Spatiotemporal transcriptome atlas of human embryos after gastrulation

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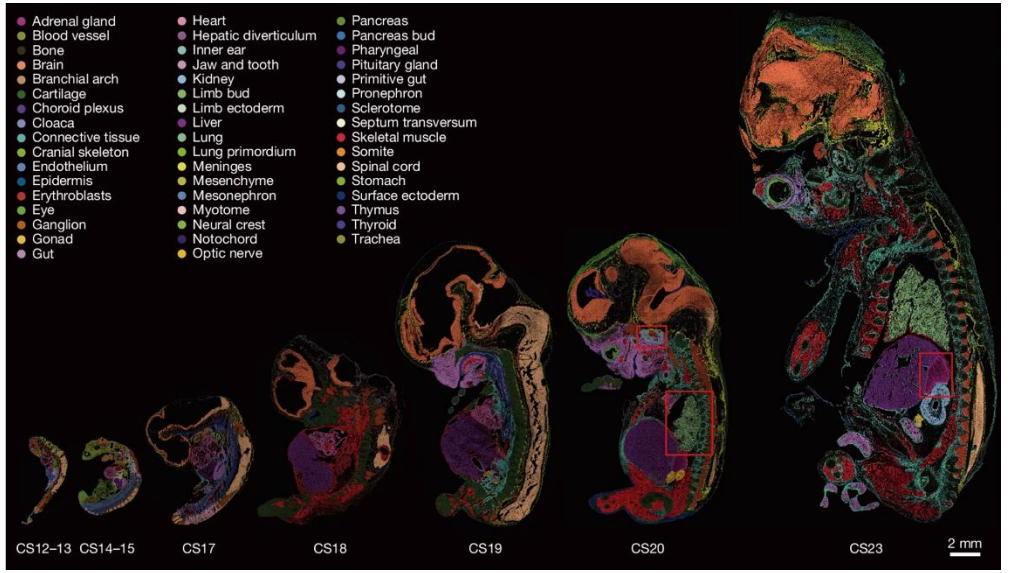
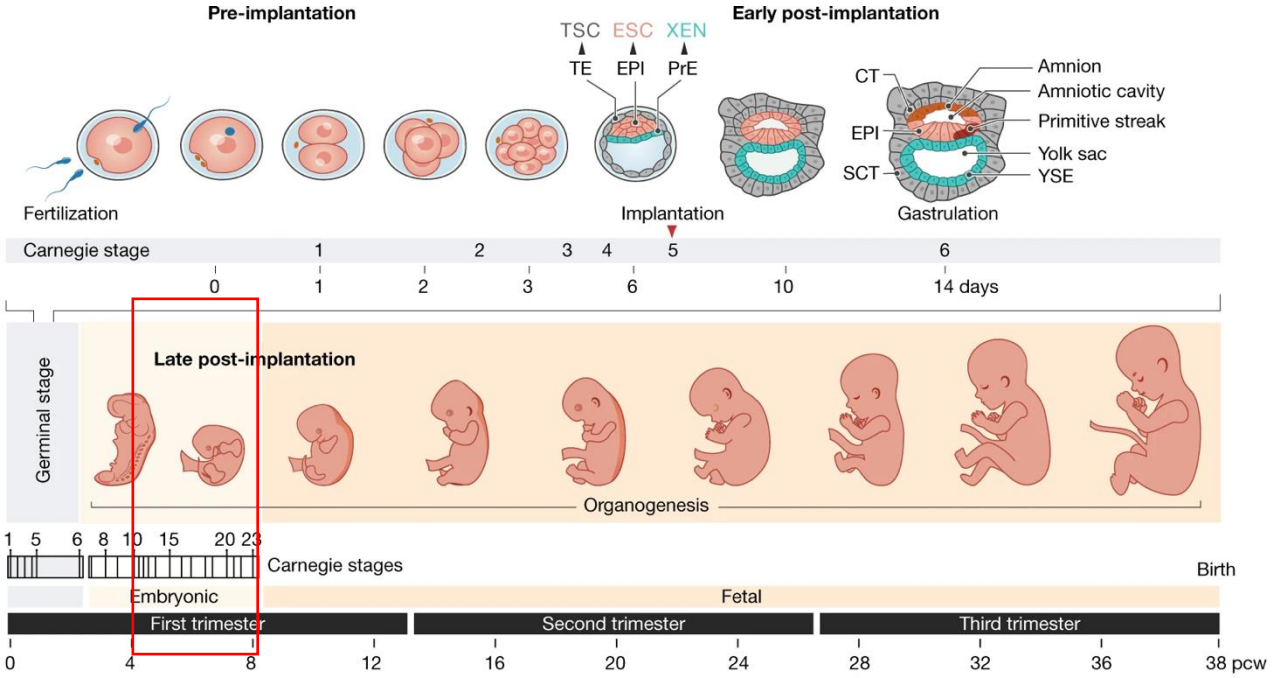
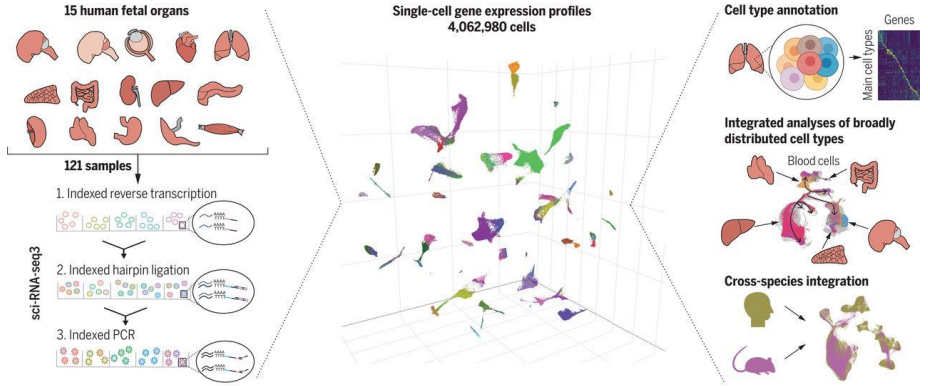
Prof. Hefeng Huang

