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A stem cell constantly faces the choice of self-renewal vs differentiation. For the proper growth and functioning of the body, the differentiation of stem cells into different lineages must be well controlled to enable the timely production of the right number and type of mature cells as well maintaining a sufficient pool of multipotent cells for future needs or in event of disease or injury. Dedicated cell-type specific splicing programs are emerging as important regulators of differentiation and lineage stability. Haematopoiesis is the process of generation of various types of blood and immune cells from rare haematopoietic stem cell progenitors (HPCs). High-throughput RNA sequencing has enabled the characterization of cellular transcriptomes to a high degree of sensitivity. While gene level characterization of HPC differentiation has seen substantial progress, most genes give rise to various mature transcript forms by alternative splicing, extending transcriptome complexity. In my project, we culture CD34+ hematopoietic progenitors isolated from umbilical cord blood driving them toward neutrophil and erythroid lineages. Using RNA-seq samples collected over time, we are trying to delineate the alternative splicing landscape that stabilises this differentiation as well as splice events that may be crucial to the branch-point of erythroid-myeloid lineage programming. Rather than looking at whole transcript forms, we analyse the differential expression of local splicing events within transcripts across differentiation time points by modelling the distribution of RNAseq read counts between splice forms at each time point using statistical models.

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