Cell
A Cell Press journal

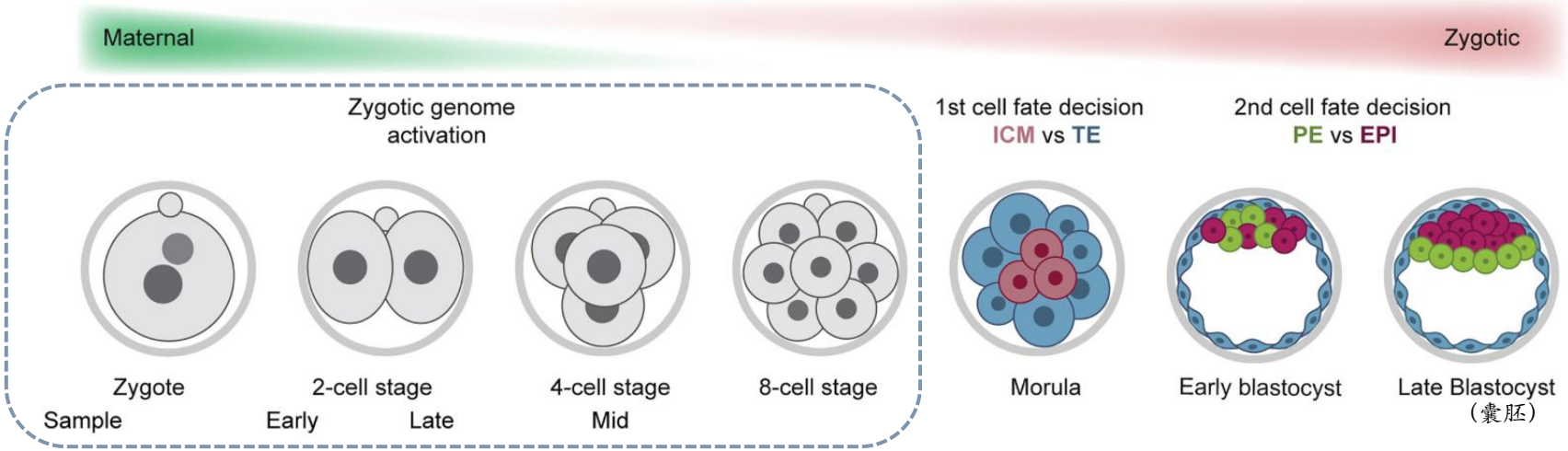
Fertilization triggers early proteomic symmetry breaking in mammalian embryos

Published: 24 Dec 2025

Reporter: Jingrui Lu **Date:** 2026.3.6

Introduction

Blastocyst formation

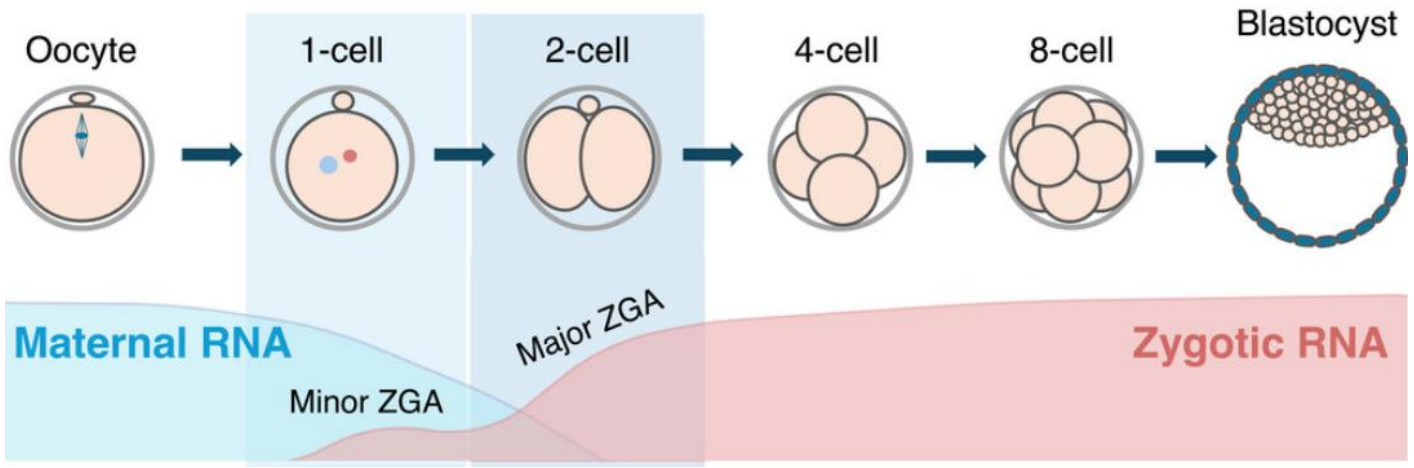


Do all blastomeres remain developmentally equivalent?