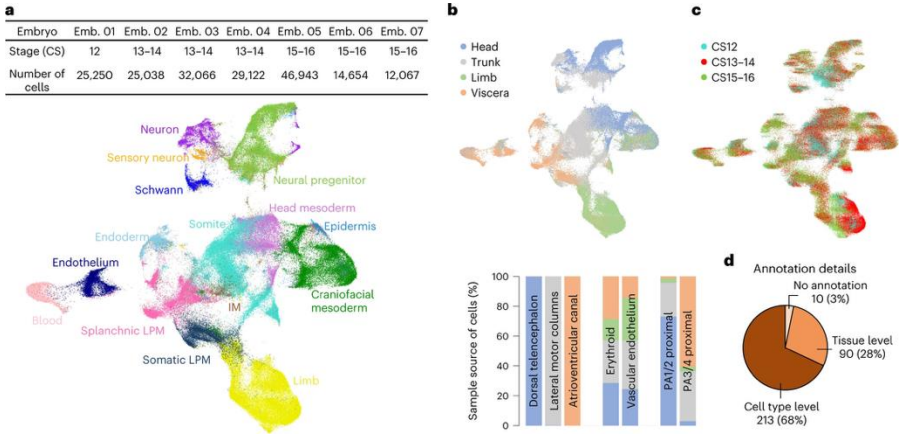


Background





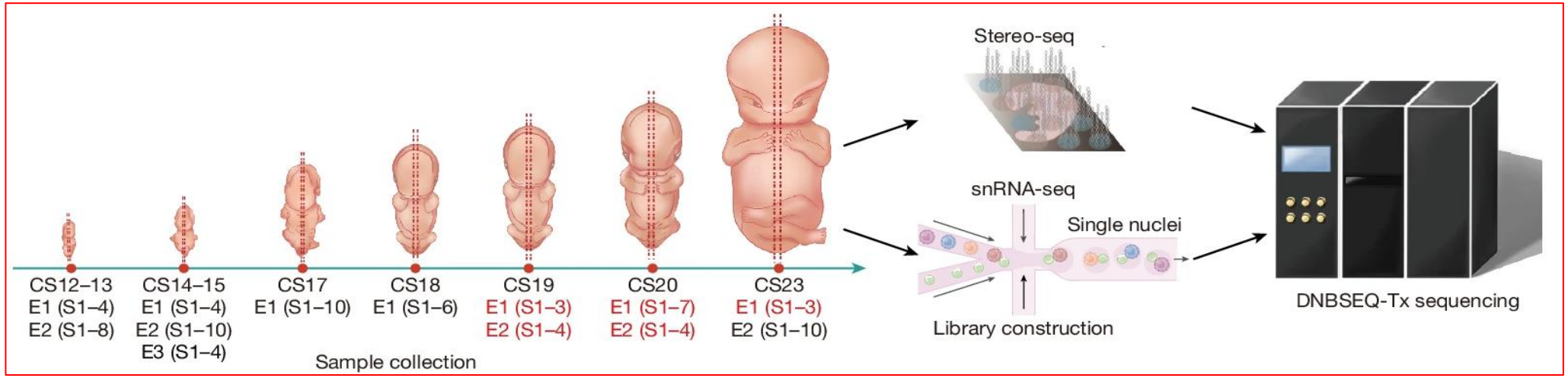
Cao *et al.* (2020) scRNA-seq of 15 organs in fetuses collected from 72 to 129 days of post-conception



Xu *et al.* (2023) single-cell atlas spanning 18 developmental systems in embryos 4–6 weeks of age

Main

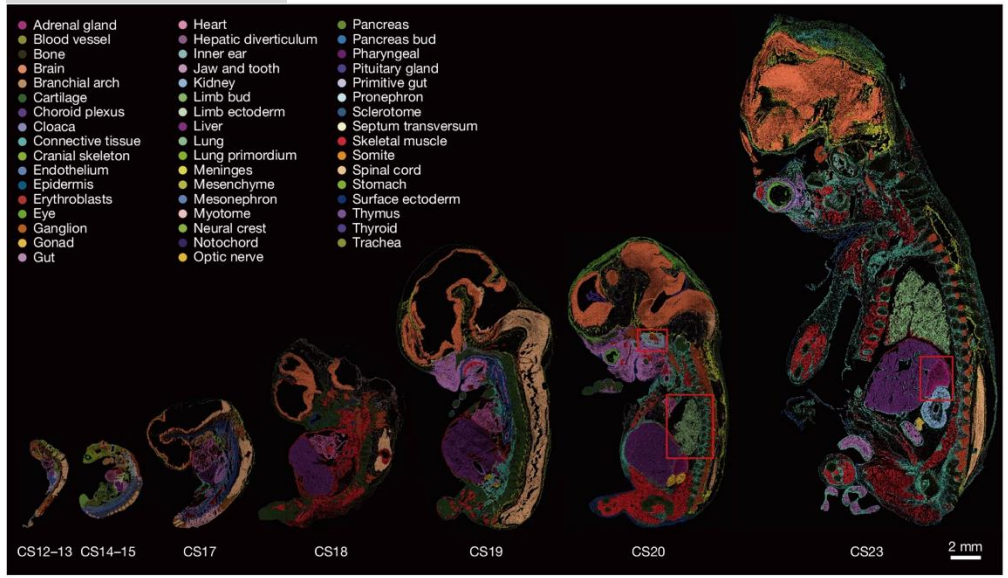
Gap: Lack whole-embryo coverage across critical stages, and comprehensive understanding of the intercellular regulatory networks and pan-embryonic transcriptional coordination during organogenesis.

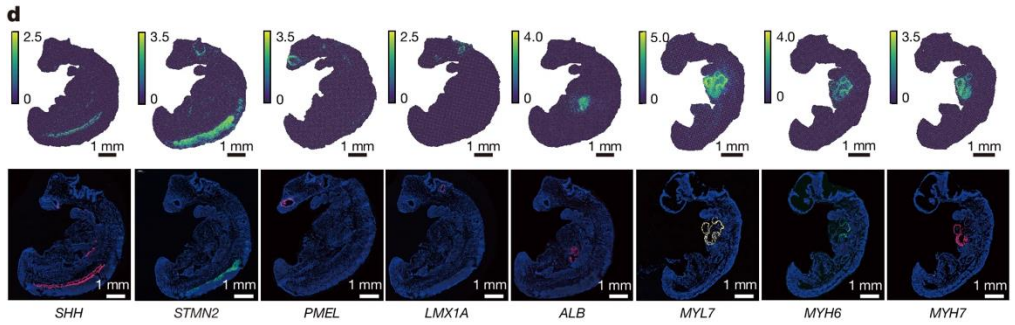


Scientific Question:
How can a spatial atlas reshape our understanding of human organogenesis?

