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## Understanding ABC transporters to navigate human diseases

### Abstract:

Membrane proteins constitute 30% of the genome in organisms and are involved in numerous physiological processes. ABC transporters is a class of membrane proteins which are ubiquitously present in all organisms, bind and hydrolyze ATP to power the solute transport and are associated with several human diseases like multidrug resistance in cancer, macular degeneration, cystic fibrosis, retinitis pigmentosa etc. ABC transporters consists of two transmembrane domains (TMDs), which form the permeation pathway and nucleotide binding domains (NBDs) to bind and hydrolyze ATP and follow alternating access mechanism. Bacterial ABC transporters like binding-protein-independent mutant of maltose transporter, MalG511 from E.coli and FtsEX-PcsB from S. pneumoniae have been characterized biochemically and biophysically to study mechanism and future higher resolution studies. Structure-function relationships were studied in mammalian ABC transporters, bovine MRP4 and human P-glycoprotein. High resolution cryoEM structures of bovine MRP4 in three different states (apo state, nucleotide bound state and substrate bound state) are determined which revealed the architecture, asymmetry of NBDs, interpreted functional effects of genetic variants, located substrate binding site, deciphered associated conformational changes in catalytic cycle of bovine MRP4. Structure based drug designing and targeting MRP4 in context of cancer and cardiac diseases will be helpful to the field of medicine. Oral excipients were screened against P-gp using calcein AM fluorescence assay and digoxin flux assay were found to be inert for their effect on P-glycoprotein. beta-Cyclodextrin and light green SF yellowish were found to be inhibitory at high macromolecular range in digoxin flux assay. This information will be helpful in preparing novel generic formulations. Additionally, the meta-analysis study provides an overview of the revolutionizing field of structural biology of ABC transporters.

### Biography

**Ruchika** has BSc (H) Biochemistry from University of Delhi and MSc. Biotechnology from Indian Institute of Technology Roorkee, India and received her PhD from Purdue University where she was trained as a Membrane Protein Biologist. Afterwards, she pursued her postdoctoral training at UCSF. She focused on ABC transporters all the way in her scientific training. She is very much passionate in elucidating mechanistic underpinning of membrane proteins using biochemical, biophysical and structural biology approaches, which could help to rationally design novel pharmacological tools to modulate the function of membrane proteins altered in disease.