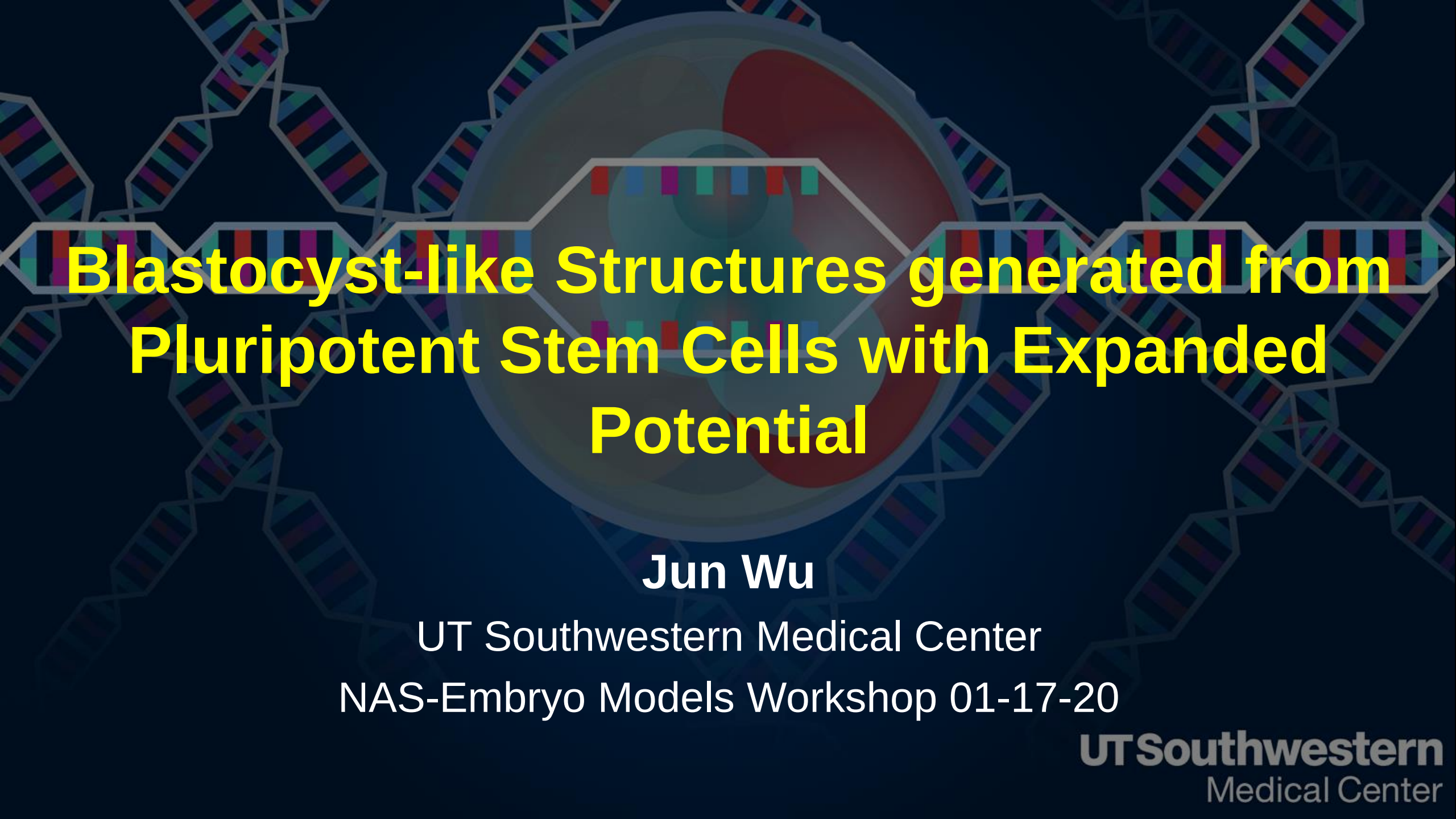




Blastocyst-like Structures generated from Pluripotent Stem Cells with Expanded Potential

Jun Wu

UT Southwestern Medical Center
NAS-Embryo Models Workshop 01-17-20

Pluripotent stem cells



Blastocyst



Somatic cells

Pluripotent stem cells

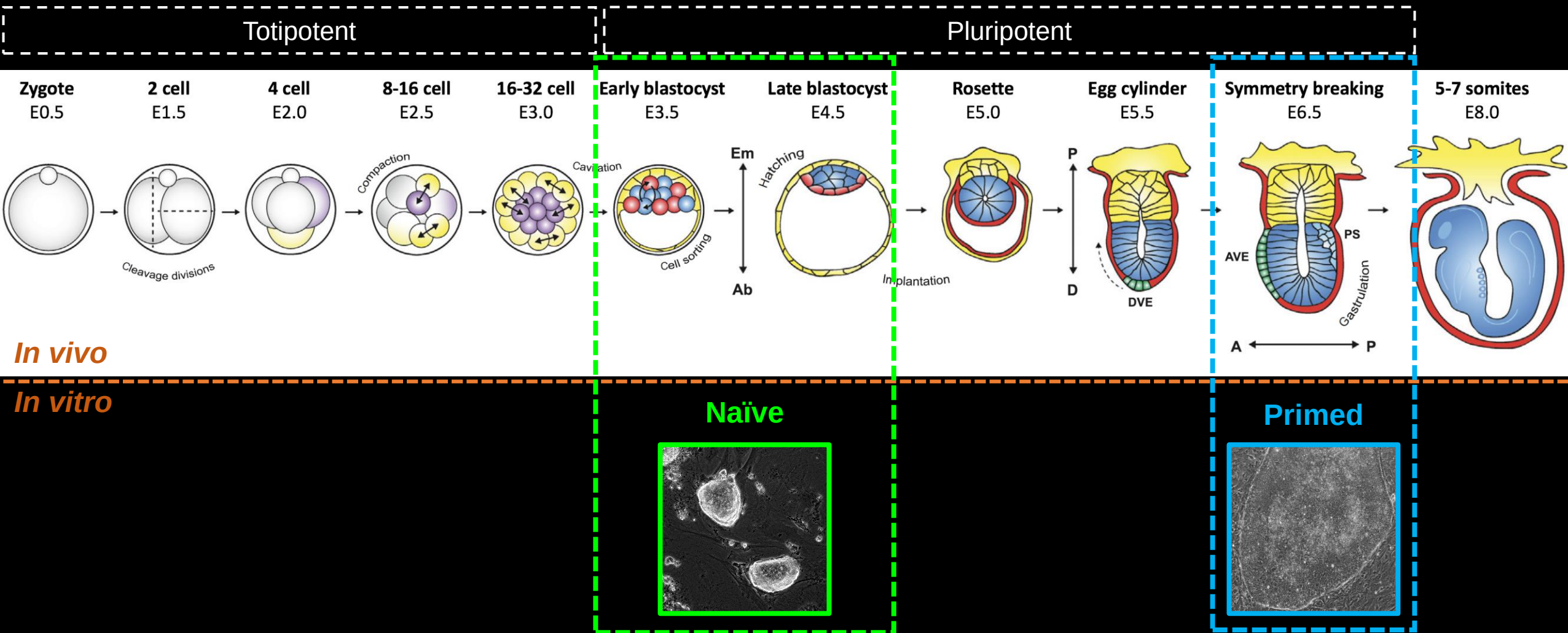


Blastocyst

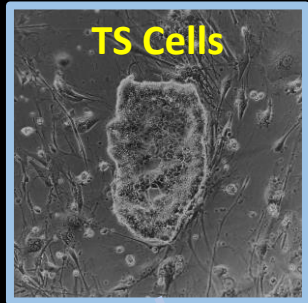


Somatic cells

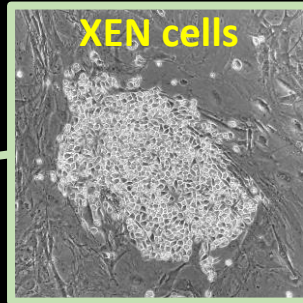
Adaptations of pluripotency continuum *in vitro*



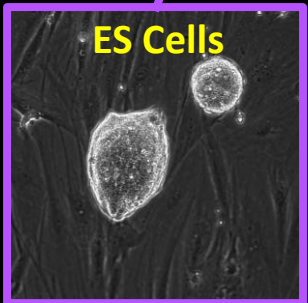
How to “build” a blastocyst using stem cells?



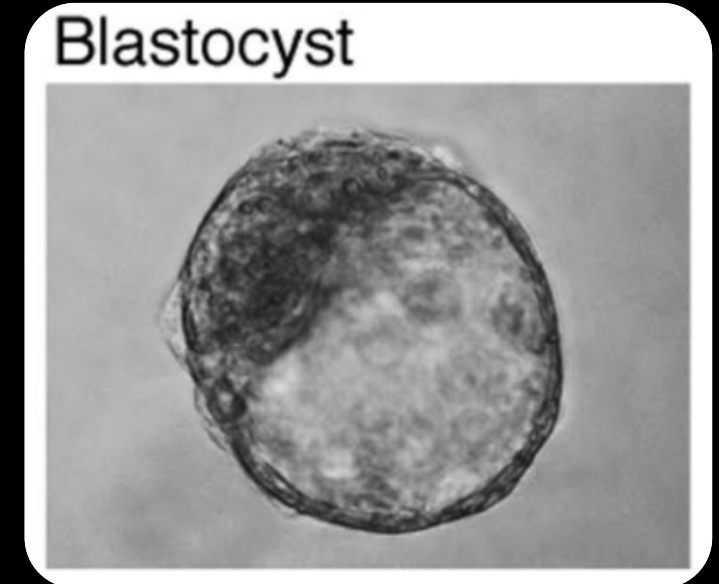
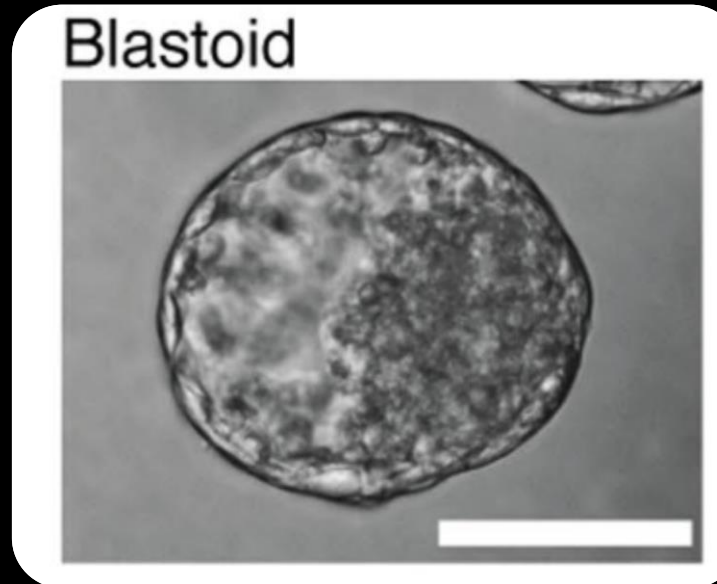
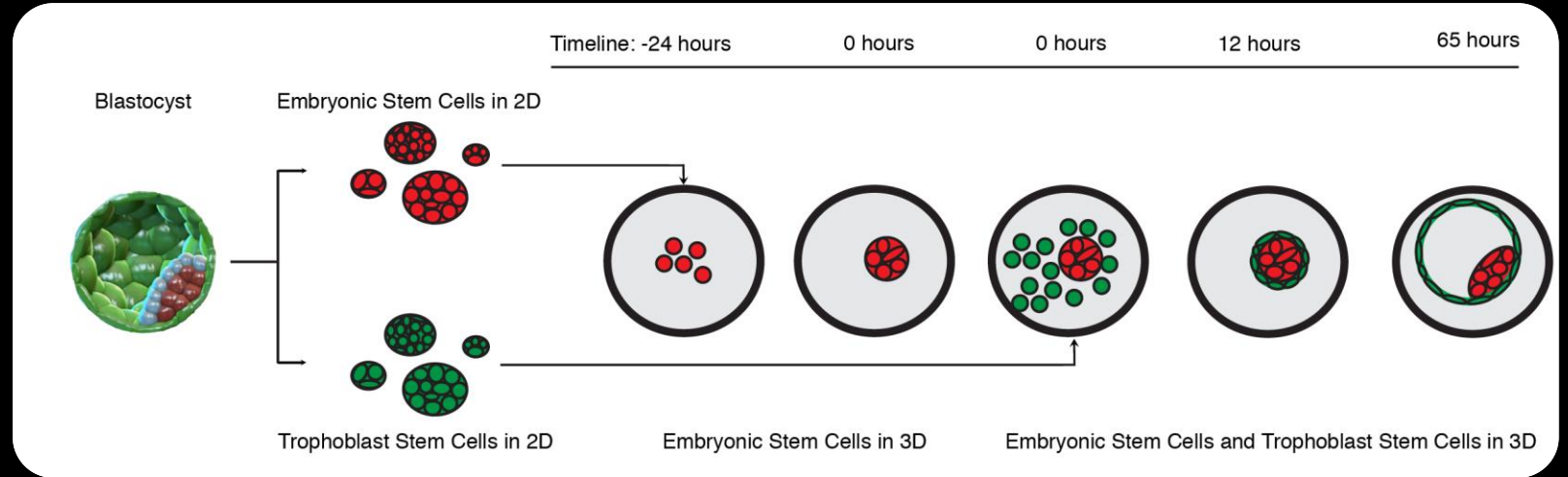
*Tanaka et al
Science, 1998*



