

Integrated short and long read single cell RNA-sequencing reveals cell type specific isoform expression and novel signature of ageing in haematopoietic stem cell and progenitors

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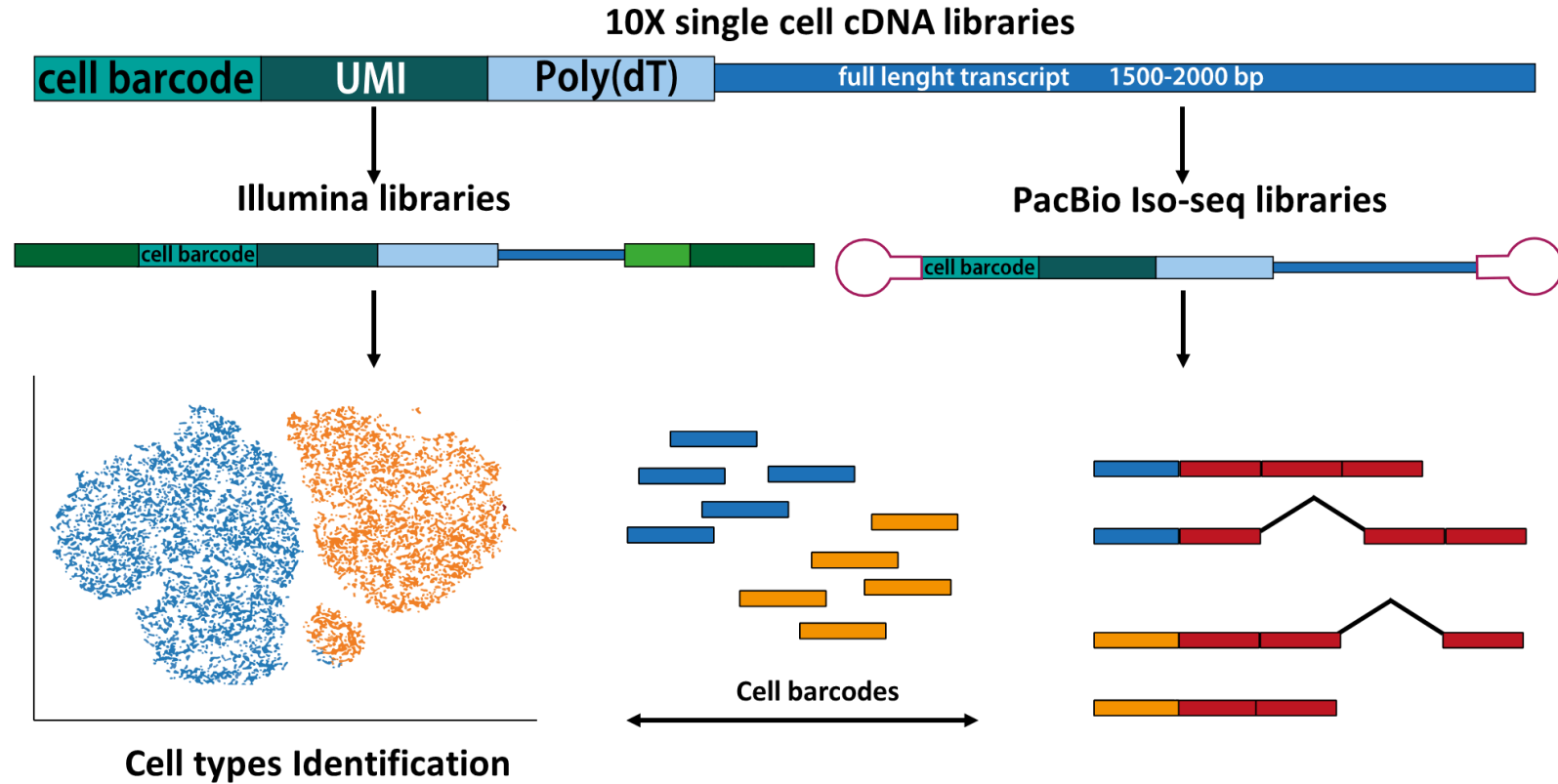
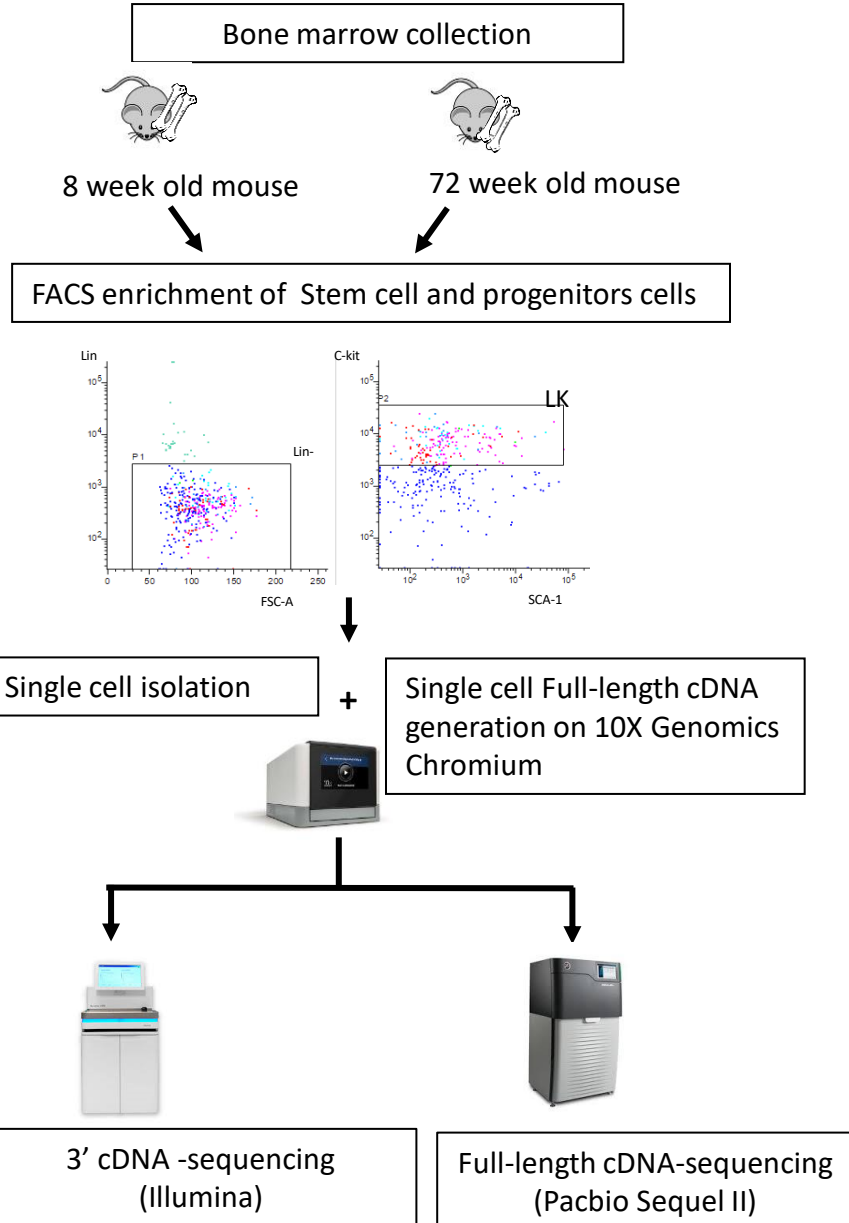
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Integrating gene and isoform expression from the same single cell