1st decision
Outer cells differentiate into **trophectoderm** (TE);
Inner cells form the **inner cell mass** (ICM)

2rd decision
ICM subdivides into **epiblast** (EPI) and **primitive endoderm** (PE)

Zygotic genome activation (ZGA)



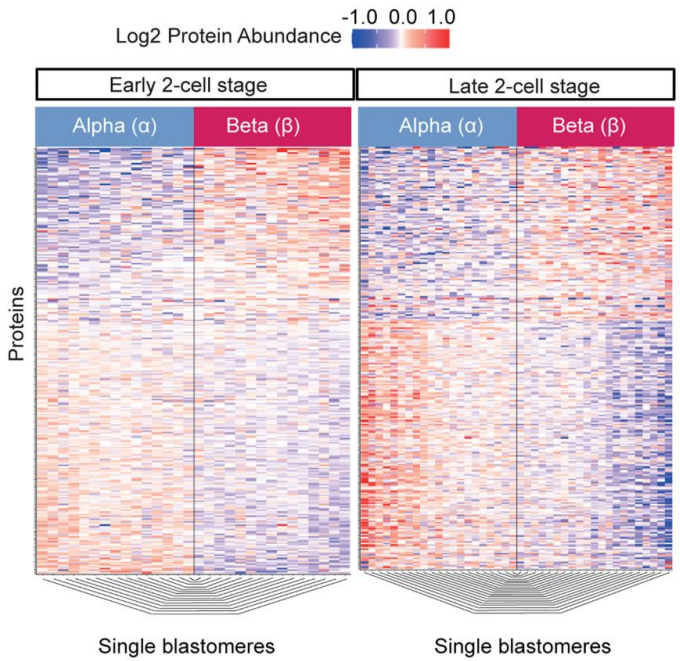
Solberg *et al.*, 2024

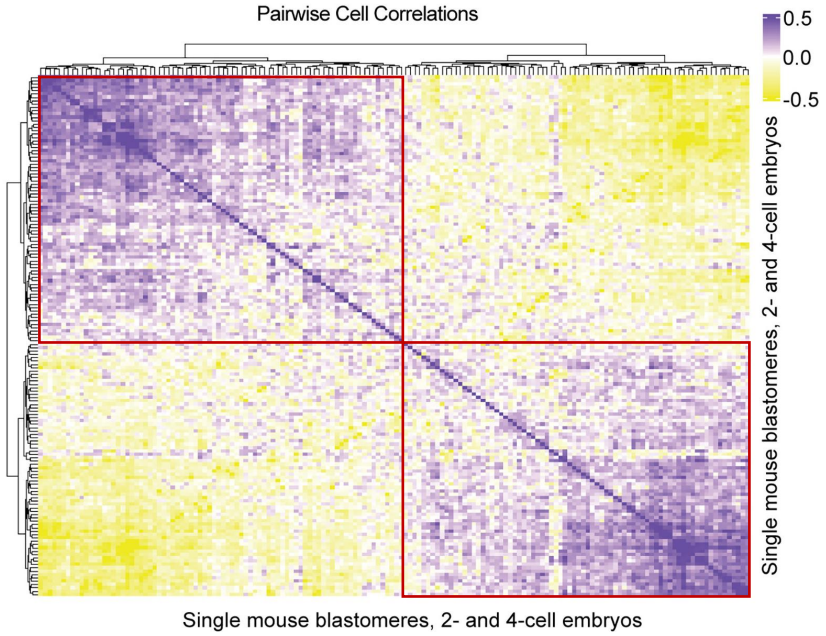
Rely on maternal ribosomes, mRNAs and proteins → Activate and transcribe its own genome

Proteomics change

- **Maternal proteins are actively degraded**
- **Zygotic proteins are actively produced**

Proteomic asymmetry in blastomeres of 2-cell- and 4-cell-stage embryos

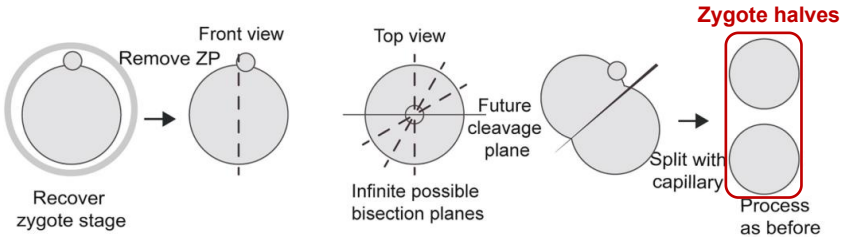


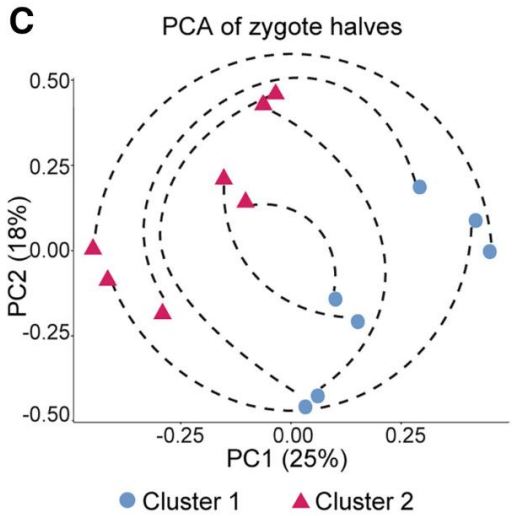


- In both early and late 2-cell stage, each embryo contains two types of blastomere (alpha and beta).
- Proteomic asymmetry persisted across 4-cell embryos.