*Kunath et al
Development, 2005*

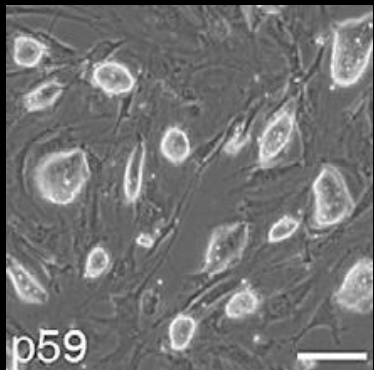
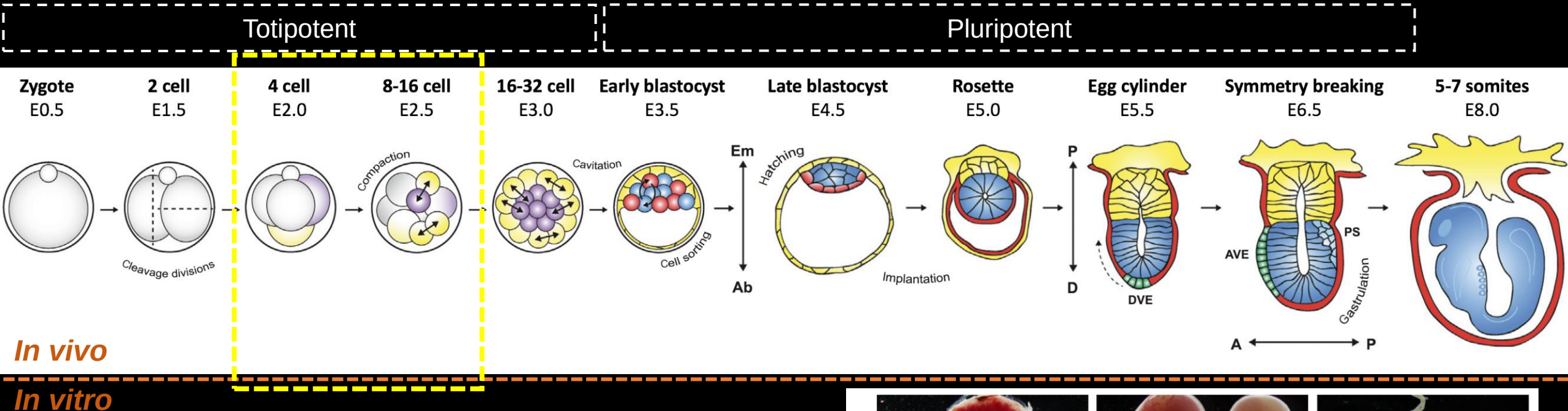


*Martin, PNAS, 1981
Evans & Kaufman, Nature, 1981*

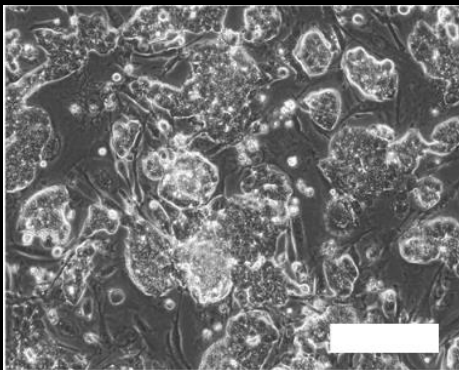


Rivron et al, Nature, 2018

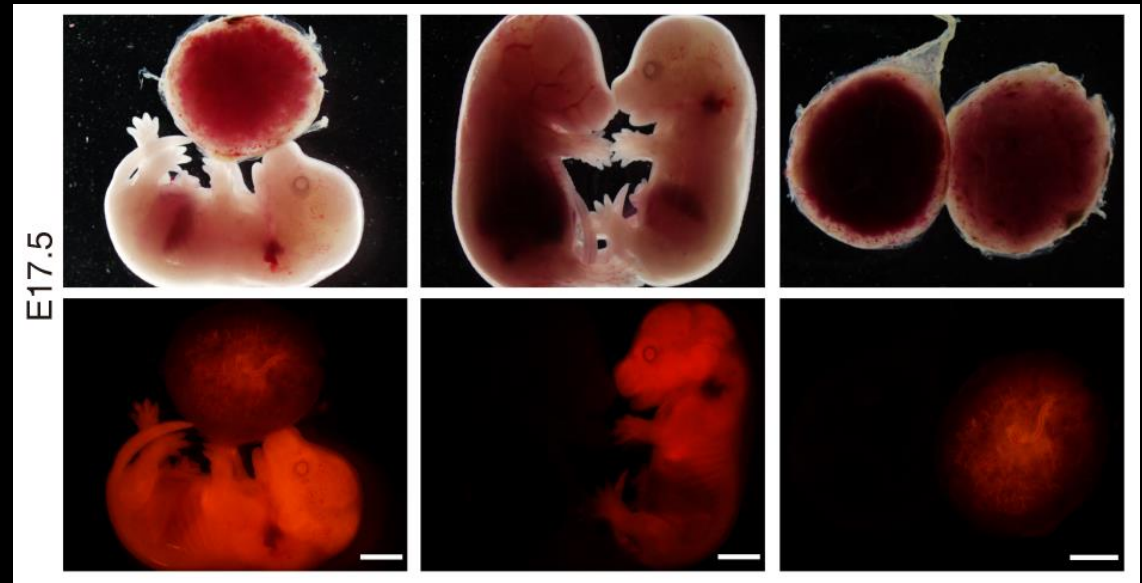
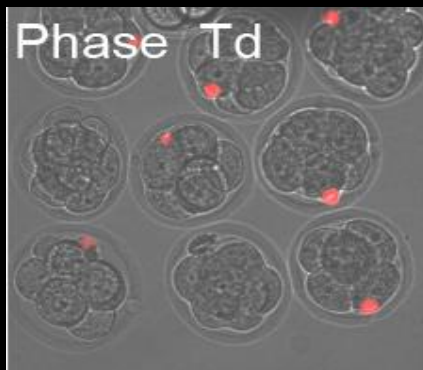
EPSCs: pluripotent stem cells with expanded potential



LIF, CH (GSK3i)
DiM (GPCRi)
MiH (PARPi)



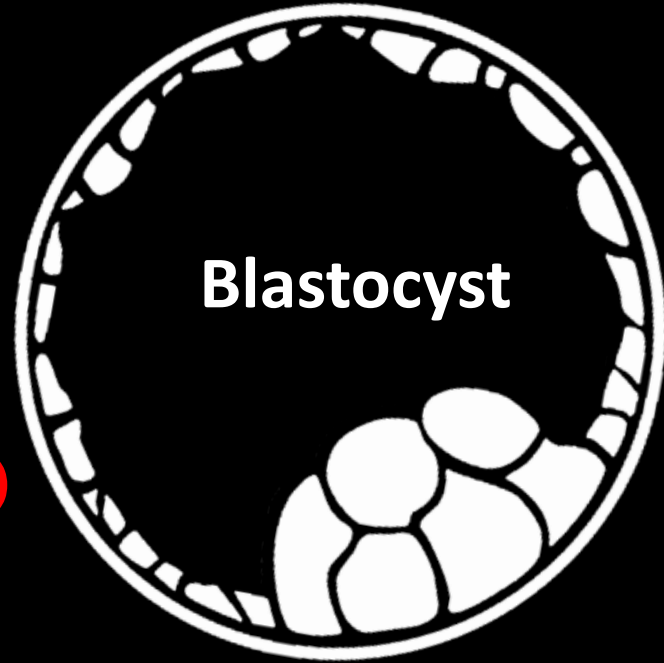
LIF, CH, PD03 (MEKi)
SB203580 (P38i)
VIII (JNKi), XAV939 (TNKSi)
A-419259 (SRCi)



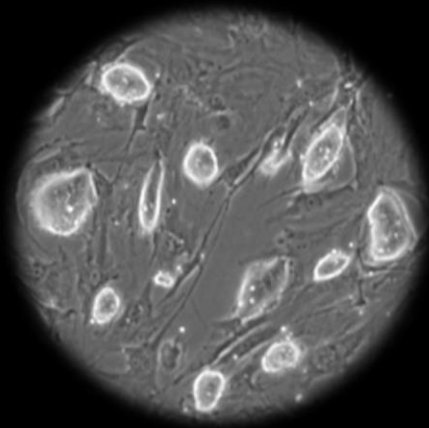
4-16 cell
blastomeres



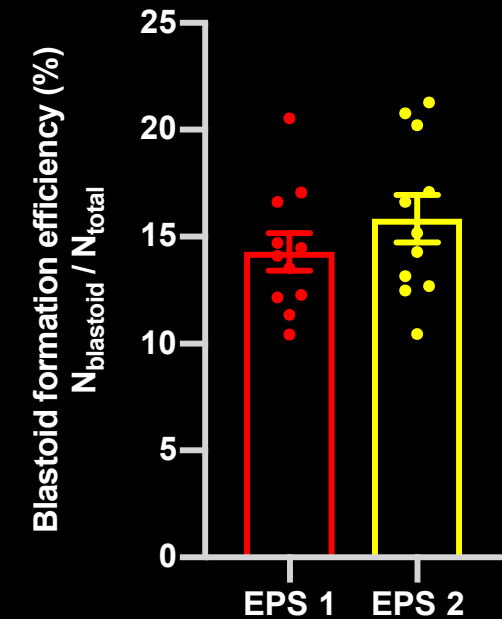
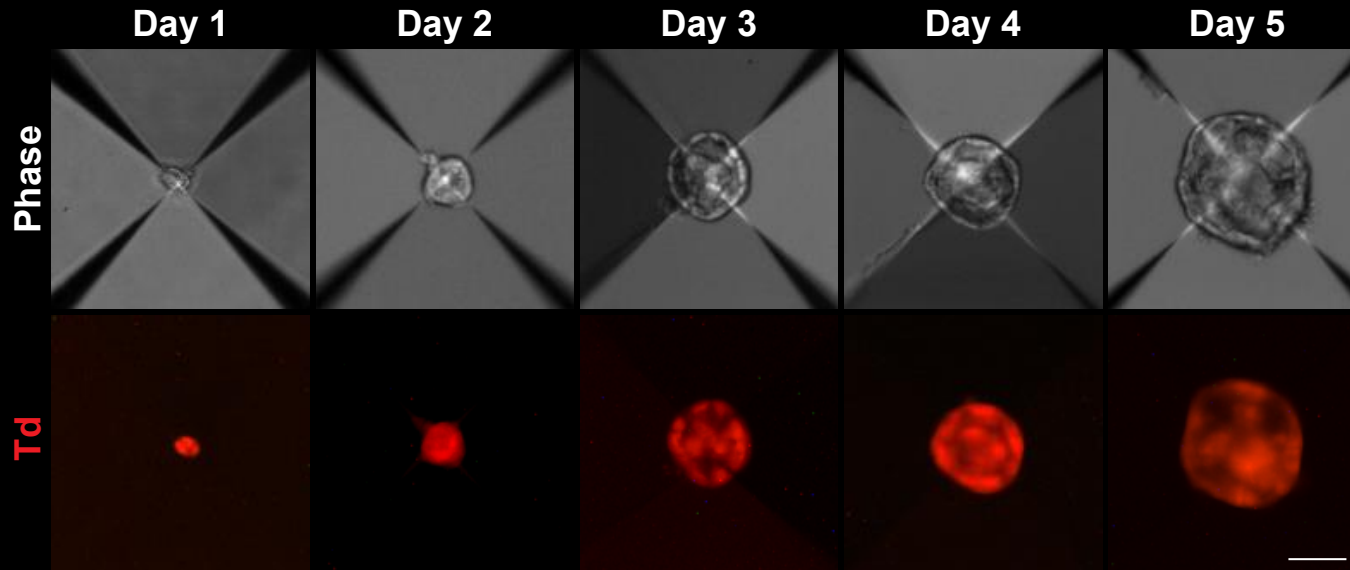
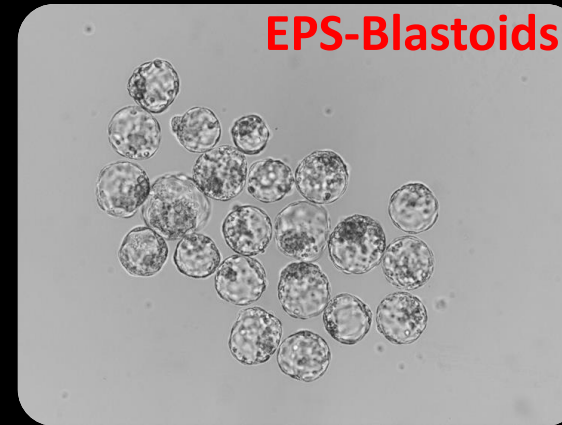
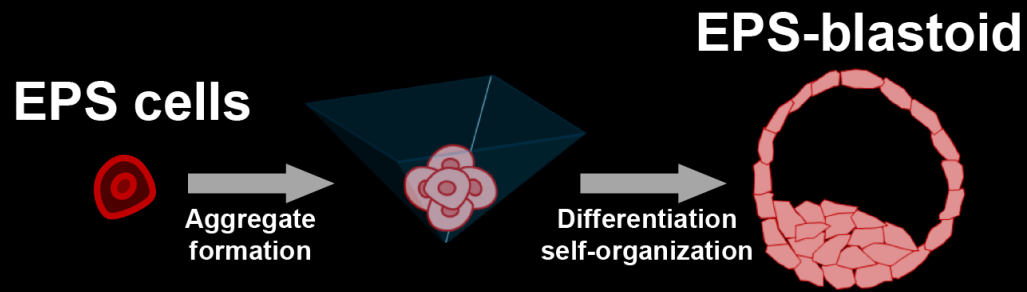
Blastocyst



