

# **A human fetal liver-derived infant *MLL-AF4* Acute Lymphoblastic Leukemia model reveals a distinct fetal gene expression program**

## **Description of Additional Supplementary Files**

**Supplementary Data 1: Differentially expressed genes in *MLL-AF4* infant-ALL vs *MLL-AF4* childhood-ALL.** List of genes differentially expressed in *MLL-AF4* infant-ALL (n=11) compared to *MLL-AF4* childhood-ALL (n=5)<sup>1</sup> (edgeR exact test; FDR<0.05), including log fold change (logFC) log counts per million (logCPM), P value and adjusted P value (FDR) for all genes.

**Supplementary Data 2: Combined table of differentially expressed genes in FL HSPC vs ABM HSPC, and in *MLL-AF4* infant-ALL vs *MLL-AF4* childhood-ALL.** List of genes differentially expressed in FL HSPC populations<sup>2</sup> compared to equivalent ABM HSPC populations<sup>3</sup> (HSC, MPP, LMPP and CBP/CLP), and/or in *MLL-AF4* infant-ALL compared to *MLL-AF4* childhood ALL<sup>1</sup>. Each FL HSPC subpopulation and *MLL-AF4* infant-ALL has its own column describing the effect in that subpopulation. “up” = FDR<0.05 and logFC>0, “down” = FDR<0.05 and logFC<0, “unchanged” = FDR>0.05. Data can be filtered by whether a gene is differentially expressed in 0-4 FL HSPC subpopulations analyzed.

**Supplementary Data 3: Significantly differentially expressed genes between *HOXA*<sup>hi</sup> *MLL-AF4* childhood-ALL, *HOXA*<sup>hi</sup> *MLL-AF4* infant-ALL and *HOXA*<sup>lo</sup> *MLL-AF4* infant-ALL.** List of genes found to be differentially expressed following a 3-way comparison between *HOXA*<sup>hi</sup> *MLL-AF4* childhood-ALL, *HOXA*<sup>hi</sup> *MLL-AF4* infant-ALL and *HOXA*<sup>lo</sup> *MLL-AF4* infant-ALL<sup>1</sup> (edgeR glm test, FDR<0.05). logFC values are given for each subtype.

**Supplementary Data 4: MLL-AF4-bound genes.** List of genes that have at least one MLL-AF4 binding site (defined as overlapping MLL-N and AF4-C ChIP-seq peaks) anywhere in the gene body in *CRISPR* MLL-AF4+ ALL, the SEM cell line<sup>4</sup> and/or an MLL-AF4 childhood-ALL patient<sup>5</sup>. Each sample has its own column describing whether an MLL-AF4 binding site is present. “yes” = an MLL-AF4 binding site is present in this gene in this particular sample. “no” = an MLL-AF4 binding site is not present in this gene in this particular sample.

## References

- 1 Andersson, A. K. *et al.* The landscape of somatic mutations in infant MLL-rearranged acute lymphoblastic leukemias. *Nat Genet* **47**, 330-337, doi:10.1038/ng.3230 (2015).
- 2 Agraz-Doblas, A. *et al.* Unravelling the cellular origin and clinical prognostic markers of infant B-cell acute lymphoblastic leukemia using genome-wide analysis. *Haematologica*, doi:10.3324/haematol.2018.206375 (2019).
- 3 Corces, M. R. *et al.* Lineage-specific and single-cell chromatin accessibility charts human hematopoiesis and leukemia evolution. *Nat Genet* **48**, 1193-1203, doi:10.1038/ng.3646 (2016).
- 4 Kerry, J. *et al.* MLL-AF4 Spreading Identifies Binding Sites that Are Distinct from Super-Enhancers and that Govern Sensitivity to DOT1L Inhibition in Leukemia. *Cell Rep* **18**, 482-495, doi:10.1016/j.celrep.2016.12.054 (2017).
- 5 Harman, J. R. *et al.* A KMT2A-AFF1 gene regulatory network highlights the role of core transcription factors and reveals the regulatory logic of key downstream target genes. *Genome Res*, doi:10.1101/gr.268490.120 (2021).