Do such asymmetries originate earlier?

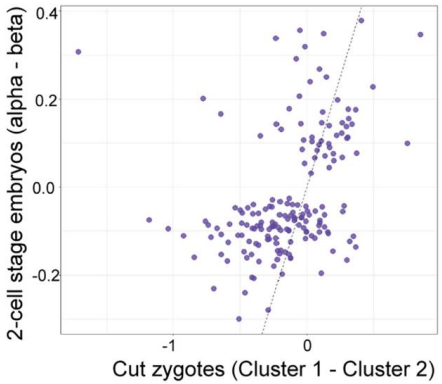
Proteomic asymmetry at zygote stage

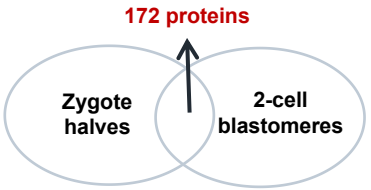




➢ Proteomic asymmetry at the zygote stage.

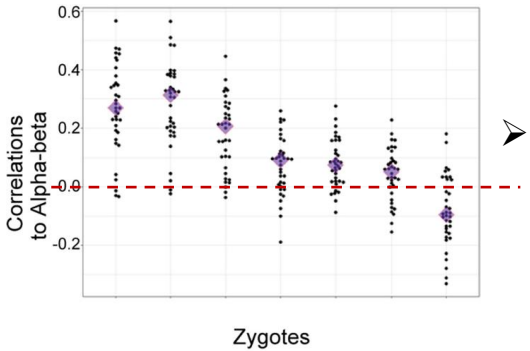
Correlation of protein fold change





Cluster 1 ➡ Alpha-like

Cluster 2 ➡ Beta-like



➢ Most zygote halves showd alpha-beta-like differences.

How alpha and beta differences evolve over time?