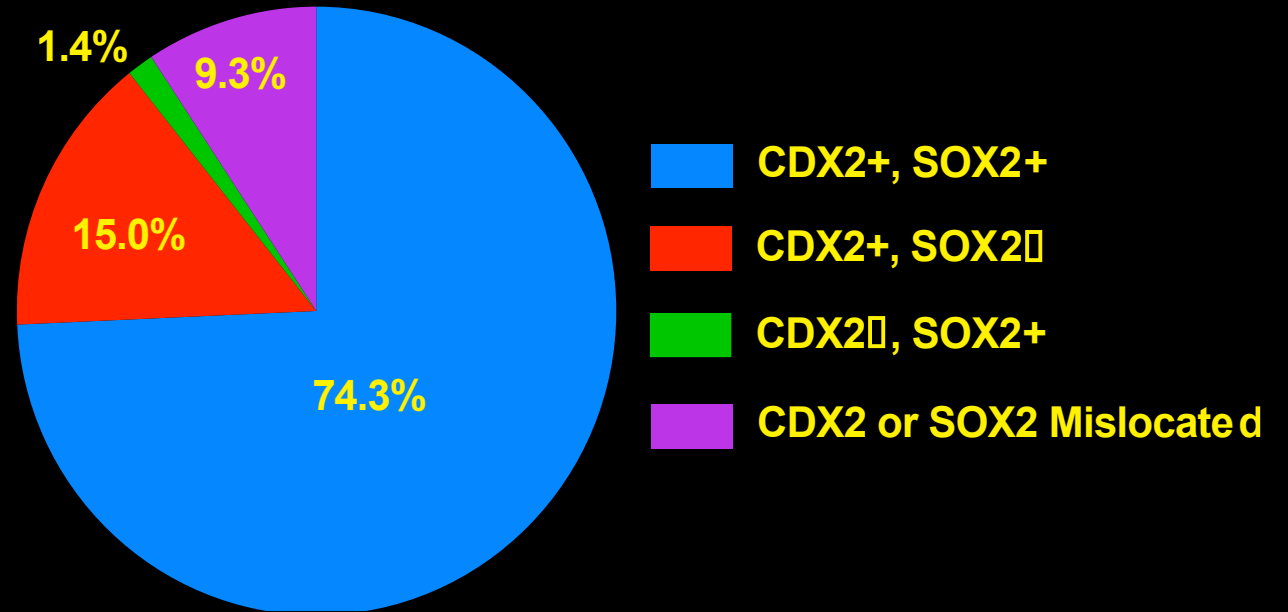
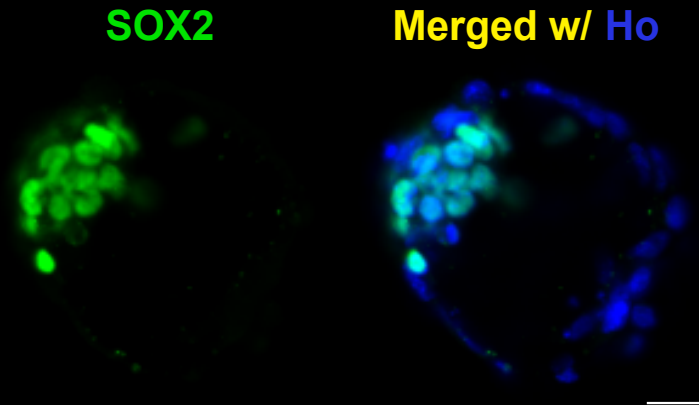
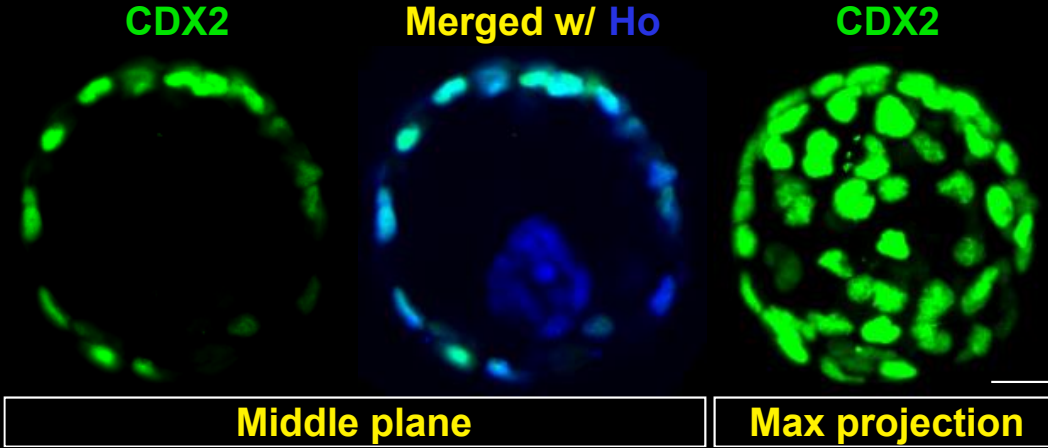
EPSCs



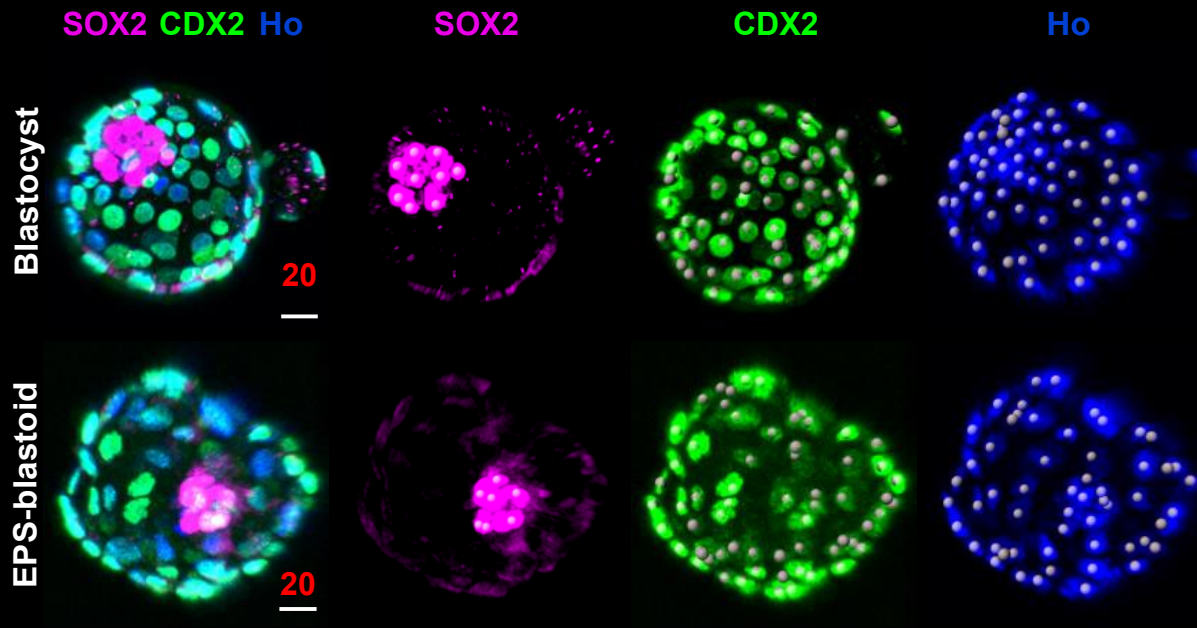
EPS cell derived blastocyst-like structure (**EPS-blastoid**)



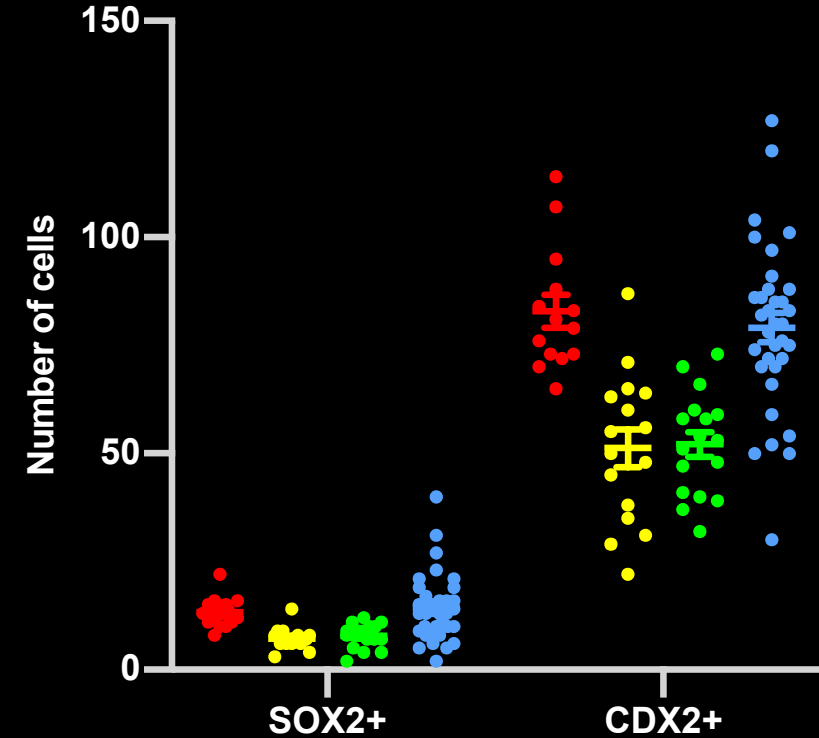
First cell fate determination in EPS-blastoids: **TE** & **ICM**



