UC RIVERSIDE

BIOCHEMISTRY 251/252 SEMINAR SERIES

Tuesday, April 28, 2026
12:00 – 12:50pm

Anjana Rao, Professor, La Jolla Institute

Seminar Title: "The DNMT-TET-ASXL-OGT axis disrupts heterochromatin integrity in clonal haematopoiesis"

Biography: Dr. Anjana Rao obtained her Ph.D. in Biophysics from Harvard University and was a Professor at Harvard Medical School until 2011, when she moved to the La Jolla Institute (LJI) and the University of California in San Diego (UCSD). Her research is focused on the regulation of gene expression, using immune cells, haematopoietic stem cells and embryonic stem cells as model systems. In collaboration with Prof. Patrick Hogan, she and her colleagues purified and molecularly characterized the calcium/ calcineurin-regulated transcription factor NFAT; defined diverse transcriptional programs regulated by NFAT proteins in T cells; identified the pore subunit of the store-operated Ca^{2+} channel, ORAI1; and defined the role of NFAT and downstream transcription factors (NR4A, TOX) in anti-tumor responses and CD8 T cell "exhaustion". More recently, in collaboration with Dr. L. Aravind, Dr. Rao and her team discovered that proteins of the TET family are dioxygenases that mediate DNA demethylation by oxidising 5-methylcytosine (5mC) to 5-hydroxy-methylcytosine (5hmC) and beyond[1, 2]. TET proteins and all three oxidised methylcytosines are now recognised as essential intermediates in all pathways of DNA demethylation[3]. Rao's lab has since explored the roles of TET proteins in gene expression and oncogenesis in the immune/ haematopoietic systems. They have demonstrated that profound TET deficiency in mouse models of lymphoid and myeloid malignancies is associated with strong signal-dependent proliferation, increased inflammation, chromosome missegregation and aneuploidies[3], and heterochromatin dysfunction connected to loss of DNA methylation in heterochromatic regions of the genome[4]. These findings led the Rao lab to investigate the mechanistic underpinnings of clonal haematopoeisis (CH), an age-related condition associated with the development of haematopoietic malignancies, inflammatory cardiovascular disease, and other inflammatory conditions[5] . The top three mutations in CH are in *DNMT3A, TET2 and ASXL1*. Rao's team has shown that each of these mutations affect heterochromatin integrity, through reduced DNA and H3K9 methylation respectively: DNMT3A and TET2 regulate DNA methylation and demethylation[3], whereas ASXL1-BAP1-EHMT1/2 complexes that lead to a global decrease in levels of the H2AK119me3 and H3K9me3 histone modifications located in facultative and constitutive heterochromatin respectively[6]. In consequence, mutations in DNMT3A, TET2 and ASXL1 are associated with increased expression of transposable elements that are normally tightly suppressed in heterochromatin and potentially with increased mutational burden. The Rao lab has shown that DNMT1, TET2 and ASXL1-BAP1 all co-immunoprecipitate with the O-GlcNAc transferase OGT (collaboration with Dr. Sam Myers, LJI). This likely involves physical and/or functional interactions of the CH-associated transcriptional regulators with OGT, a component of both TET-OGT and ASXL1-BAP1-containing protein complexes in the nucleus[6,7]. In ongoing studies, the Rao lab has shown a reciprocal regulatory interaction within the TET-OGT complex in which Ogt gene deletion or OGT inhibition "unleashes" TET activity throughout the genome, resulting in increased 5hmC, decreased 5mC and striking derepression of TEs[7]. Reciprocally, TET deficiency increases O-GlcNAc levels in the genome. Dr. Rao is an elected member/fellow of the US National Academy of Sciences, the American Academy of Arts and Sciences and the American Association for the Advancement of Science. She has received numerous other awards. She has mentored more than 100 post-doctoral fellows, students and technicians, many of whom have gone on to leadership positions in science-related fields.

Location: Genomics Auditorium 1102A
Seminar Host: Dr. Russ Hille & Dr. Jikui Song