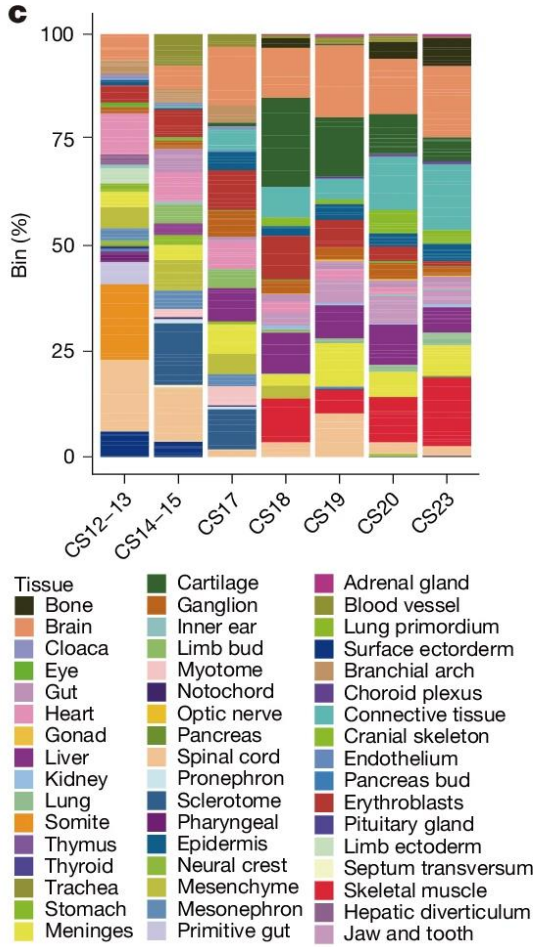
Human organogenesis spatiotemporal atlas