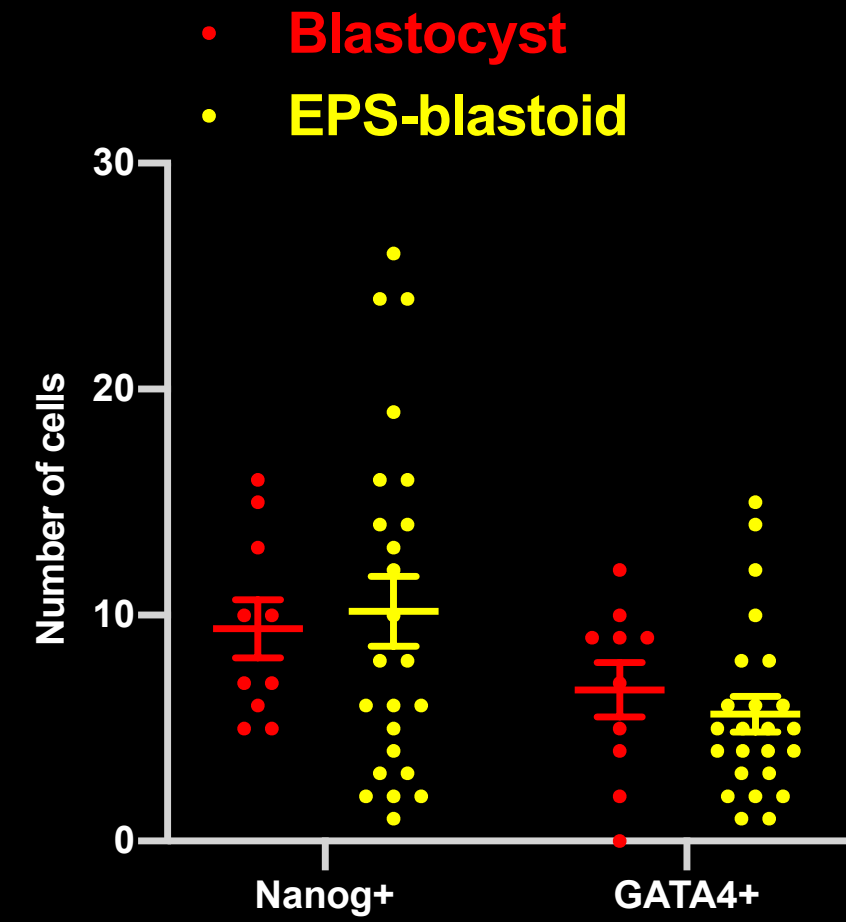
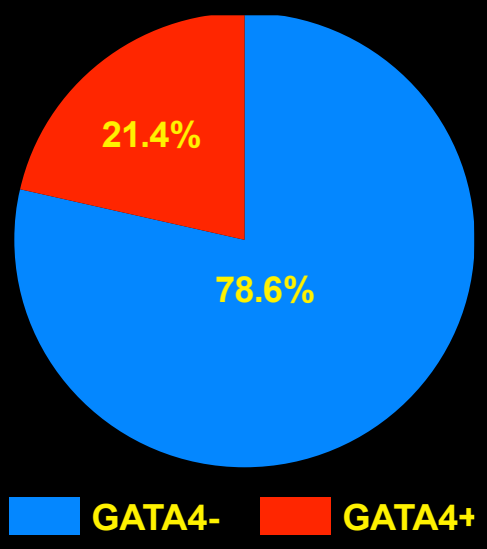
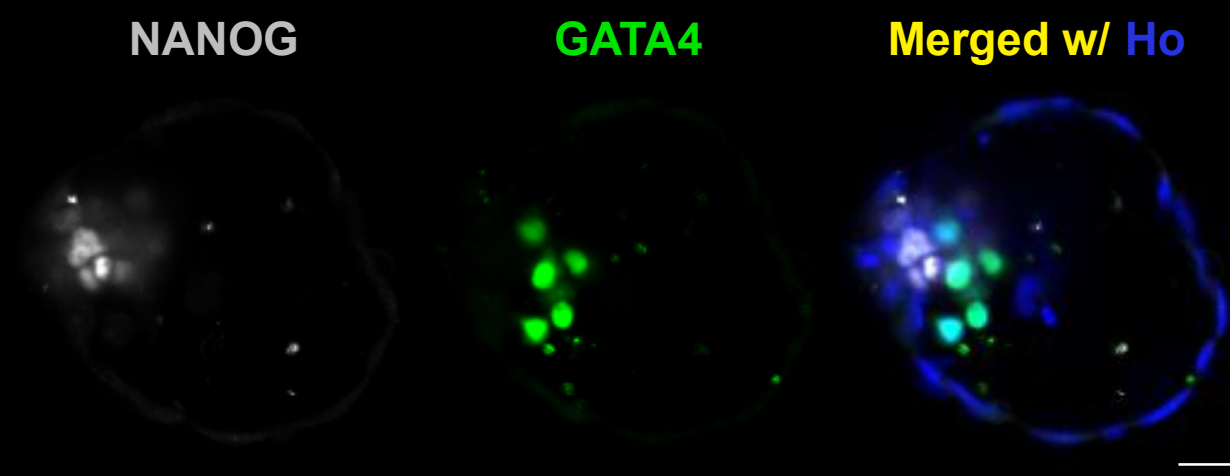
First cell fate determination in EPS-blastoids: **TE** & **ICM**



- **Blastocyst**
- **EPS-blastoid (day 4)**
- **EPS-blastoid (day 5)**
- **EPS-blastoid (day 6)**

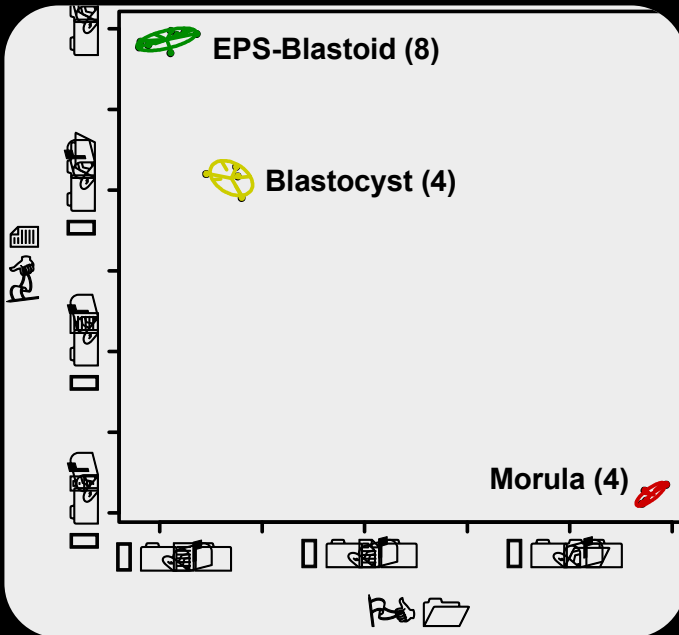


Second cell fate determination in EPS-blastoids: **EPI** & **PE**

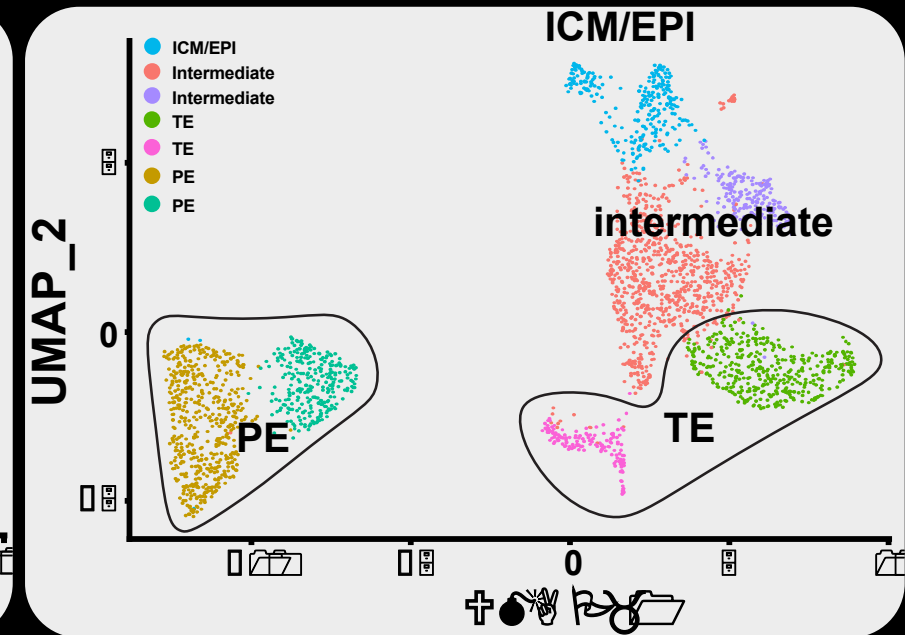
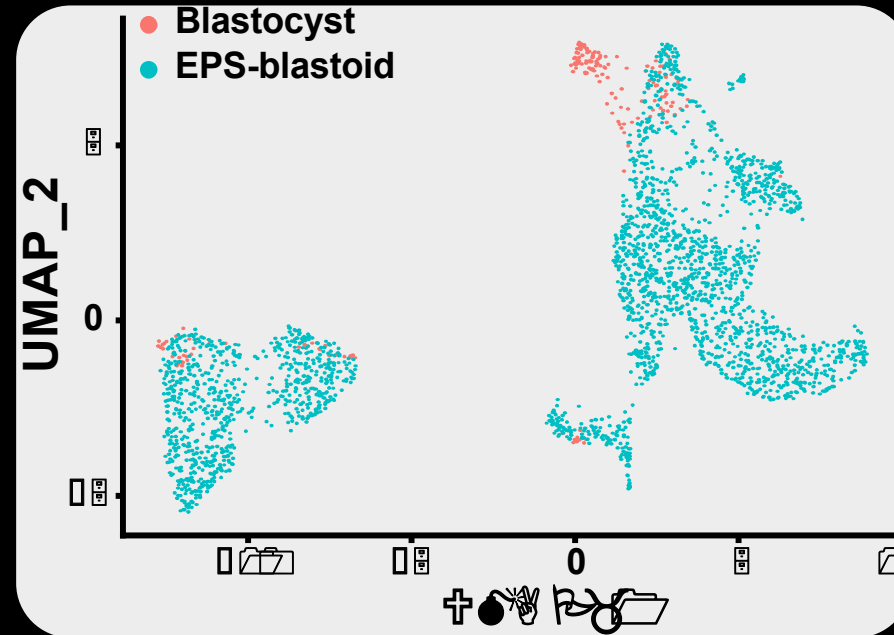


Transcriptomic features of EPS-blastoids

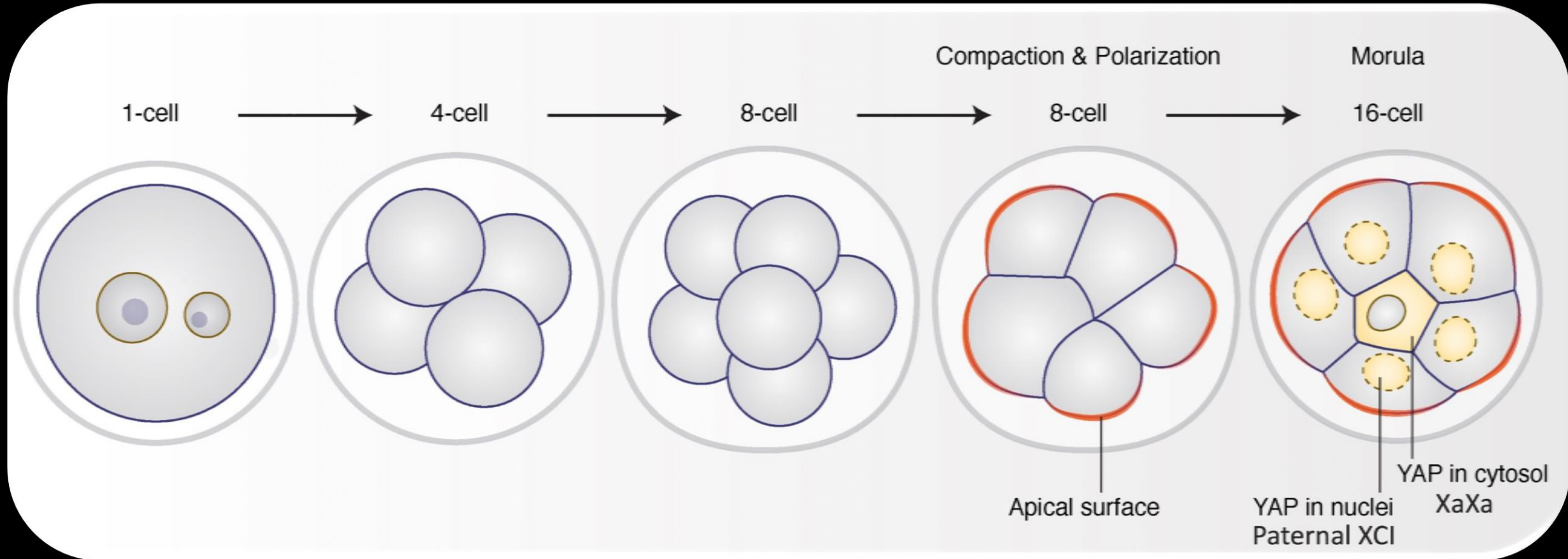
Bulk RNA-Seq



scRNA-seq

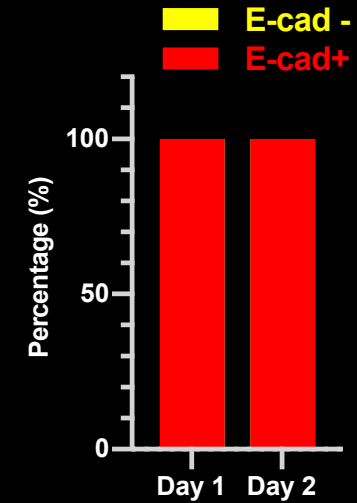
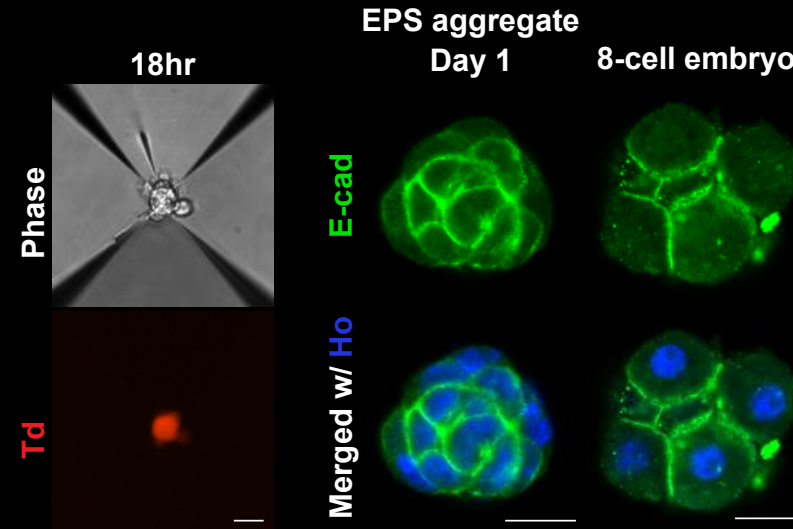