Stem and progenitor cells (Lineage negative, cKit+) were isolated from young and aged mice.

Full length cell-barcoded cDNA was produced using 10X genomics platform and then used for standard Illumina sequencing (short-read) and parallel PacBio sequencing (long-read).

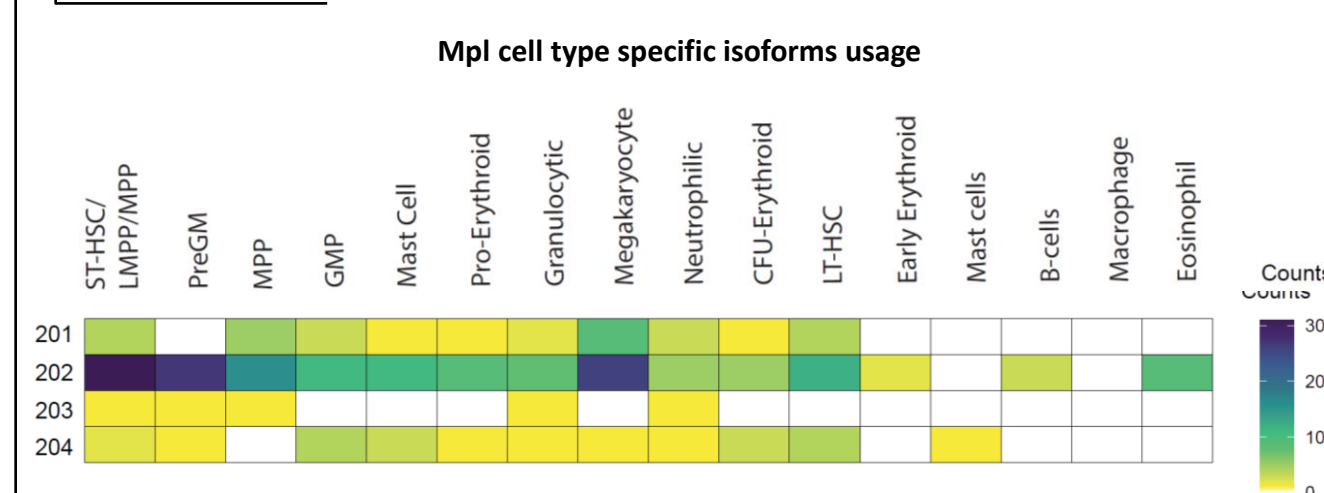
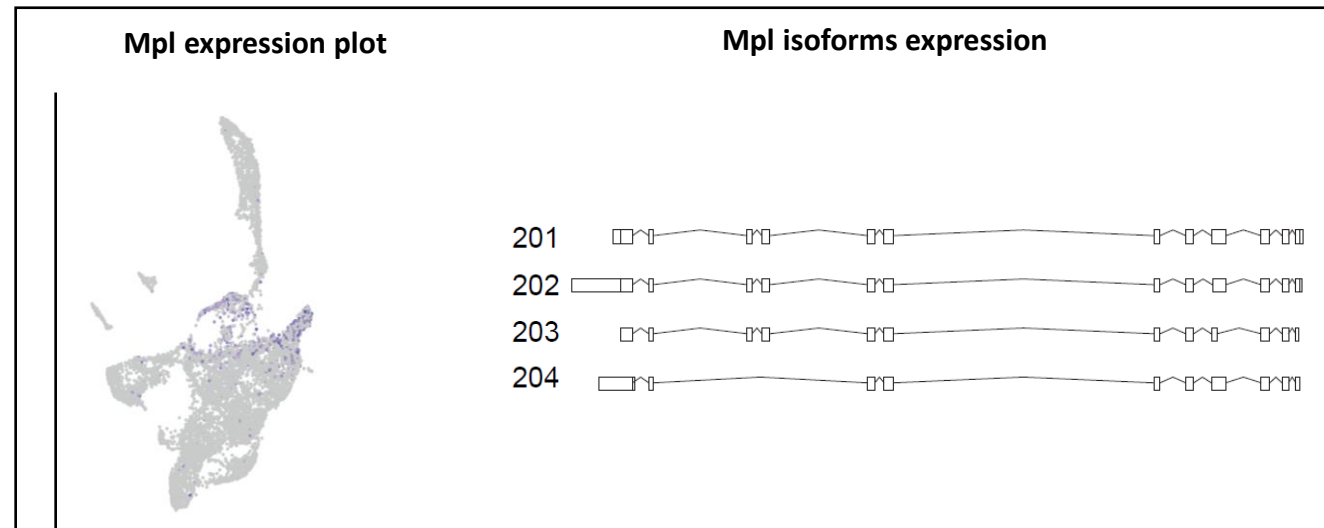
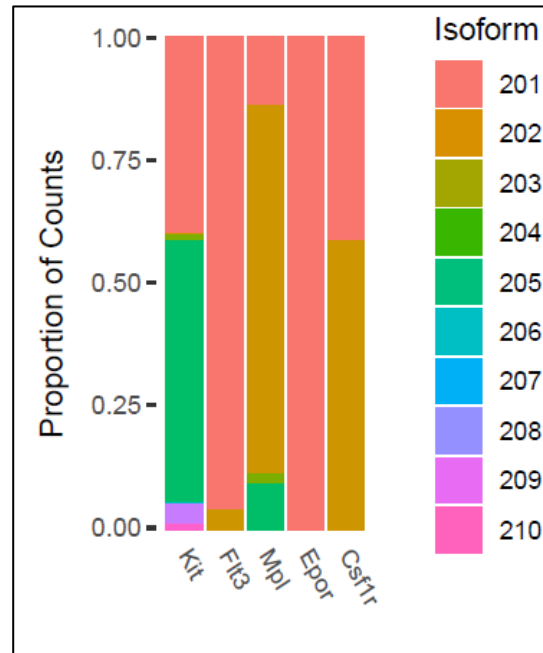
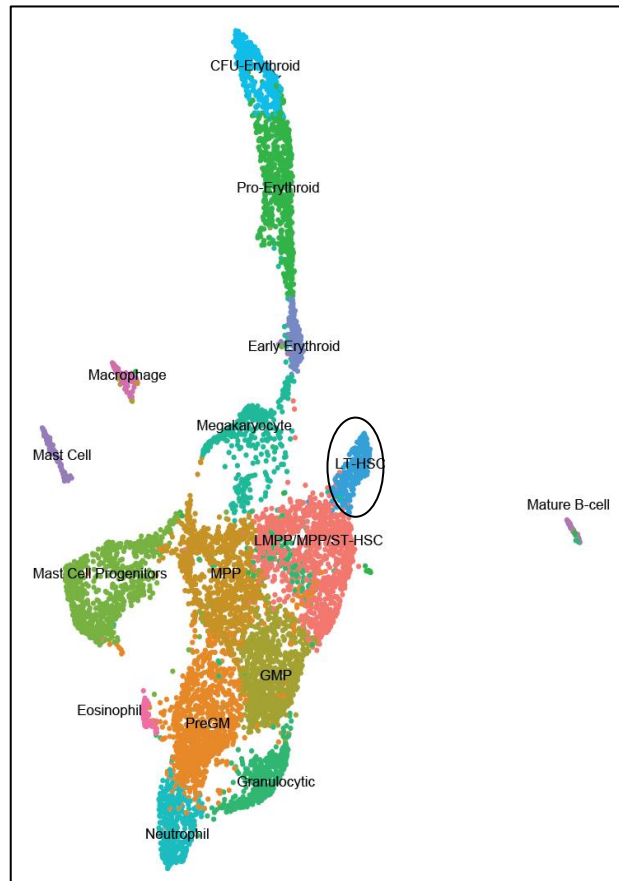


Integrating gene and isoform expression from the same single cell

Short-read analysis identified cell type clusters corresponding to stem and progenitor cell types.

Long-read analysis revealed multi-isoform expression of key regulators of hematopoiesis, such as cytokines.

Integration of short and long read data enabled assignment of AS isoforms to individual cells and cell-type clusters, revealing cell-type specific expression of isoforms with distinct functional domain. Here we show cell type specific usage of functionally distinct isoforms of the thrombopoietin receptor, *Mpl*



Signature of ageing

Long read data described a pan-hematopoietic increase in noncoding transcripts including lncRNAs, and transcripts with retained introns

Show read data showed upregulation of (*Sult1a1* and *Nupr1*) as well as un-expected upregulation of *Igkc* transcripts in the stem cell subpopulation

Furthermore, long read data revealed that the *Igkc* arising from aged LT-HSC population consisted of fully VJ-recombined transcripts