Annotation

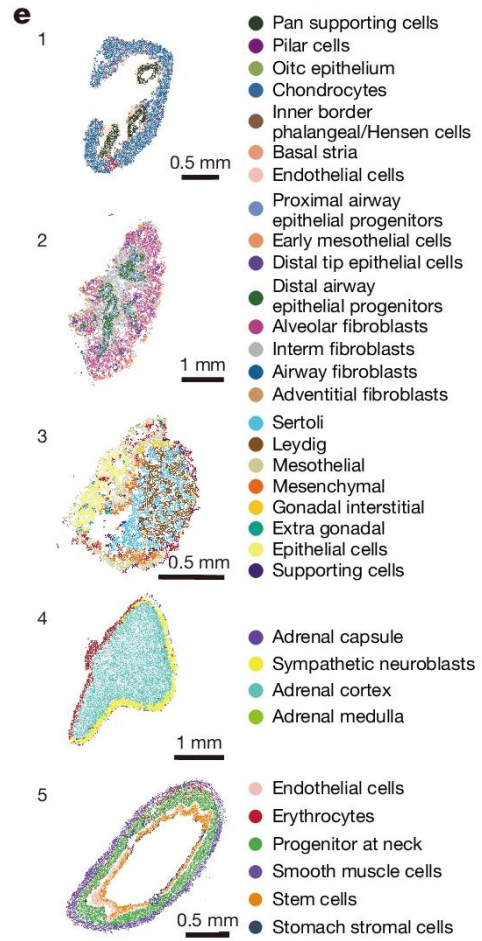




The reliability of this atlas

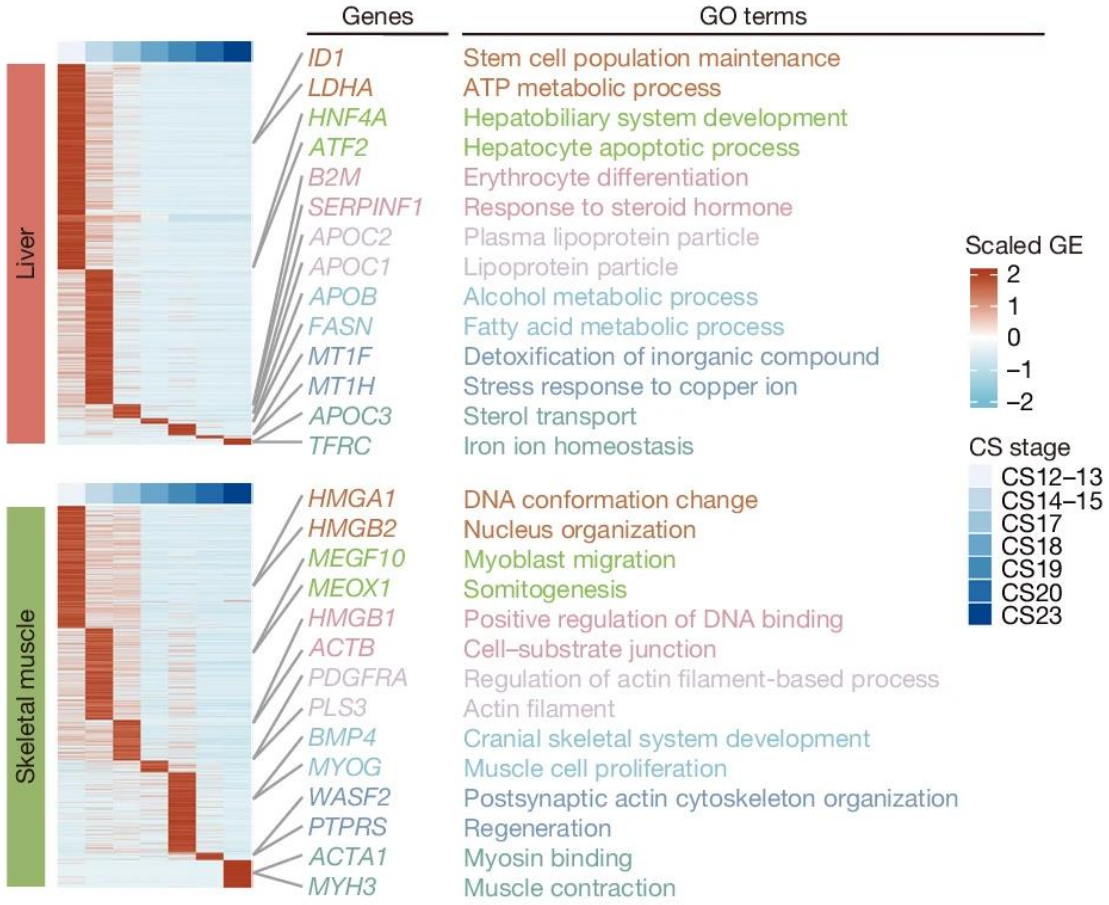


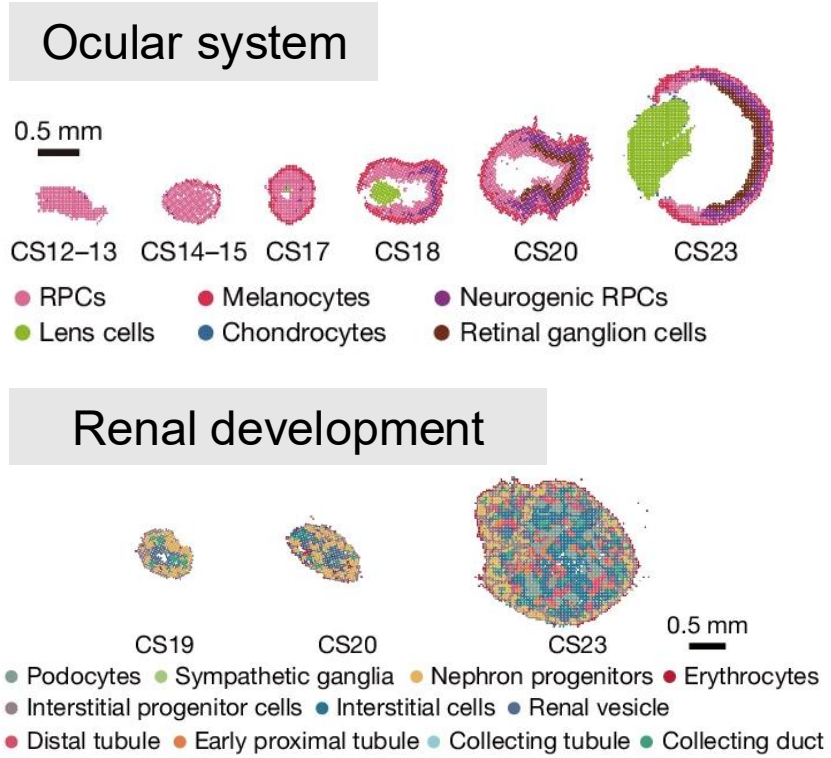
Dynamic changes of Tissue distribution



Substructure mapping

Different organs establish distinct molecular identities early