EPS-blastoid formation mimic pre-implantation development

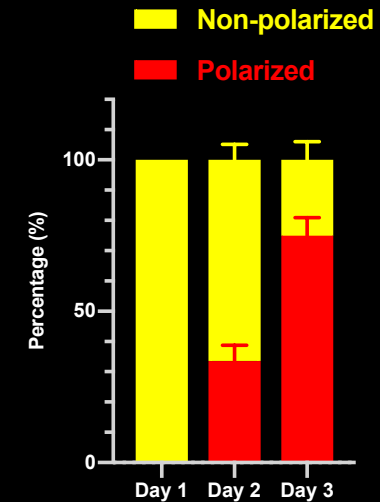
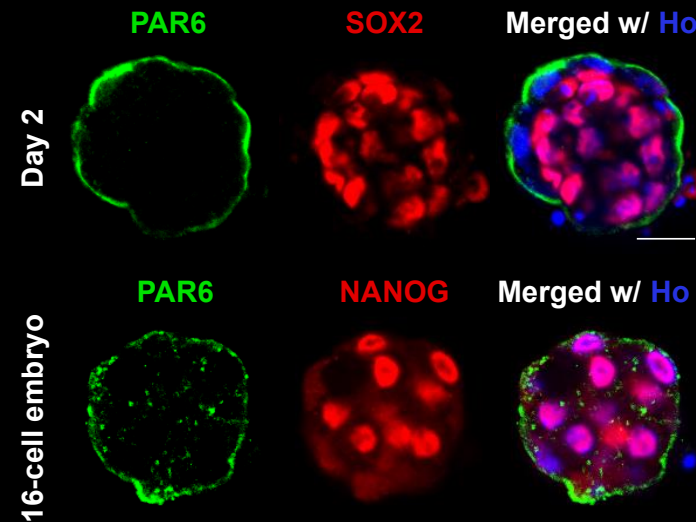


Compaction and Polarization

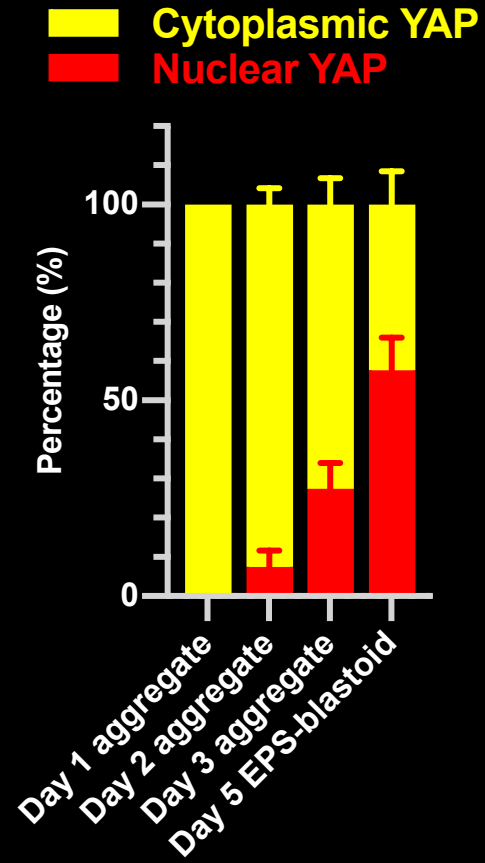
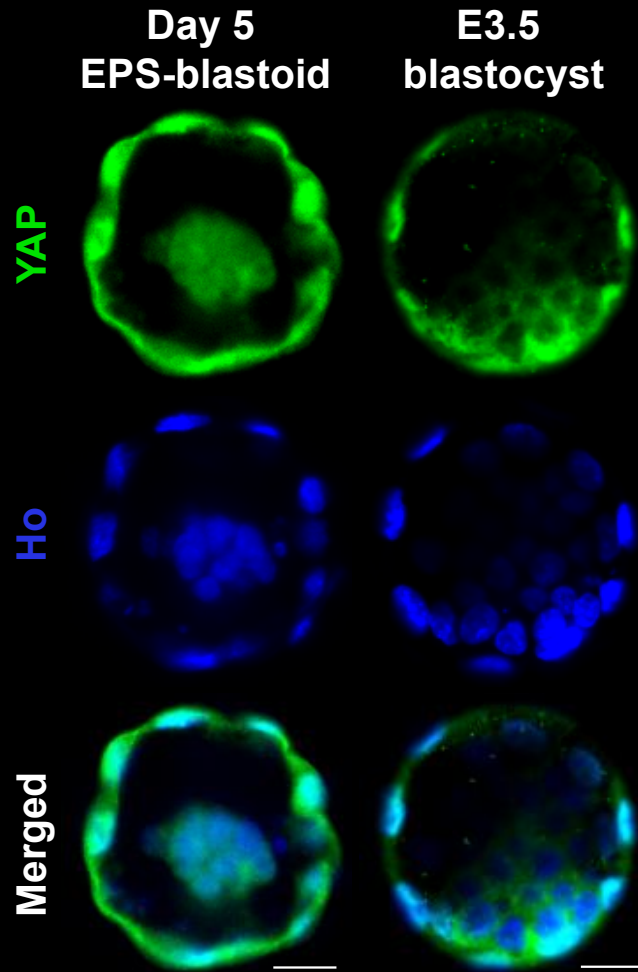
Compaction



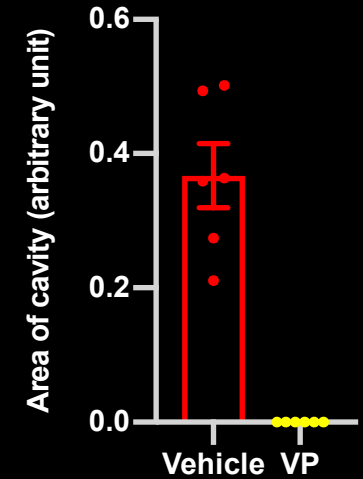
Polarization



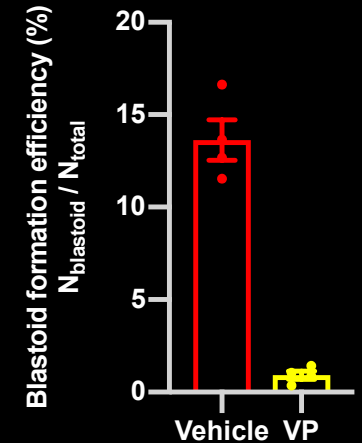
Hippo-YAP signaling



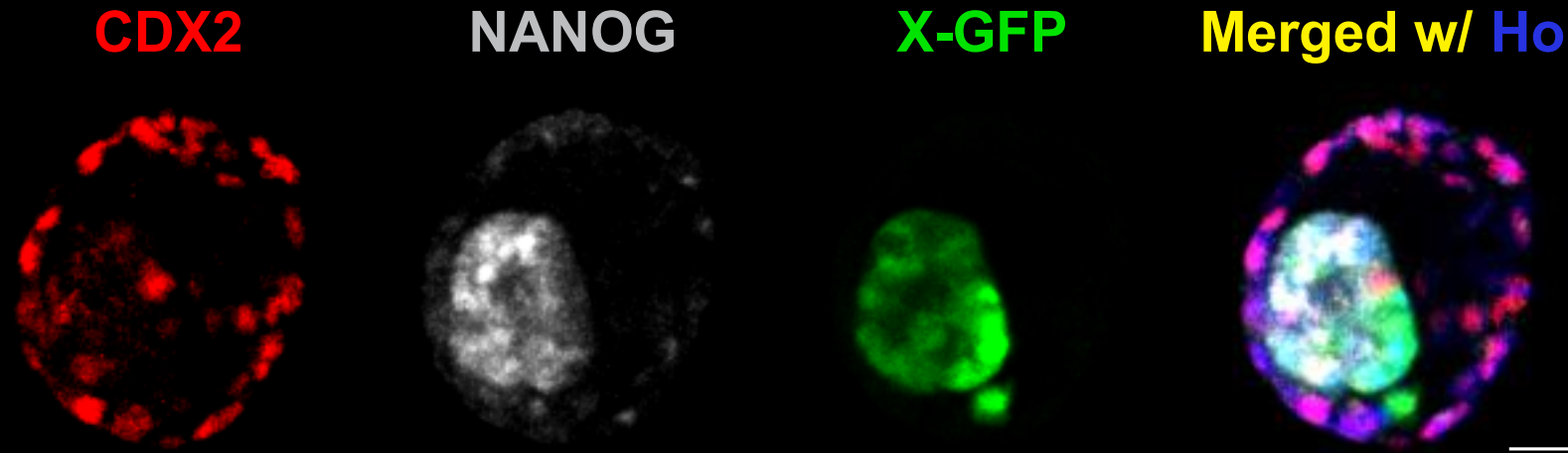
Mouse embryos



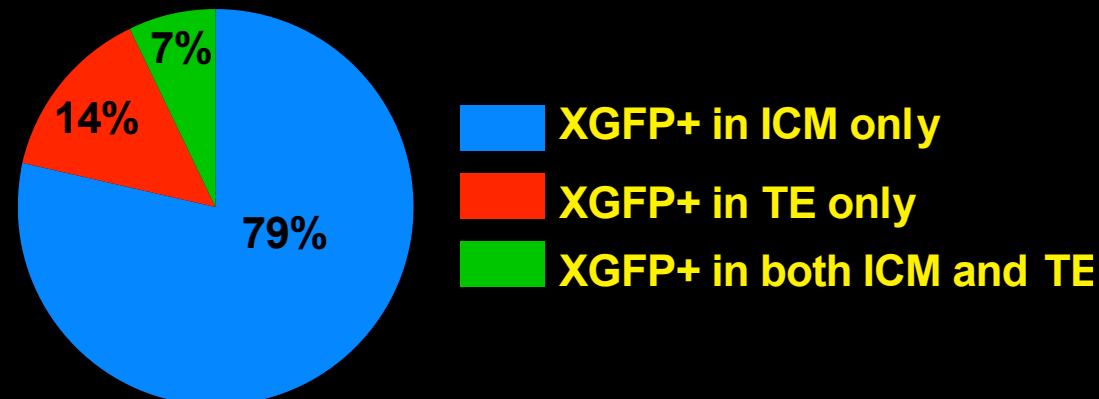
EPS cell aggregates



Paternal X-inactivation in TE

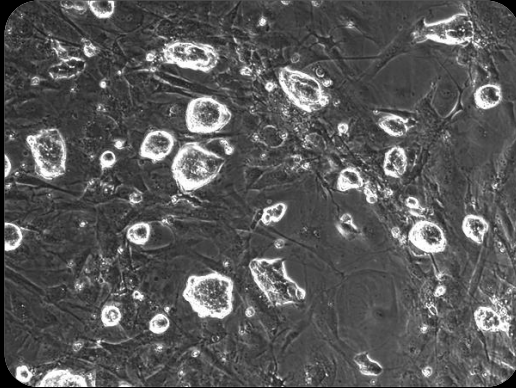


Frequency of EPS-blastoid categories

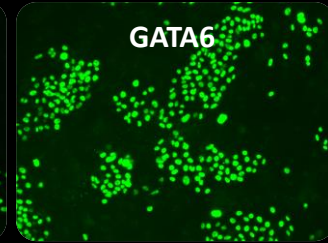
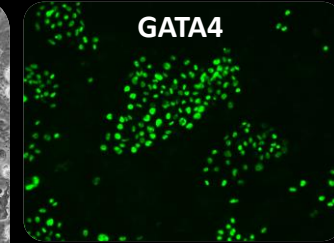
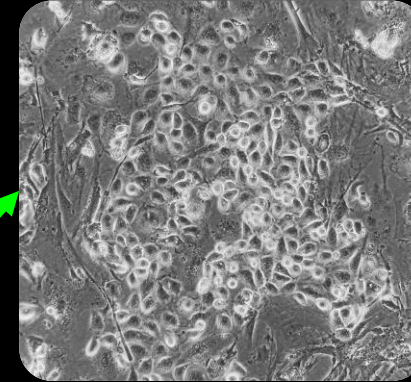


