During mouse embryonic development, hematopoiesis has been well studied. At the stage of our sample (E11.5), embryonic erythrocytes can be found in circulation system and are undergoing differentiation to mature erythrocytes as cells are decreasing diameter and will start enucleation soon [1][2][3]. In our t-SNE projection, blood-related signals were detected in several clusters by GSEA. One of the three clouds presents ‘erythrocytes’ signals (**FIGXXX**). By analyzing its sub clusters ~~at IBS i5 resolution~~, all of them show comparable results. Interestingly, this cloud shows a crescent like structure, which may indicate a transition of differentiating erythrocytes along its axis. To test this hypothesis, we first projected several hemoglobin genes onto this structure (**FIGXXX**). ~~Adult β-globin (~~*~~Hbb-βS~~* ~~and~~ *~~Hbb- βT~~*~~) shows an opposite gradient trend as embryonic β-globin (~~*~~Hbb-Y and Hbb-h1~~*~~), while the same as adult α-globin (~~*~~Hba-a1~~*~~).~~ As we expected, the expression level of *Hba-a1* shows a gradient along the crescent axis (**FIGXXX**), while embryonic β-globins (*Hbb-Y and Hbb-h1*) show the opposite. The gradient of these gene expressions matches up with reported gene switching during primitive erythropoiesis [2][4] and supports our hypothesis. On the other end, we re-computed PCs for this cloud to see genes driving this crescent structure **(FIGXXX**). By running GSEA on top genes contributing to negative and positive PC1, we found that cells from one end of the cloud show a stronger signal of house-keeping biological processes such as ‘mitotic division’ and ‘translation’, indicating a transition along the development trajectory.

We also found clusters with other blood-related signals which can be potential cell types differentiated from hematopoietic stem cells, such as monocytes (**FIGXXX**), megakaryocytes (**FIGXXX**). These cell types should be considered as progenitors as they are not committed at this time point (**REF**). Marker gene projections were made to support GSEA results (**FIGXXX**). Interestingly, one of these clusters shows a remarkable three axes structure. To further study the underlining meaning of this structure, we divided this cluster into sub clusters (**FIGXXX**). **MABYE WE SHOULD TALK ABOUT IBS HERE**. By analyzing sub clusters using GESA, the three axes show unique signals for hematopoietic stem cells (HSC), megakaryocytes and erythrocytes signals, respectively (**FIGXXX**). This is another example of differentiation along cell lineage, showing HSC differentiate into ~~megakaryocytes-erythroid progenitor cells and branch to~~ two different cell types (**REF**).

To better understand HSC signals in our data set, we studied differentially expressed genes for HSC originated from yolk sac and [aorta-gonad-mesonephros](https://en.wikipedia.org/wiki/Aorta-gonad-mesonephros) (AGM) (**REF**). We calculated sum UMI of related genes from two origins and projected on our tSNE plot (**FIGXXX**). Projection of genes related to AGM originated HSC largely overlap with our monocytes progenitors cluster, which agrees with literature (**REF**). But we have no further evidence showing if these cells are in a transient form of HSC or are committed to monocytes. On the other hand, projection of genes related to yolk sac originated HSC highlights one axis of the cluster we talked above (**FIGXXX**), which also agrees with literature (**REF**). (One thing to keep in mind is that, YC-HSC data was from E9.0 according to reference). (A general conclusion could be added here).

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