How do blood stem cells differentiate? A single-cell approach to solving an age-old question.

Dr Julie Thoms and Prof John Pimanda

Circulating blood cells are replenished throughout adult life by the controlled expansion and differentiation of haematopoietic stem cells (HSCs) in the bone marrow. During this process, stem cells transit through multiple progenitor states and progressively commit to specific terminal cell lineages such as monocytes, lymphocytes, and macrophages (Figure 1).

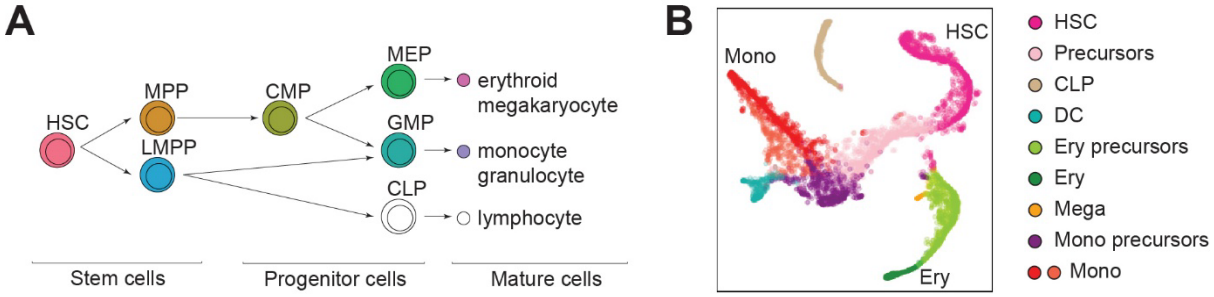

Figure 1: (A) Haematopoietic differentiation tree. (B) Haematopoietic differentiation at the single cell level. Adapted from Thoms et al Blood 2021.

Haematopoietic differentiation is controlled by orderly changes in gene regulation and expression, which when disrupted can lead to leukemic transformation. However, knowledge of the gene regulatory changes underpinning this process is elusive. Stem and progenitor cells are relatively rare, and although regulatory changes occur in single cells, experimental techniques to study gene regulation in single cells are still under development.

This project will primarily use bioinformatics techniques to integrate existing datasets that characterise gene expression and chromatin organisation in single cells with genome-wide transcription factor binding and genome organisation data.

Hypothesis: Genome-wide transcription factor binding and genome organisation data from highly purified blood stem and progenitor cells can be used to scaffold single cell datasets from corresponding cells to increase understanding of how gene regulation controls cell fate decisions in individual cells.

Aims:

1. Use single cell RNAseq and ATACseq data sets to learn essential bioinformatics skills for visualising multidimensional data.
2. Use existing genome wide gene regulation datasets to identify candidate regulatory regions to study in single cells.
3. Integrate single cell and bulk datasets to identify specific patterns of gene regulation across the haematopoietic differentiation hierarchy.

Dr Thoms and Prof Pimanda will be available to discuss this project on zoom from 4pm – 5pm on Wed 6th July using this link:
https://unsw.zoom.us/j/87426296169?pwd=C2Gp3PP1MeQOqXeGGeaW3TvEHBv8GM.1