Functional characterization of EPS-blastoids

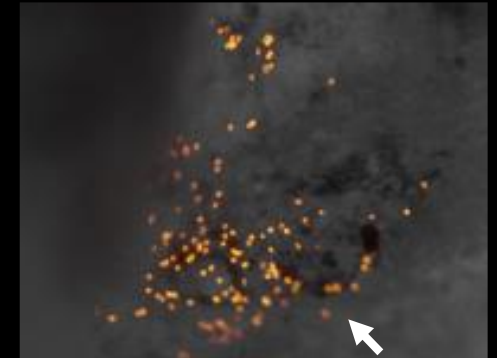
Blastoid-ESCs



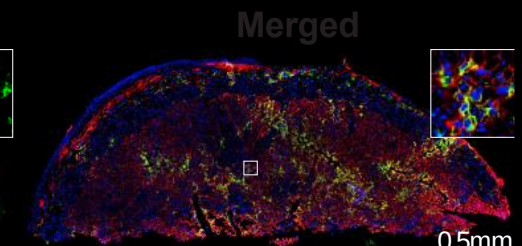
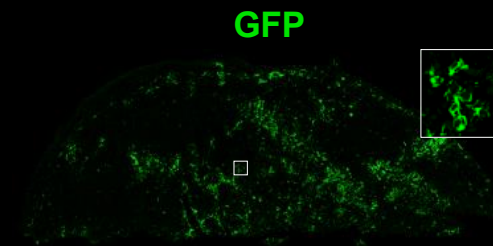
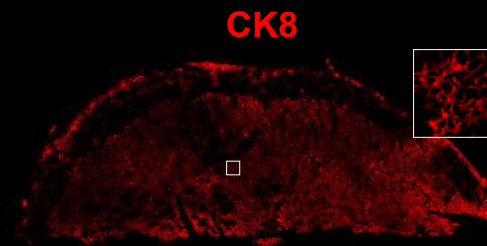
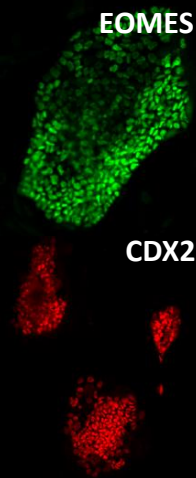
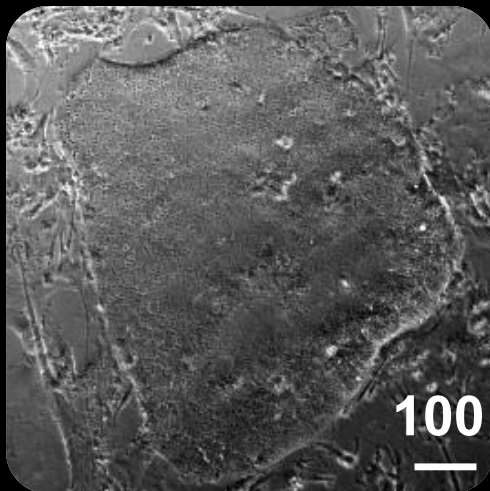
Blastoid-XEN cells



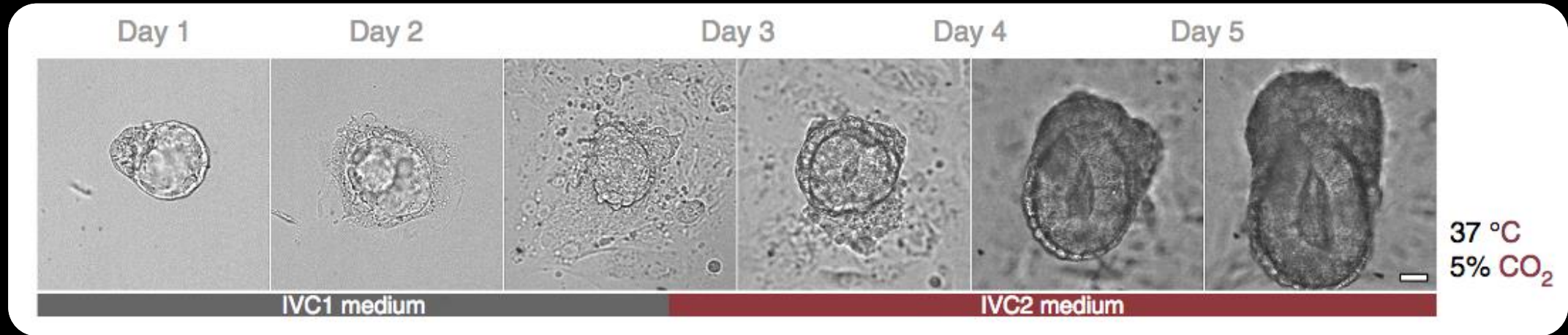
Td



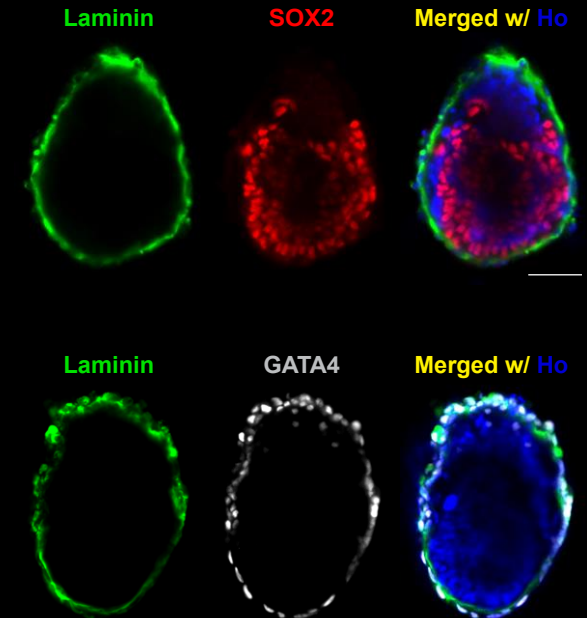
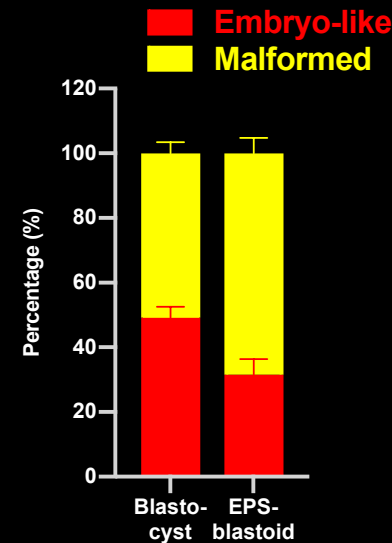
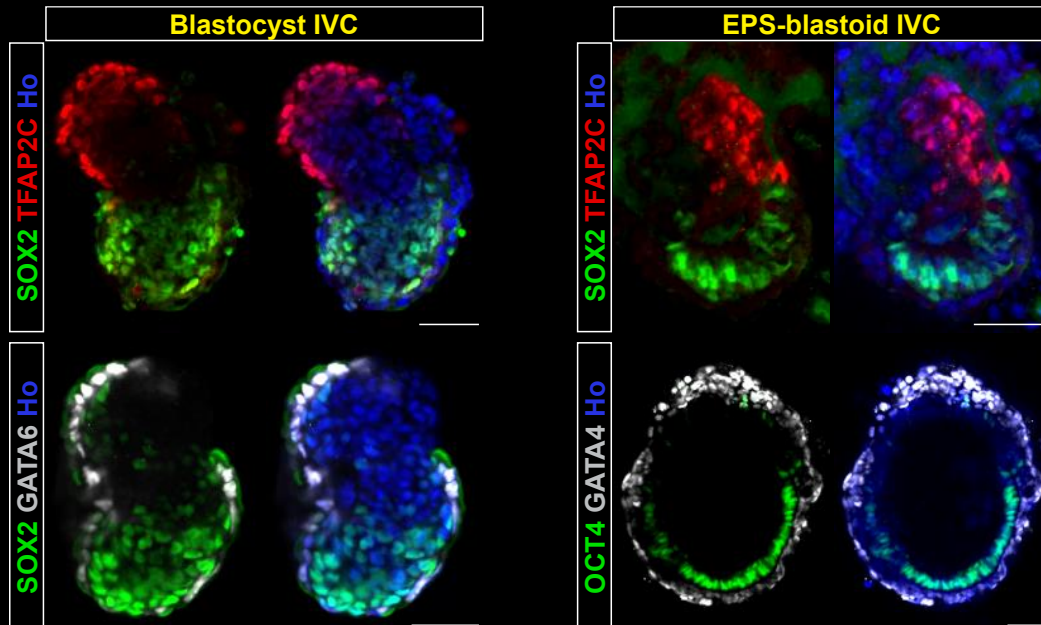
Blastoid-TSCs



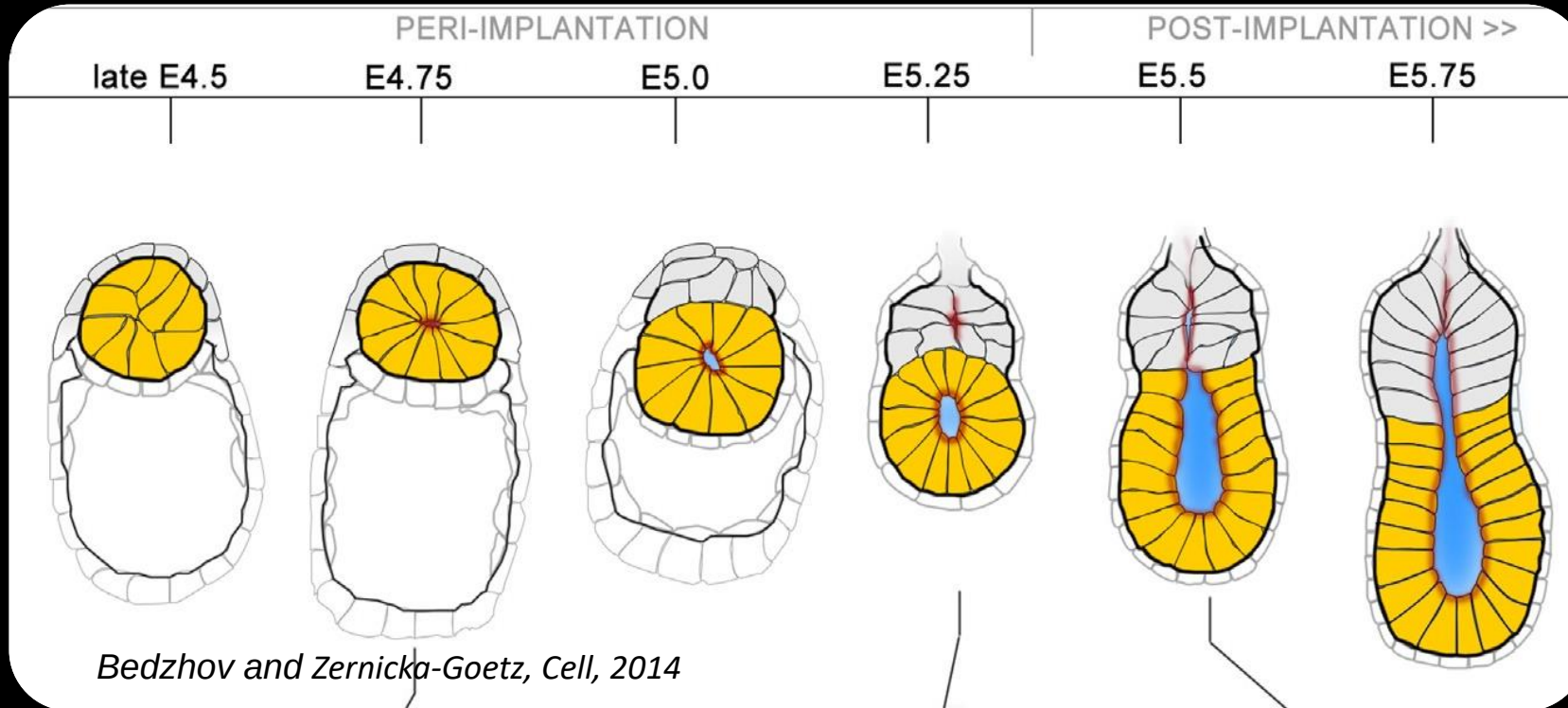
In vitro culture of EPS-blastoids to **post-implantation** stages



