Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Seminar

How does human blood get its red color? A tale from RNA perspective

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Millions of people globally suffer from Thalassemia, a red blood cell disorder and underpinnings of causality for is poorly understood. India has one of the largest populations of thalassemia global load and this continues to rise. Thalassemia are hemoglobin gene disorders and leads to suboptimal RBC's impacting quality of life.

Hemoglobin (Hb) mRNAs are highly expressed and translated during erythropoiesis. Here, we identify N6-methyladenosine(m6A) modifications on hemoglobin RNA and explore their role in post-transcriptional regulation. We performed transcriptome wide MeRIPseq(methylated RNA immunoprecipitation sequencing) for detection of post-transcriptional RNA modifications on human $CD34^{+}$ hematopoietic stem cells and differentiating erythropoietic cells. The 5'end m6A of Hb RNA is a cap modification, m6Am, that would stabilize the Hb transcript relative to other transcripts. RNA modifications are reported to be dynamic and change in context dependent manner. The presence of 5'end m6A impart resistance to degradation, RNA degradation and are preferred for translation. Our 5'end m6A finding explains high Hb RNA and protein levels. On the contrary, the m6A modification decreased along the mRNA body of many transcripts, including Hb, signifying potential demethylation events by ALKBH5, a known RNA demethylase. During GATA2 to GATA1 switch during erythropoiesis, a new enhancer peak occurs in the ALKBH5 locus, and ALKBH5 levels were upregulated. RNA immunoprecipitation using anti-ALKBH5 antibody showed interaction between Hb RNA and ALKBH5 protein. In summary, RNA methylation and selective demethylation provides a posttranscriptional mechanism regulating erythropoiesis by directly governing Hb RNA translation.

Friday, Jan 11th 2019

4:00 PM (Tea/Coffee at 3:30 PM)

Auditorium, TIFR-H