Dynamics of alpha and beta differences

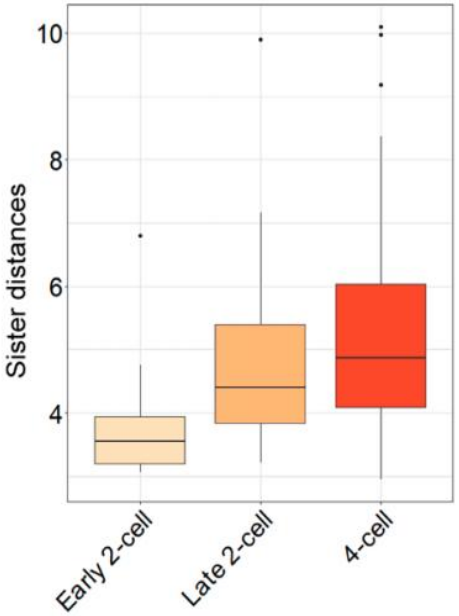
Alpha identity

Psmc4

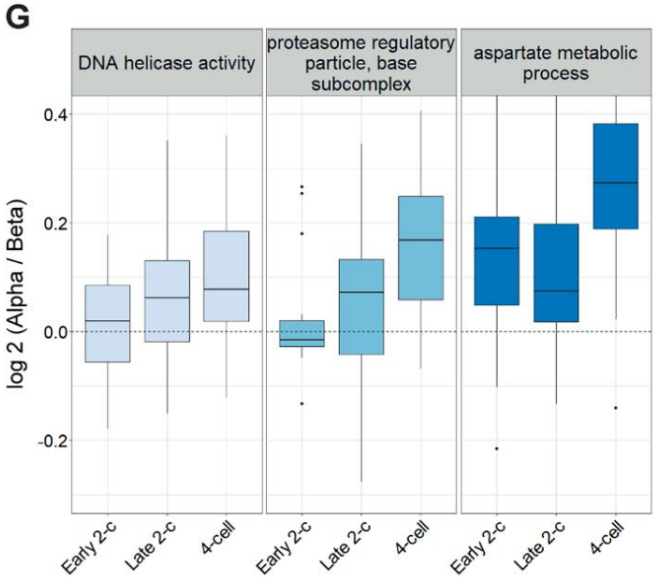
Beta identity

Gps1
Nedd8

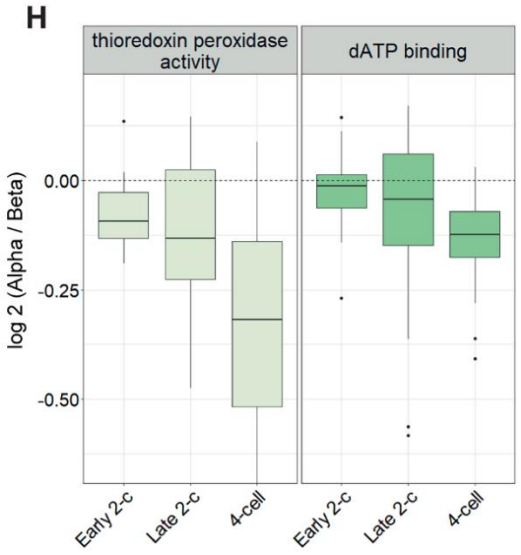
Proteomics difference



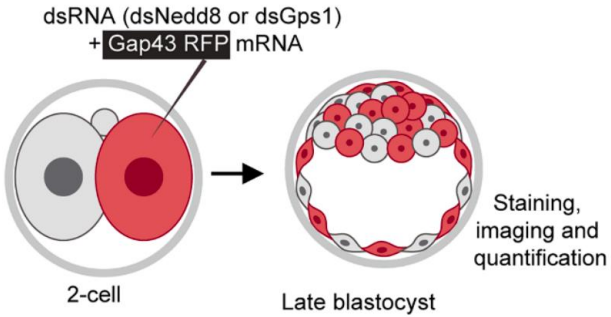
Alpha identity



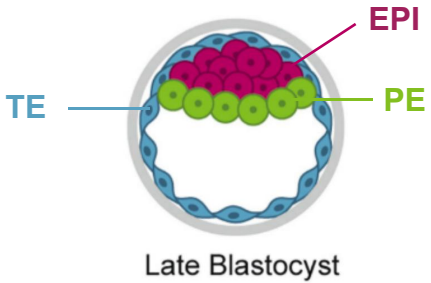
Beta identity



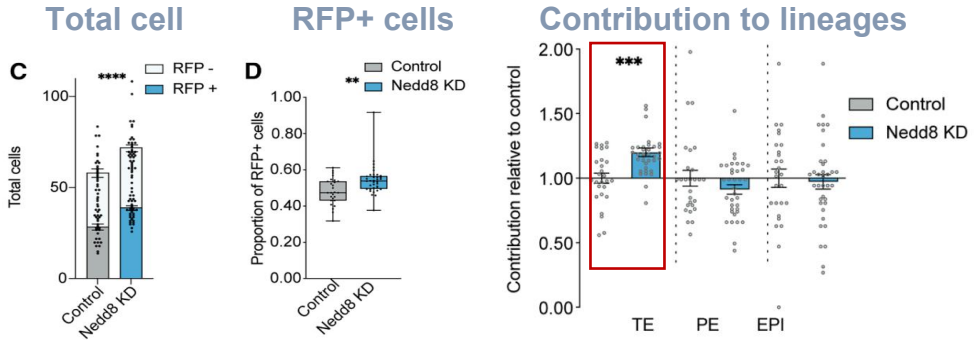
The role of beta-enriched proteins in lineage fate



Psmc4 | Alpha identity | Beta identity | Gps1 Nedd8

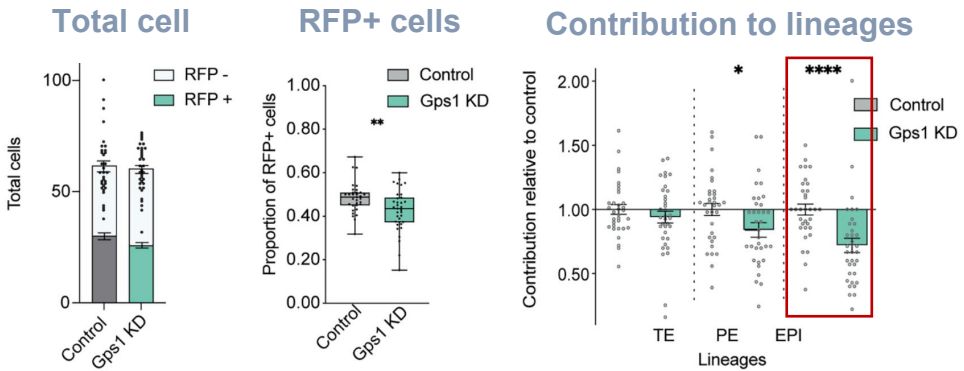


Nedd8



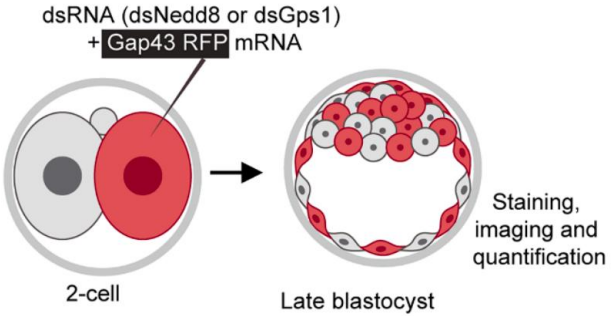
➢ Nedd8 restricts proliferation and TE differentiation