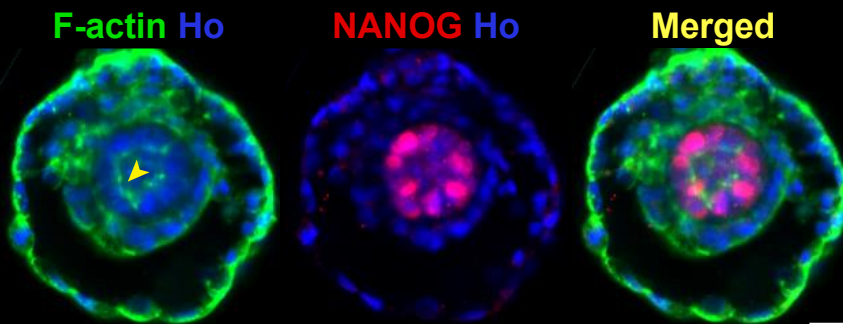
Bedzhov et al., Nature Protocol, 2014



Modeling **peri/post-implantation** development

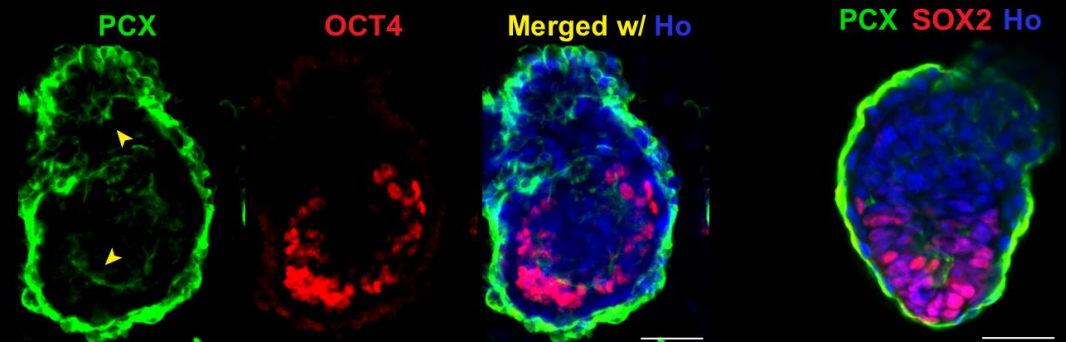


Epiblast polarization



Blastoid - Day 3

Pro-amniotic cavity formation



Blastoid - Day 5

Blastocyst - Day 5

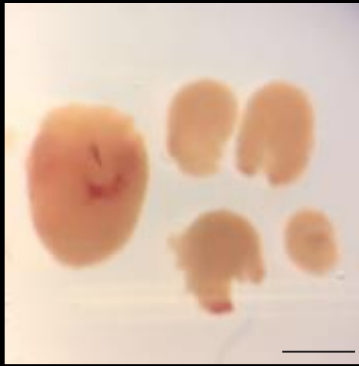
In utero developmental potential of EPS-blastoids



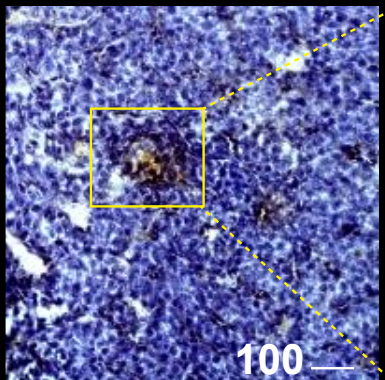
Control
deciduae at 7.5dpc



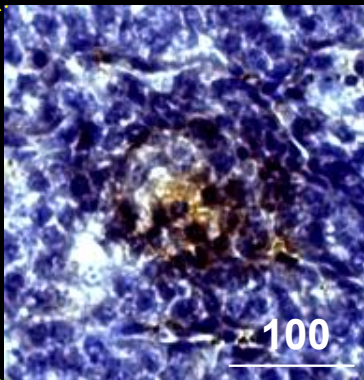
EPS-blastoid-induced
deciduae



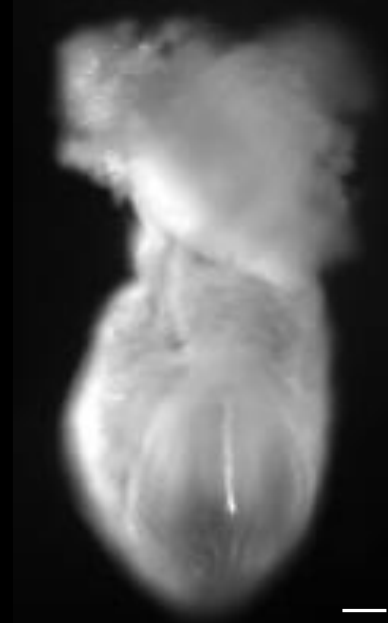
tdTomato



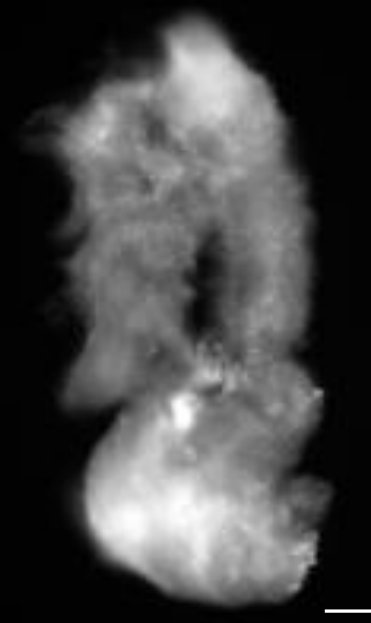
tdTomato



Control 7.5dpc

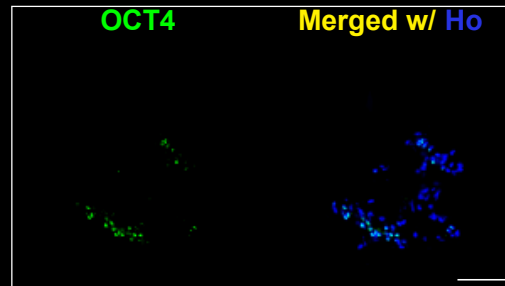


EPS-blastoid 7.5dpc



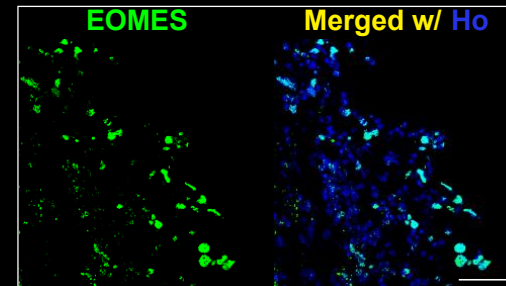
OCT4

Merged w/ Ho



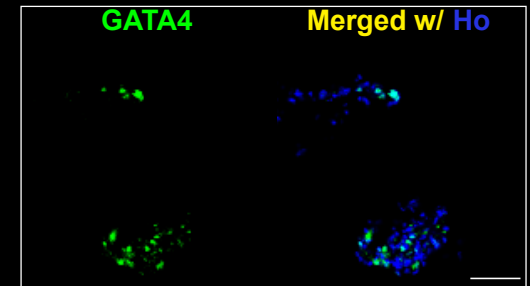
EOMES

Merged w/ Ho



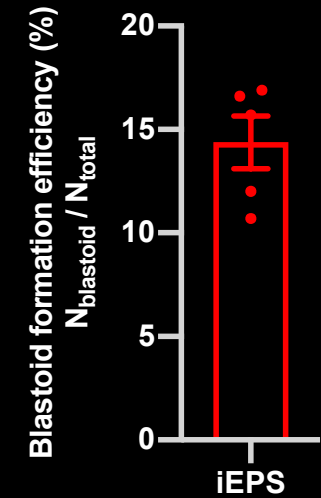
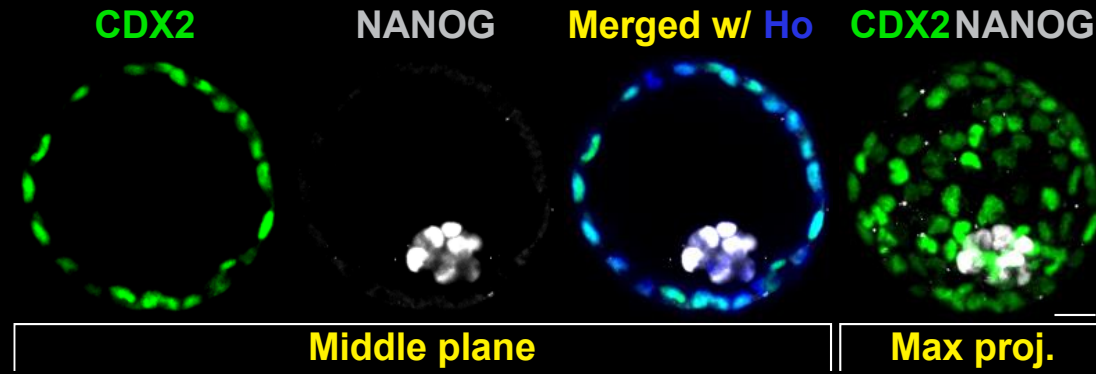
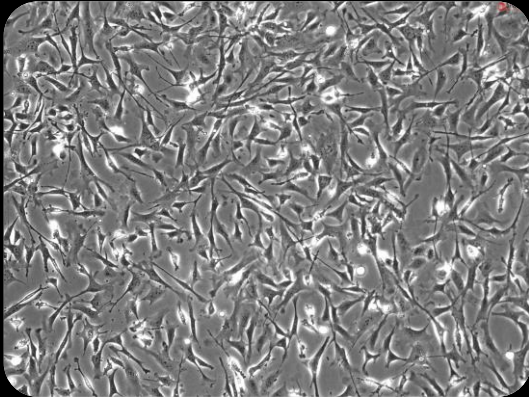
GATA4

Merged w/ Ho

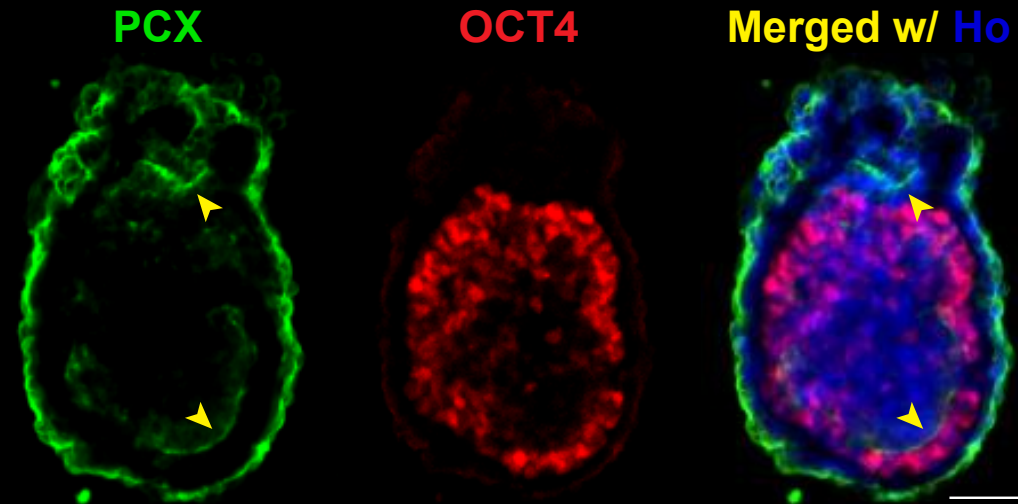
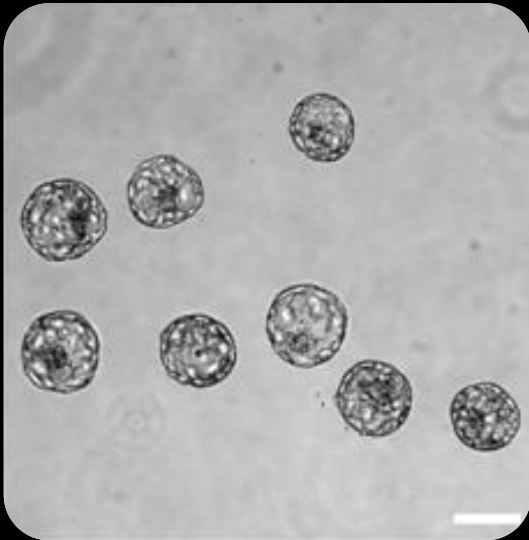


