Human embryo

Yolk sac

Contents

Membrane

Vitelline duct

Liver

Single cell multiomics

10x chromium

→*CITE-seq*

→*scRNA-seq*

→*SMART-seq2*

Spatial validation

2D/3D Imaging

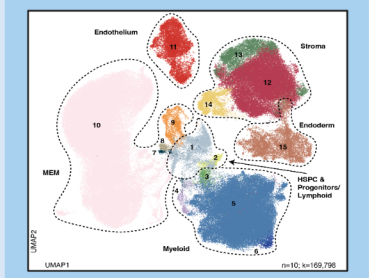
→*RNAscope*

→*Immunohistochemistry*

→*Fluorescence microscopy*

External data integration

+ *in vitro* iPSC dataset



Integrated Yolk Sac atlas

Anatomy

Yolk sac

Endoderm → Metabolic/coagulation functions

Evolutionary conserved metabolic functions

	Human	Rabbit	Mouse
Met./Coag.	✓	✓	✓
EPO/THPO	✓	✓	✗

Mesoderm → Transient YS hemogenic endothelium

Across gestation

Pre-AGM
Early hematopoesis

Myeloid

Post-AGM
Definitive hematopoesis

Lymphoid/Megakaryocyte

Monocyte-independent Mac

HSPC → Pre-Mac → Mac

CS14

AGM

Monocyte-dependent Mac

HSPC → Mono → Mac

Recapitulated in vitro
Alsinet et al., 2022

Across organs

Human

YS-restricted early erythropoiesis

≠

Mouse

YS and Liver early erythropoiesis

Pre-AGM derived Mac

Skin Gonad Liver AGM

TREM2+ Mac

Skin Gonad Brain AGM

Multiorgan functions of the human yolk sac

We characterized functions of the developing human YS, combining scRNA-seq and CITE-seq, with 2D and 3D imaging techniques providing spatial context and validation. Our findings revealed YS contributions to metabolic and nutritional support, and early hematopoiesis. We characterized myeloid-bias in early hematopoiesis, distinct myeloid differentiation trajectories, evolutionary divergence in initial erythropoiesis, and YS contributions to developing tissue macrophages.