Gps1

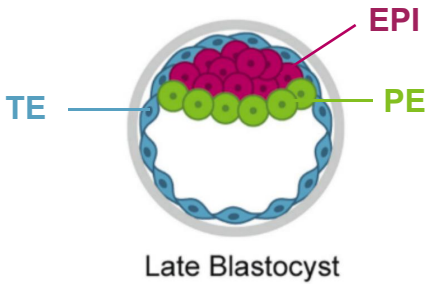


➢ GPS1 promotes proliferation and EPI differentiation

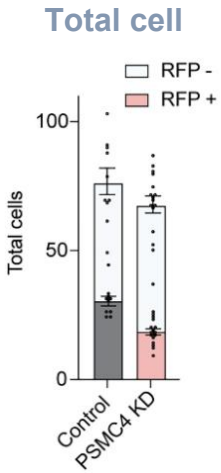
The role of alpha-enriched proteins in lineage fate

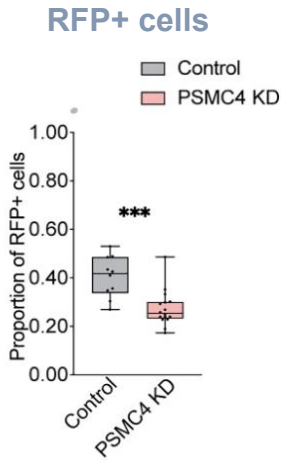


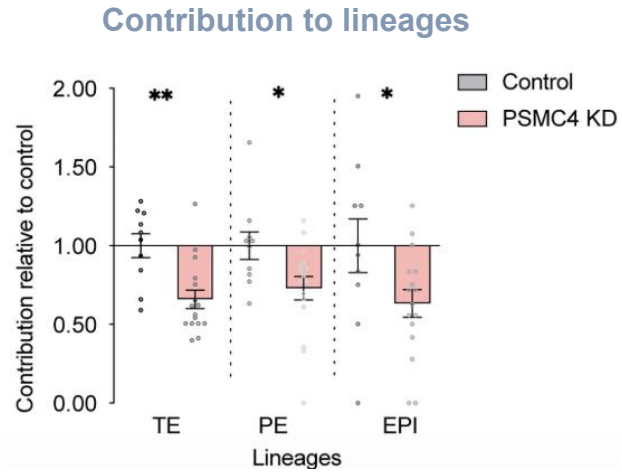
Psmc4 | Alpha identity | Beta identity | Gps1 Nedd8