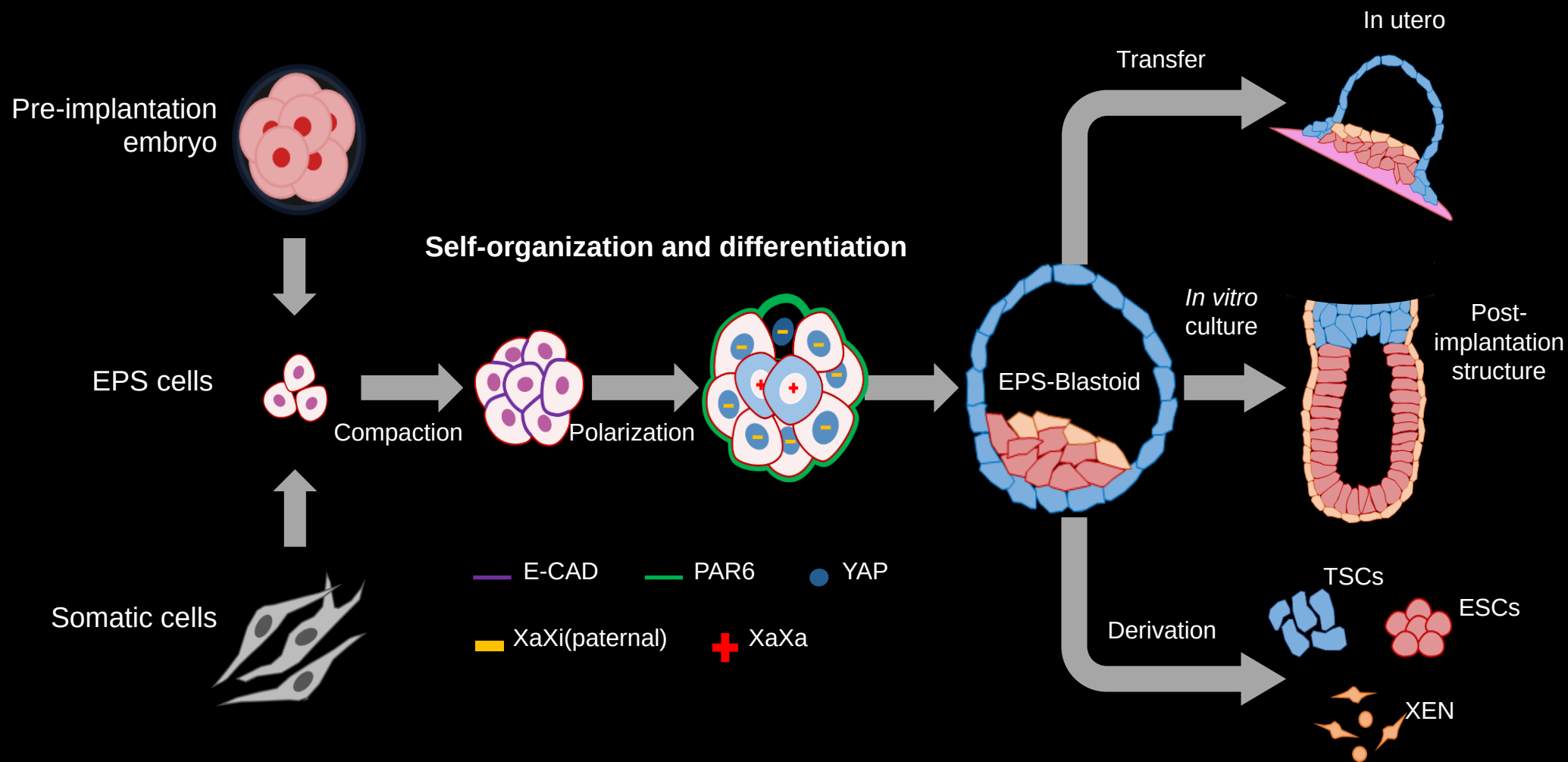
iPS-EPS cells derived blastoids

Fibroblasts

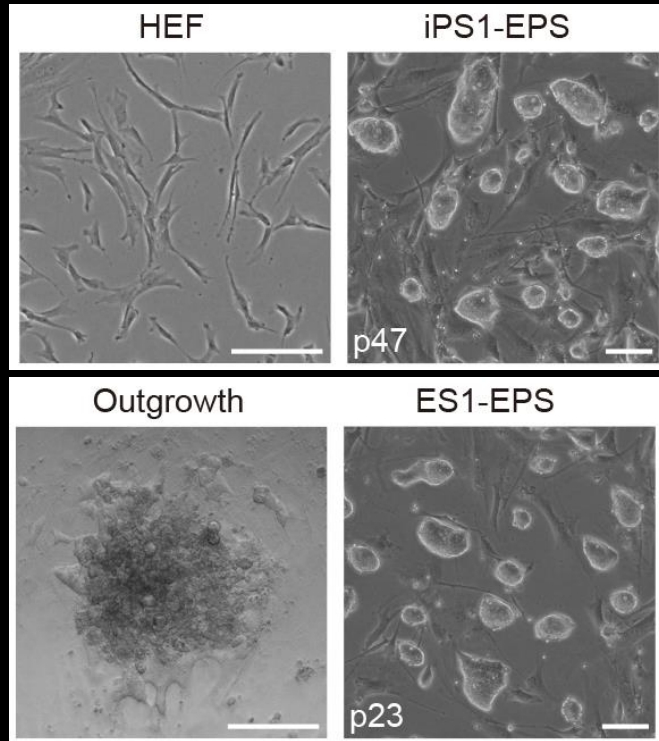


iPS-EPS blastoids

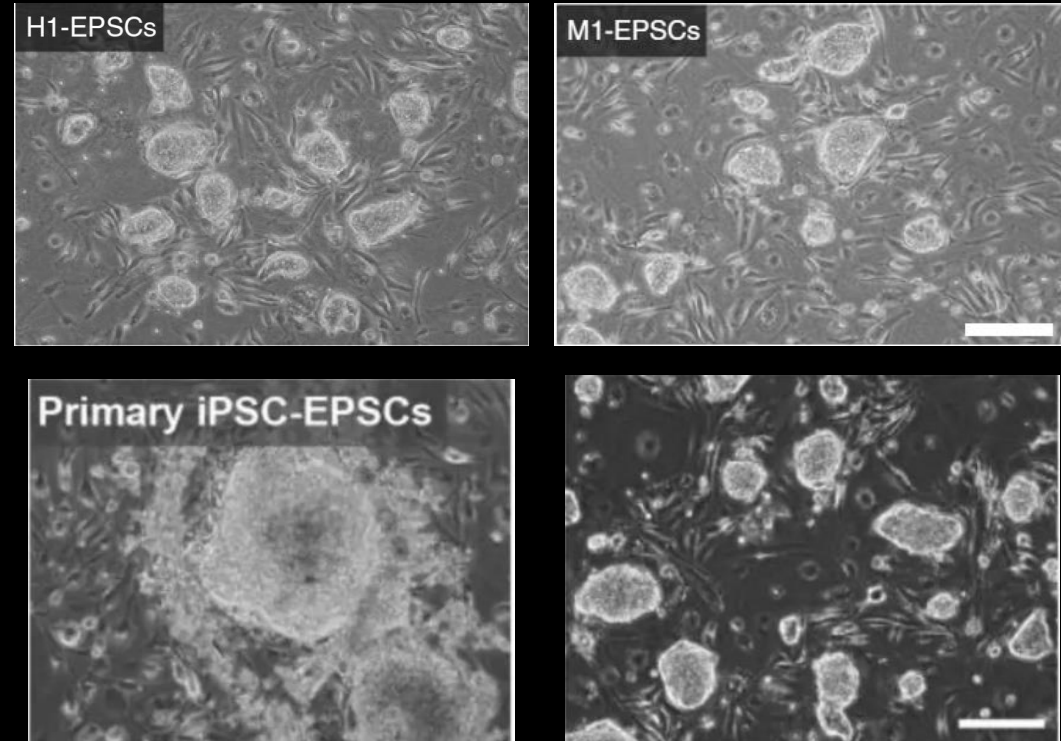




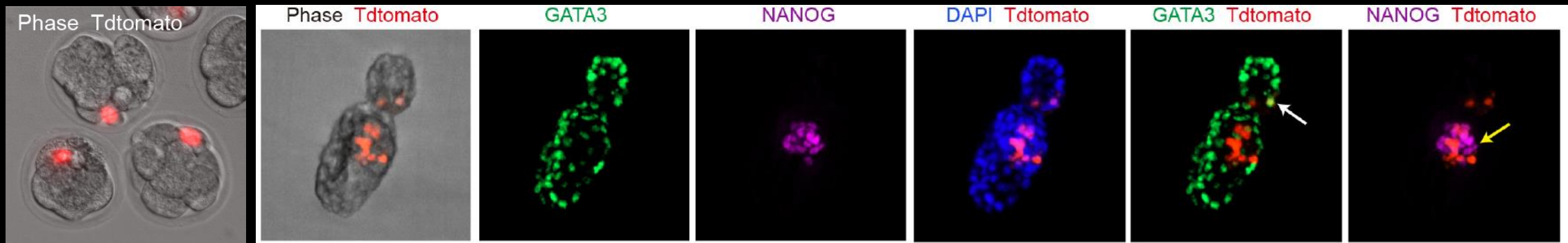
Human EPSCs

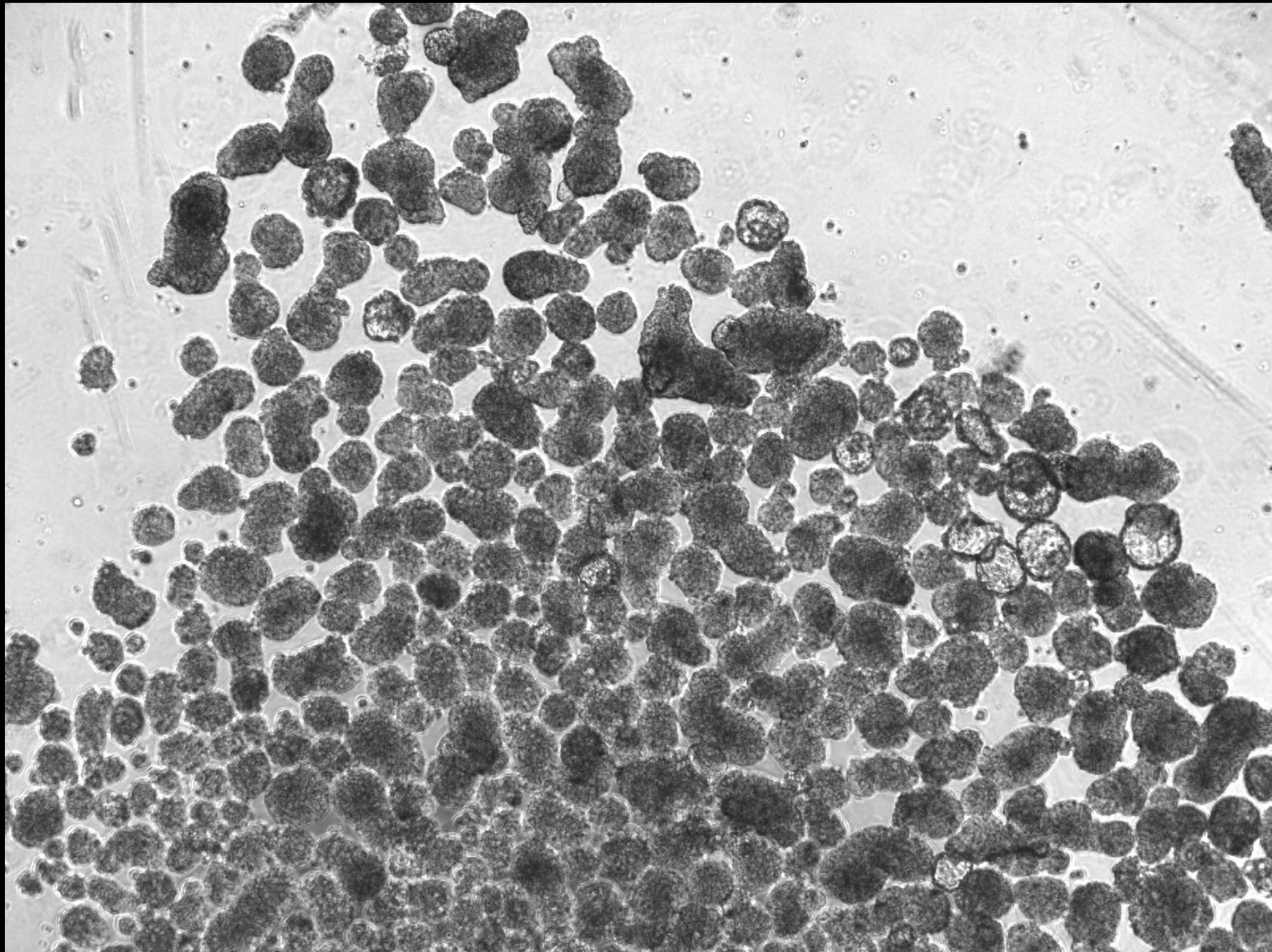


Yang Liu* Xu* Wang* Wu* et al, Cell, 2017*



Gao Nowak-Imialek* Chen* Nature Cell Biology, 2019*





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CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

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