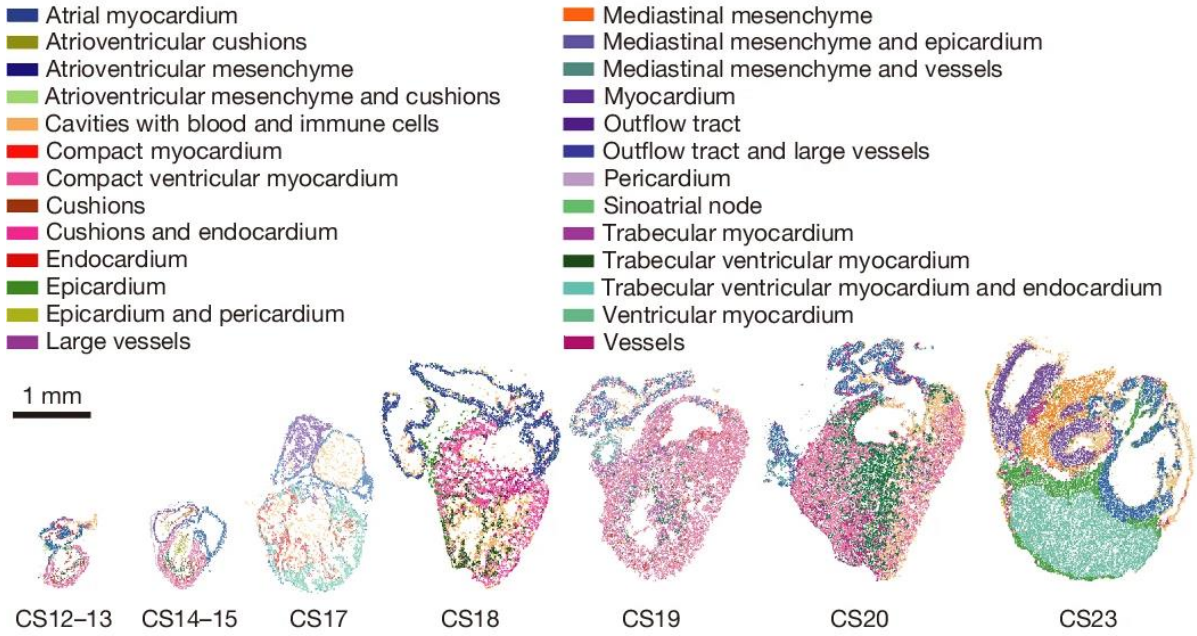


- Identified the orchestrated timeline of organ function and development.

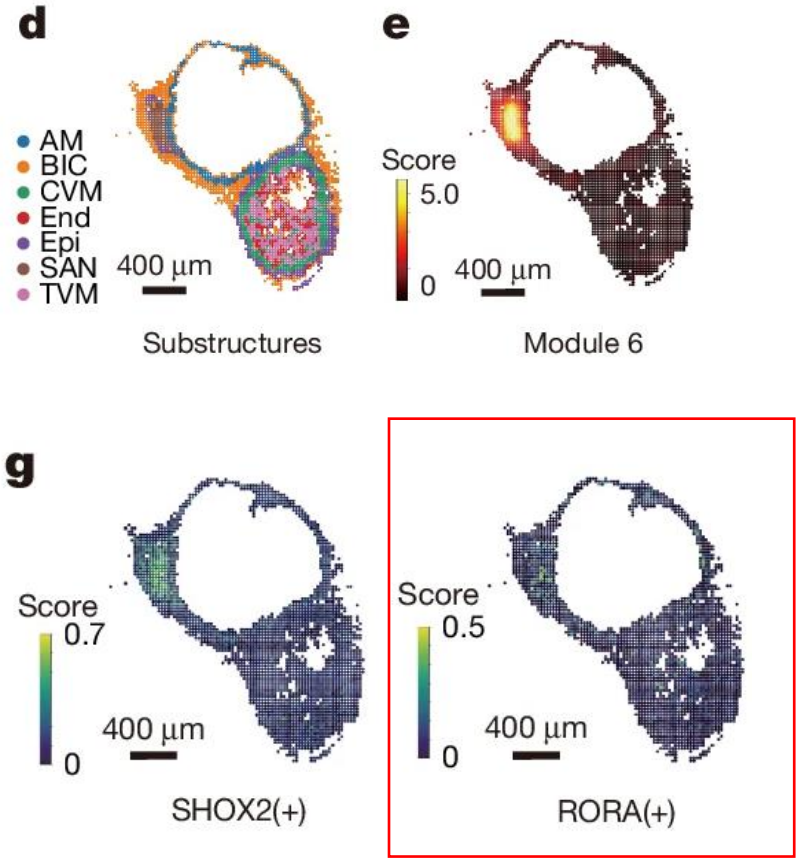
- Spatial transcriptomics resolves intra-organ patterning.
- Different organs forms different regulatory programs.