Psmc4

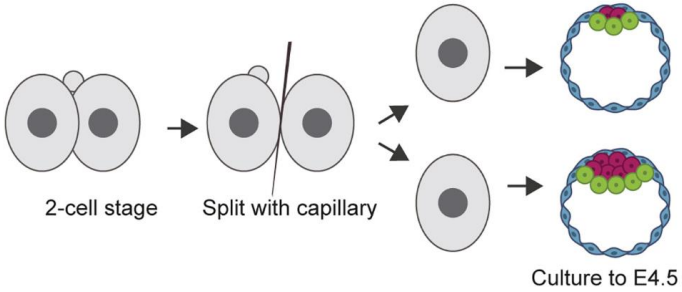


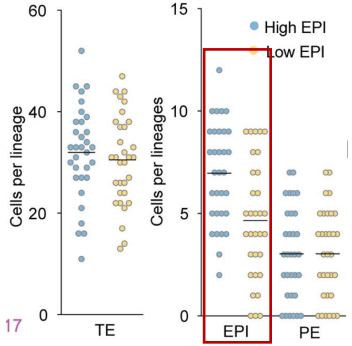


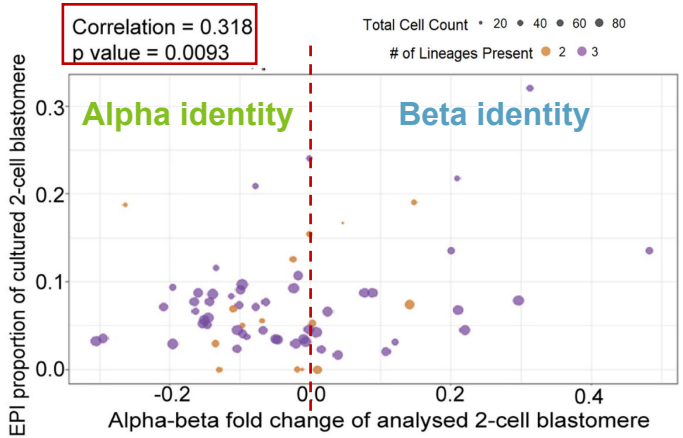


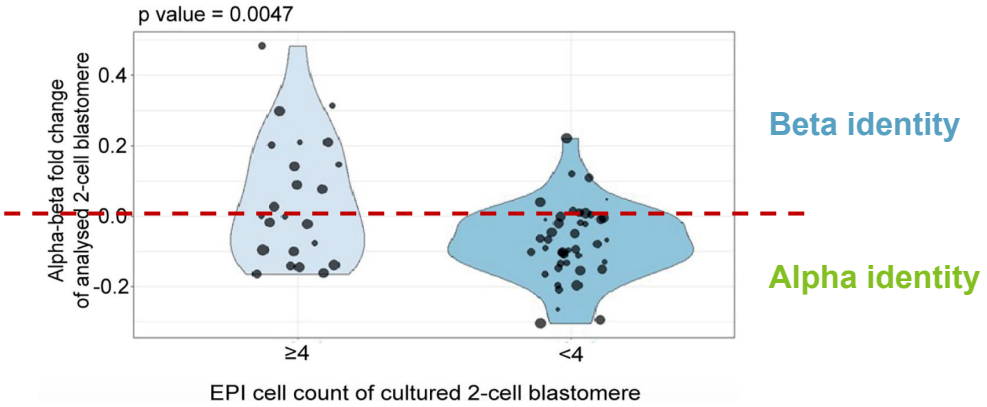
➢ **Psmc4 promotes proliferation and support all lineage specialization**

Different developmental potential of alpha and beta blastomeres





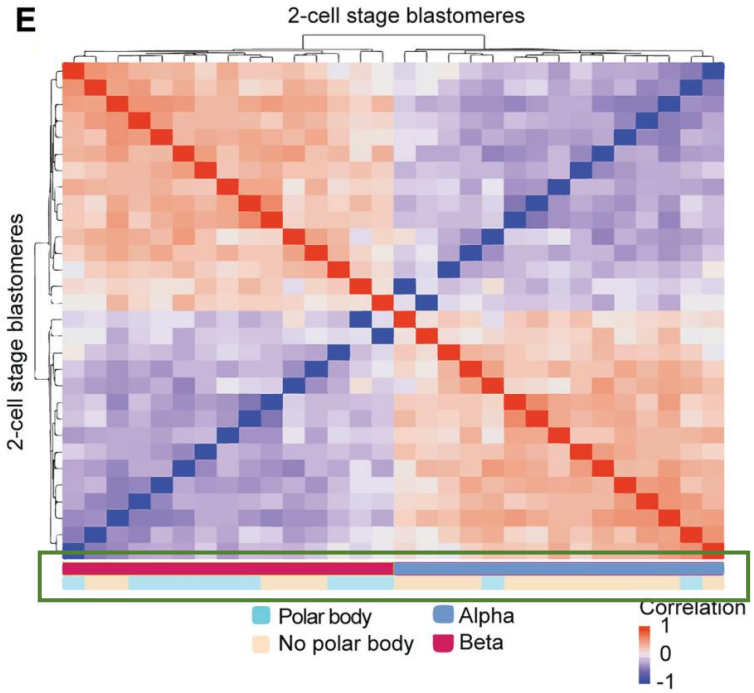


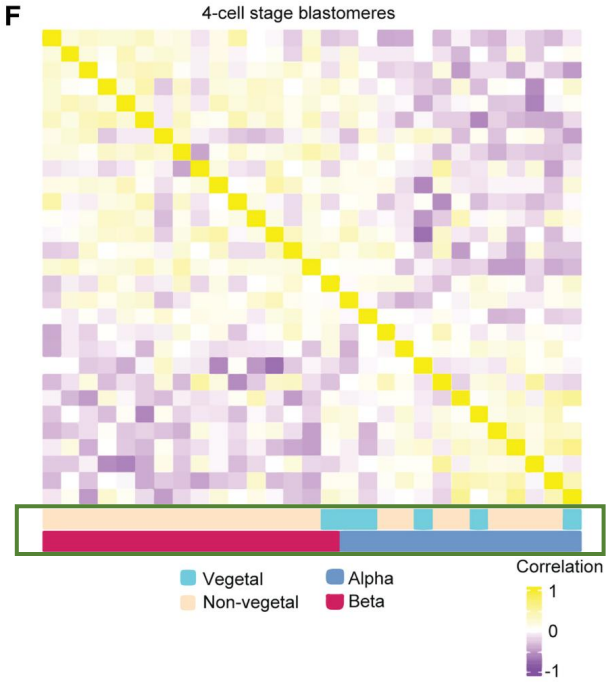


Beta blastomeres → Higher proportion of EPI
Alpha blastomeres → Lower proportion of EPI

