

RESYS Project

Differentiation of hematopoietic precursors in embryos

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2019 – 2020

The Dataset

The Early Hematopoietic process

The biological process we are studying is one of differentiation of multipotent precursor cells *Hemangioblasts* into hematopoietic and endothelial cells alike. In the mouse embryo, there is emergence of blood cells at day 7 in the yolk sac and this is the marker of the beginning of the hematopoiesis. Both the Hematopoietic Stem Cells (HSC) and the Endothelial Stem Cells (EPC) originate from these multipotent precursor cells. The blood cells will be formed by differentiation of the HSCs while the vasculature (tissue of the blood vessels) will be formed through differentiation of the ESCs.

The Experiment

In the paper *Decoding the Regulatory Network for Blood Development from Single-Cell Gene Expression Measurements*, single-cell gene expression data was used in order to infer the regulatory networks at work during the hematopoietic differentiation process. It is known that blood development initiates at gastrulation from mesodermal cells, which initially have the potential to form blood, endothelium and smooth muscle cells. They showed that single-cell analysis of a developing organ coupled with computational approaches can reveal the transcriptional programs that control organogenesis.

In order to acquire the data necessary they sampled single-cells in *in vivo* mice embryos. The cells were sampled from the mesoderm and their potential to differentiate into blood cells was asserted thanks to expression of Flk1 and Runx1 expression. The sampling was done at four distinct time points.

Those four times points define groups of cells, which are not homogeneous since the differentiation process is asynchronous. That is to say some cells begin their differentiation process earlier than others :

E7.00 At this time point the cells are labeled "PS"

E7.50 ————— "NP"

E7.75 ————— "HF"

E8.25 At this time points cells were categorized into two different set. Those cells which expressed *GFP* were labeled "4SG" and where considered as putative blood cells while those that did not where labeled "4SFG" and considered as putative endothelial cells.

At each time points gene expression of a set of genes was measured in each cell, these genes were selected by hand as they were known to play a role in the process. Forty-six genes were selected, out of those : four were housekeeping genes in order to assess the quality of the measures. Nine were markers known to identify the different cell states and thirty-three were transcription known to play a role in the transcriptional program underlying

the differentiation process.

Categorizing Genes

To be pertinent in our analysis we first need to categorize the genes into the different cell states they belong to. We use the literature to guide us in our task. In the article, the authors underlign groups of genes as being characteristic of the two end states :

- For Hematopoietic Cells : Hbb-bH1, Gata1, Nfe2, Gfi1b, Ikzf1 (Ikaros) and Myb
- For Endothelial Cells : Erg, Sox7, Sox17, Hoxb4, Cdh5

In order to support our categories we plotted the distribution of the mean gene expression levels in the different stages :

Their Network Inference

Using MIIC

Appendix

