The research work performed by Ms. Urbi Roy involves elucidating the primary reason behind the deregulation of the transcription factor, BCL11B and its impact on the pathogenesis of T-cell acute lymphoblastic leukemia. It was reported by multiple groups that the exon 4 of *BCL11B* harbours several driver mutations, which abrogates its DNA-binding ability. The high frequency of C>T or G>A conversion at the close vicinity of AID-binding motifs in the deregulated gene prompted her to investigate the role of the physiological mutator, Activation-induced cytidine deaminase (AID) in the fragility of *BCL11B* gene. Using various experimental assays, she has demonstrated the aberrant expression of AID in T-ALL cells and patients and its ability to bind to *BCL11B* fragile Region I in exon 4. She has further shown that the endogenous expression of AID can generate a signature mutation pattern in this region inside cells which is enhanced upon overexpression of AID, thus reinforcing its binding to exon 4 and generation of mutations upon aberrant repair. Another part of her work involved the characterization of different non-B DNA structures in *BCL11B* fragile Region I where she has successfully determined the formation of non-canonical structures and binding of AID to this region, thus explaining the fragility of this region. Taken together, her results reveal that AID binds to exon 4 due to the formation of non-B DNA, leading to a U:G mismatch, which when repaired erroneously generates deleterious mutations, resulting in loss of functionality of *BCL11B*.

Sathees C. Raghavan, Ph.D.
Professor
Department of Biochemistry
Indian Institute of Science
Bangalore - 560 012.