- **Beta blastomeres promote epiblast formation**

Different developmental potential of alpha and beta blastomeres



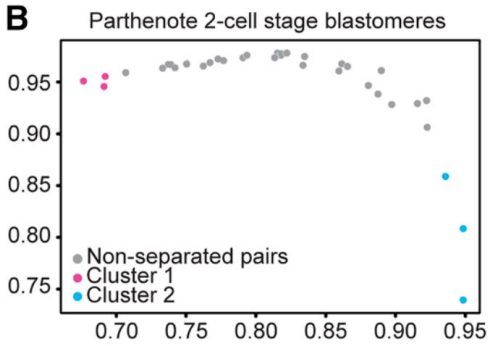


- Blastomere **inheriting the second polar body** was more likely to be classified as **beta**
- **Vegetal blastomeres** were significantly more likely to be classified as **alpha**

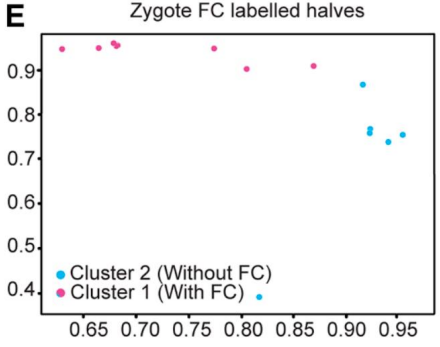
How to trigger such proteomics asymmetry?

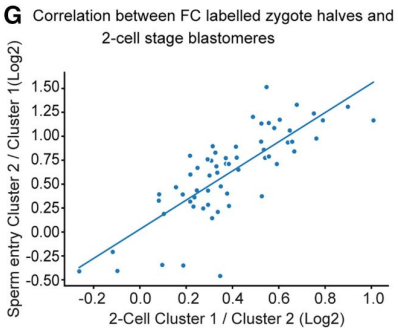
Fertilization triggers the breaking of symmetry

Parthenogenetic embryos (孤雌胚胎)



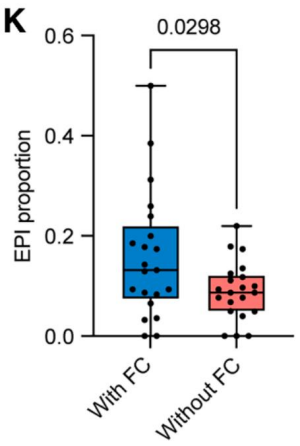
Fertilized embryos





FC: Fertilization cone (受精锥)