Cardiac substructures revealed by GRNs

Heart annotation

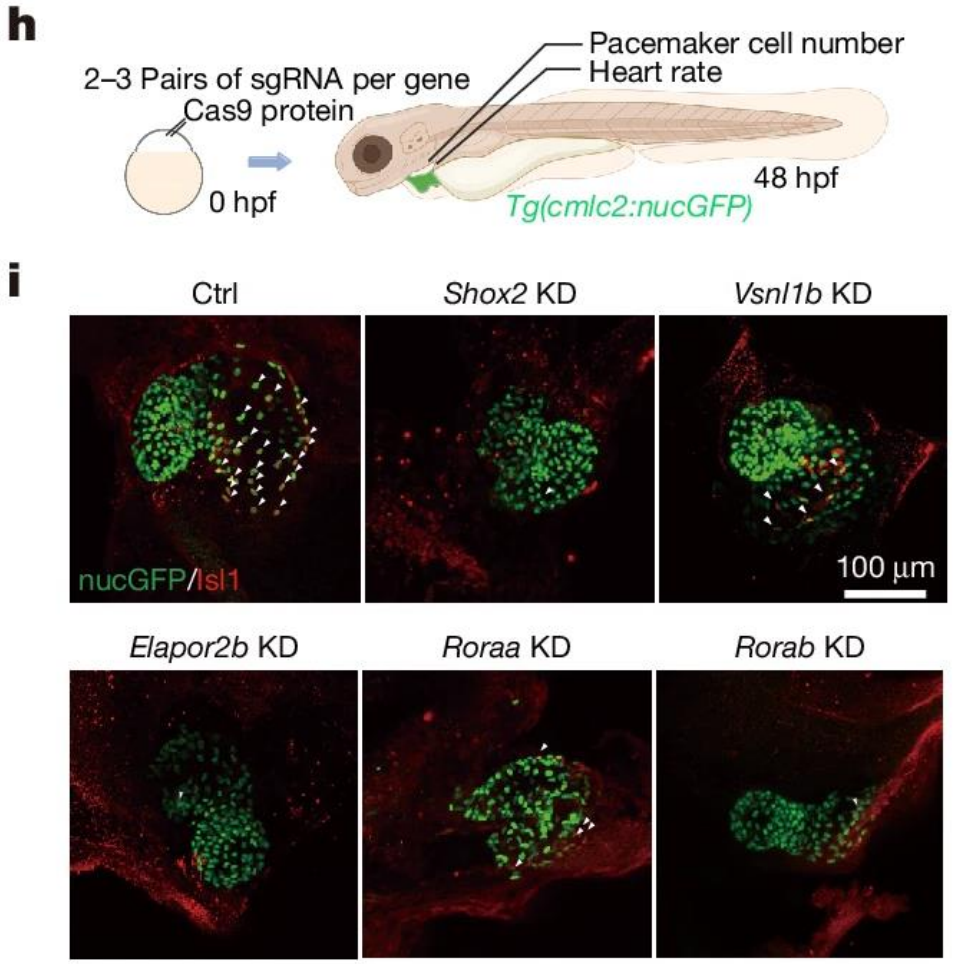


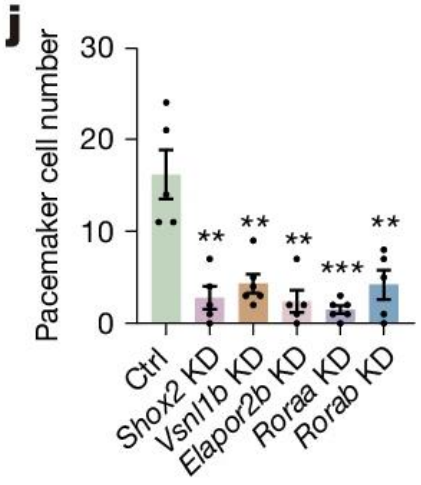
Pacemaking markers

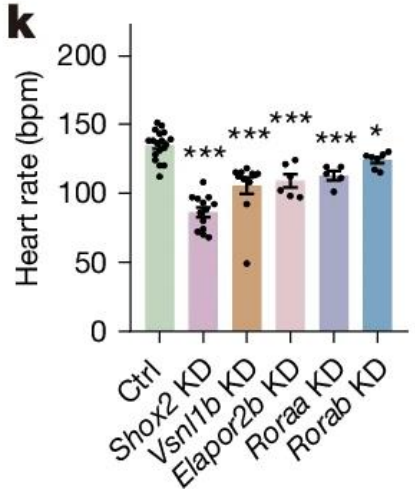


New finding: RORA

Regulators for cardiac function



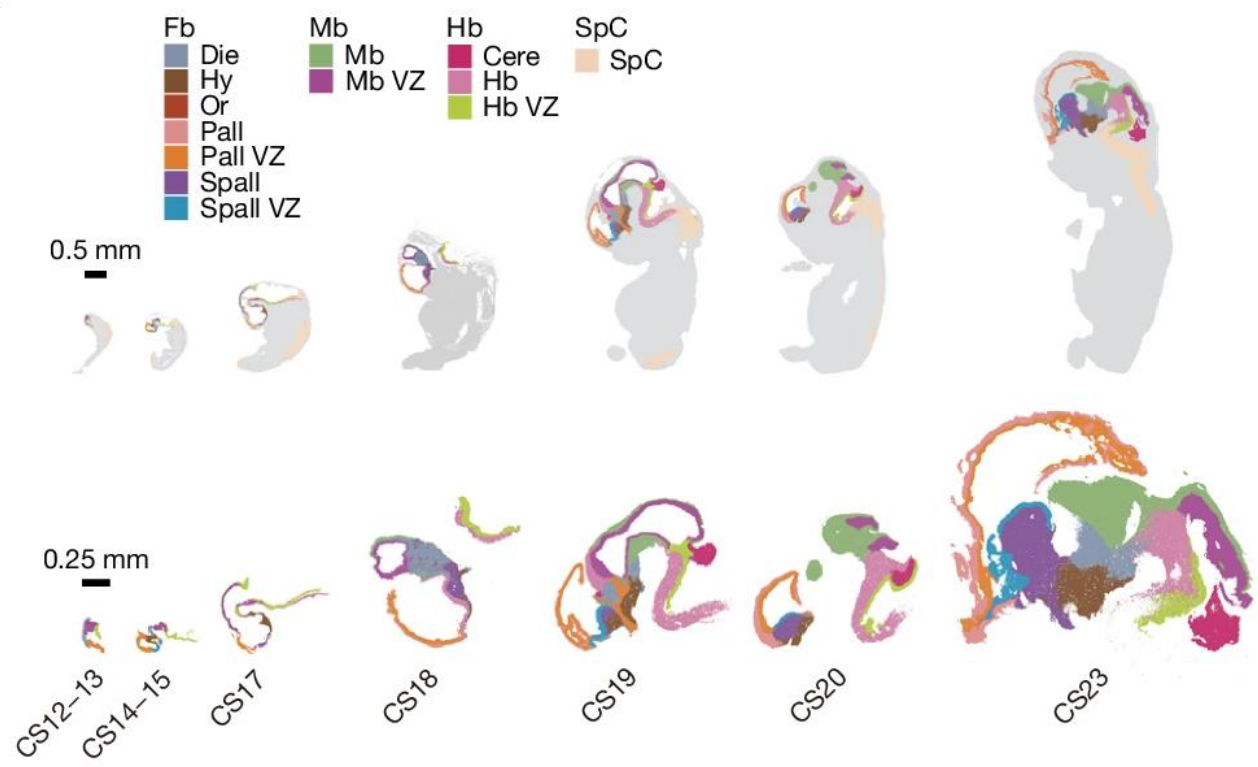




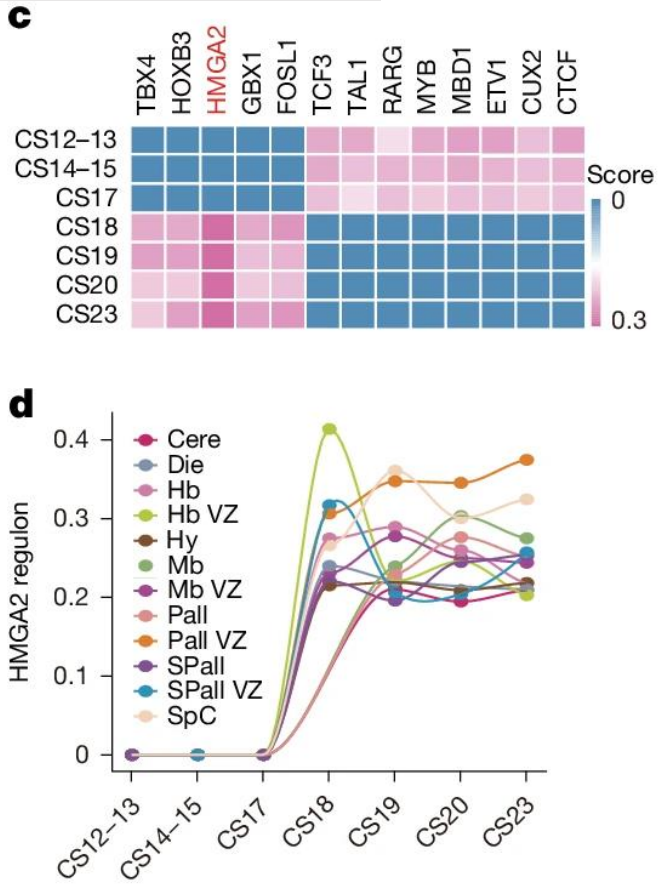
- Regulatory roles of SHOX2 and RORA in the human SAN, providing novel insights into the molecular mechanisms governing cardiac pacemaker cell function.

