art spectroscopic and microscopic techniques, comprehensive biophysical characterization of the structural and conformational changes in Ras isoforms, upon incorporation into heterogeneous model membrane systems, was accomplished. The main results elucidate key codecs for Ras isoform diversity, providing critical hints to target Ras in an isoform-specific manner.

The second part focusses on the small molecule-mediated modulation of signaling pathways. Wnt signaling is a branch of a functional network involved in a broad range of biological processes, such as development and homeostasis. It is one of the fundamental oncogenic pathways, and is implicated in multiple cancers. Thus targeting this pathway is an attractive therapeutic approach. Within the framework of biology oriented synthesis (BIOS), screening of the natural product inspired with anolide-based compound collection revealed potent inhibitors of Wnt signaling (IC<sub>50</sub> = 100 nM) in human colorectal cancer cells. An assortment of different biochemical, cell biological and proteomic methods-based primary and secondary assays, were used to validate the bioactivity of our „lead compound“ in the Wnt pathway. Our efforts towards identification of the compound’s target protein will be discussed. Through a similar approach in a parallel project, a potent and selective small molecule inhibitor of cytokinesis was identified and validated.

#### About the speaker:

Shobhna Kapoor completed her Bachelor’s degree from St. Stephen's College in University of Delhi, followed by an Master’s at IISc, specializing in Chemistry. She then went on to do a PhD in Biophysical Chemistry at TU Dortmund and had a Postdoctoral stint at MPI Dortmund. Some of her awards include the Dissertation Prize, Faculty of Chemistry and Chemical Biology, TU Dortmund, PCCP Hot Topic Prize for poster presentation, NRW Young Scientist Award in Chemistry and Dr. A. Nagaraja Rao Medal for the “Best Master’s Student” .