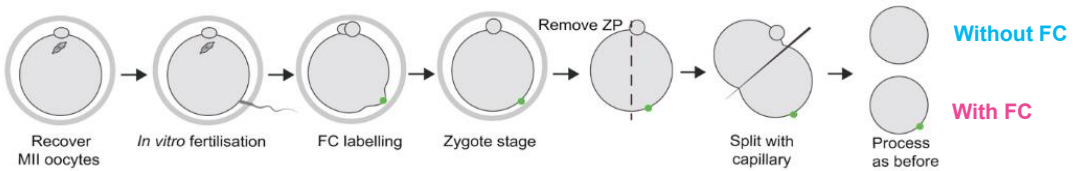
Lineage development



➢ **Fertilization triggers proteome asymmetry in the zygote.**

➢ **Fertilization leads to higher EPI proportion.**

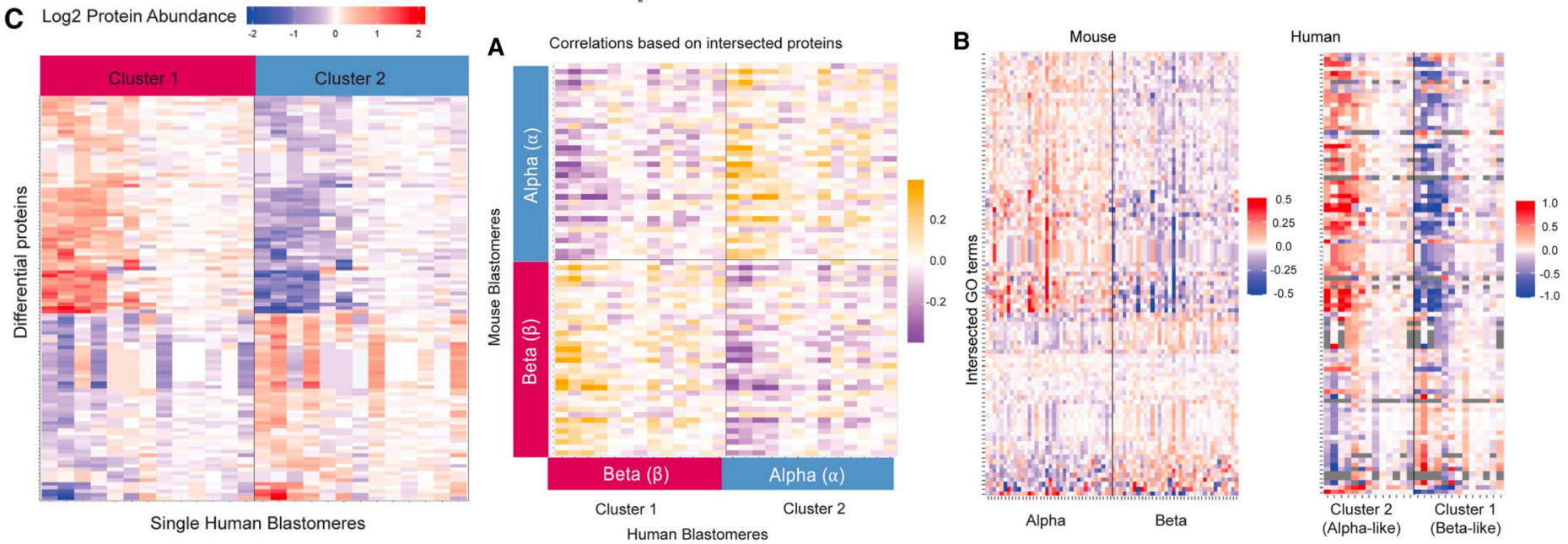
Fertilized embryos processing procedure



Whether the proteomic asymmetry is conserved in human embryos?

Proteome asymmetry is conserved in human 2-cell_x0002_stage embryos

Cross-species annotation

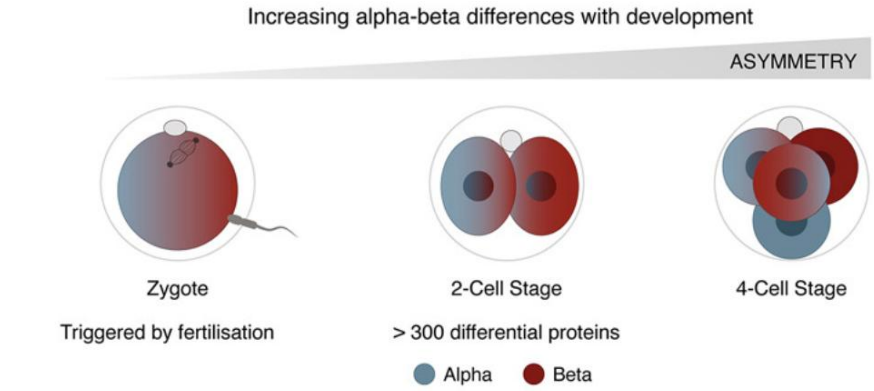


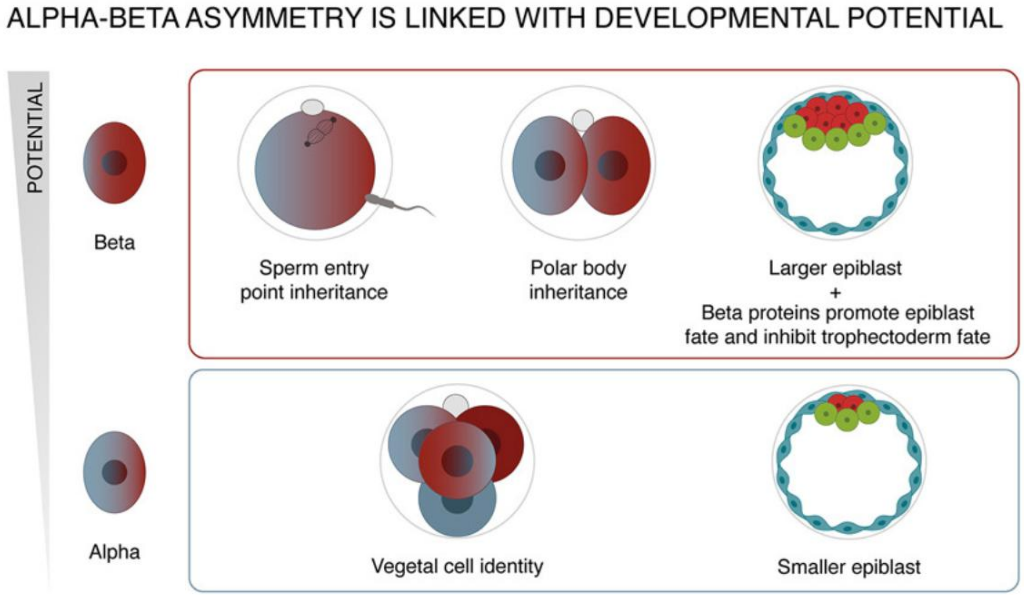
➢ **Strong directional concordance between mouse and human.**

Summary

Summary

- Single-cell proteomics reveals early proteome asymmetry in human and mouse.





Thanks for your listening!

—