Central nervous system regionalization

Brain annotation

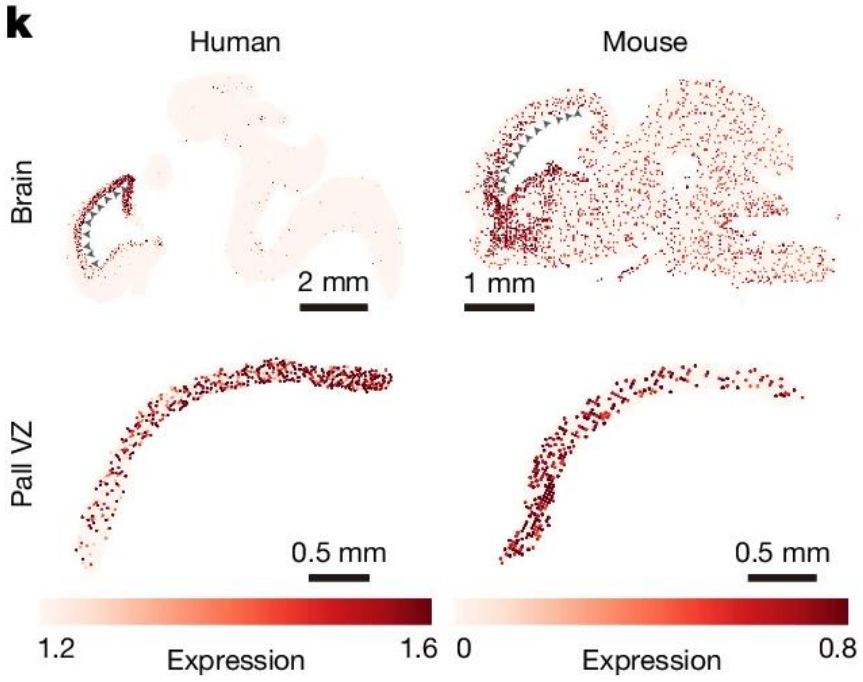


HMGA2 regulon



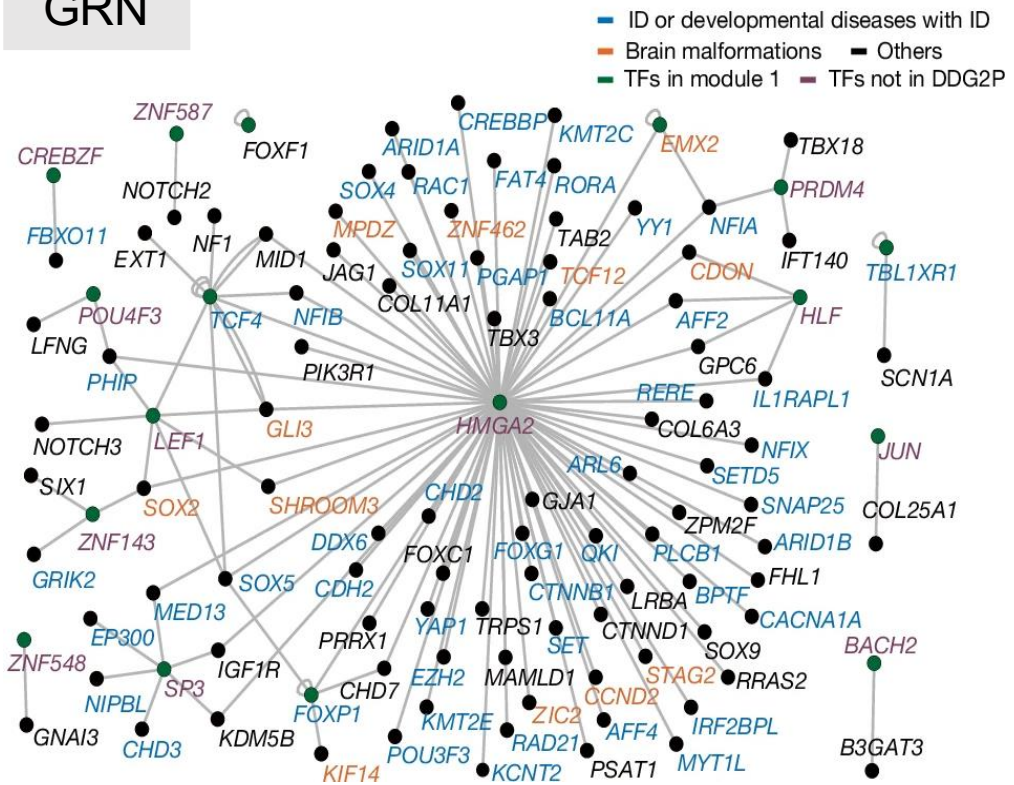
HMGA2 is important in human brain development

Human specificity



- Human *HMGA2:* rostral Pall VZ
- mouse *Hmga2:* caudal

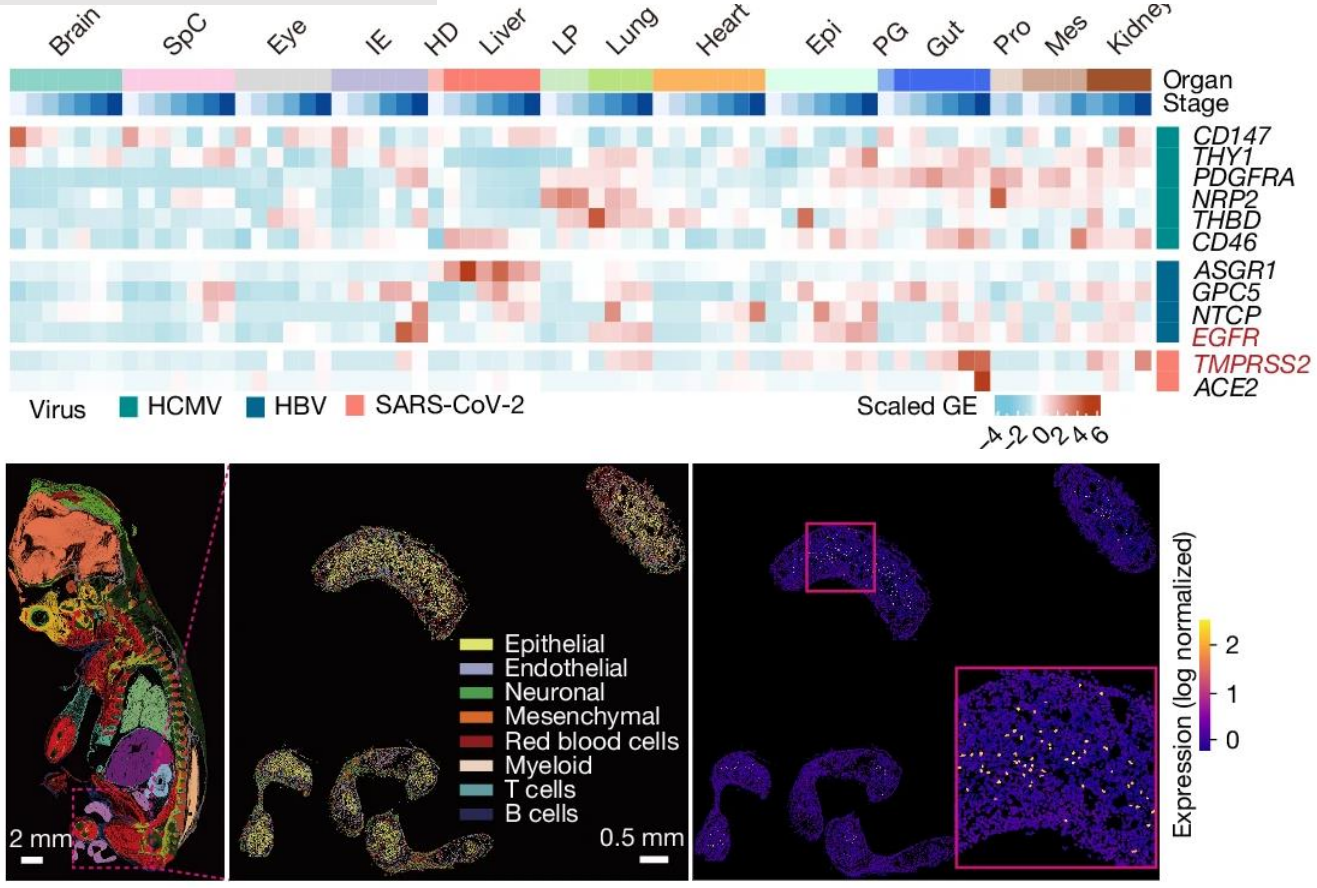
GRN



- 51 TFs specifically linked to intellectual disability

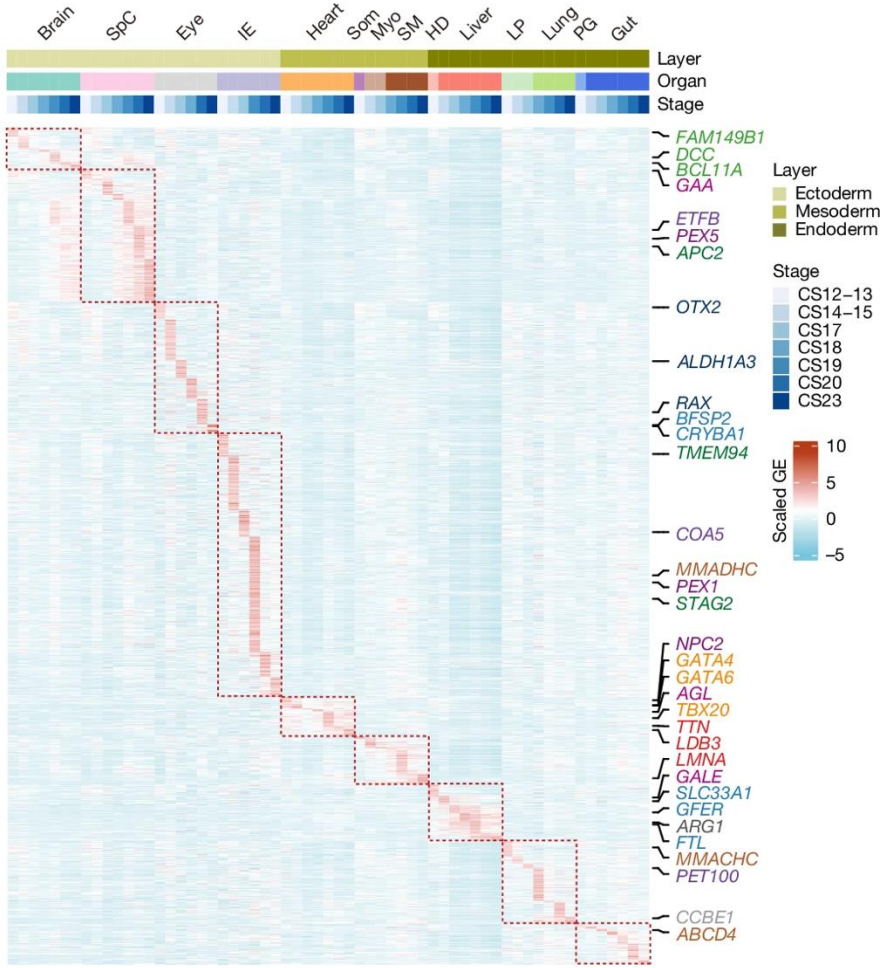
Clinical Applications

Viral susceptibility



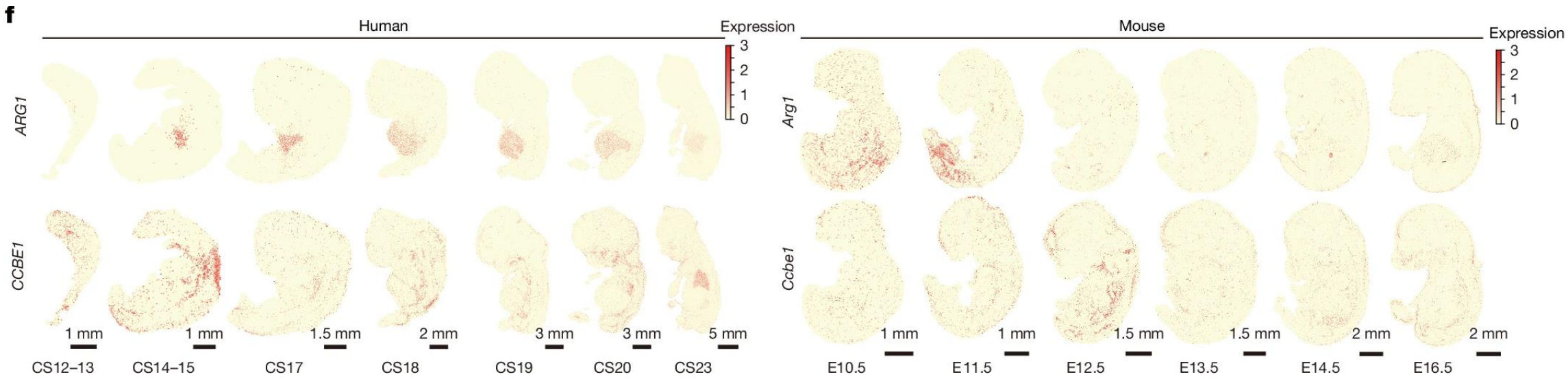
- By profiling host factors essential for virus attachment and entry, this atlas provides insight into the potential molecular basis of prenatal viral infection.

Disease gene patterns



- Developmental transcriptomes reflect genotype–phenotype relationships across diverse disease contexts.

Human specific pattern



- Human ARG1: hepatic dominance from CS14–15
- Mouse Arg1: only became liver enriched at E16.5

- Human CCBE1: high lung-specific expression after CS19,
- Mouse Ccbe1: minimally expressed in the lung between E10.5 and E16.5

- Illustrated the differences in genes across species.
- Emphasized the limitations when applying mouse models for certain human disease studies.

Summary

- A high-resolution spatiotemporal atlas of post-gastrulation (CS12-23) human whole-embryos has been established.
- Spatial organization is a key determinant of organ-specific developmental programs.
- Spatial atlas reveals human-mouse expression divergence.
- The atlas serves as a foundational resource for developmental biology, regenerative medicine and evolutionary studies.
- The HESTA database (Human Embryogenesis Spatiotemporal Transcriptomic Atlas - HESTA) is publicly available. You can map your scRNA-seq data onto it to infer spatial localization.

Future directions

- Integrating spatial transcriptomics with spatial epigenomics, proteomics and metabolomics will further advance our understanding of human embryogenesis.

Thanks for your attention!

Any Questions?