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Adrien Dufour, Cyril Kurylo, Jan B Stöckl, Yoann Bailly, Patrick Manceau, Frédéric Martins, Stéphane Ferchaud, Bertrand Pain, Thomas Fröhlich, Sylvain Foissac, et al.

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# Gene networks controlling functional cell interactions in the pig embryo revealed by omics studies

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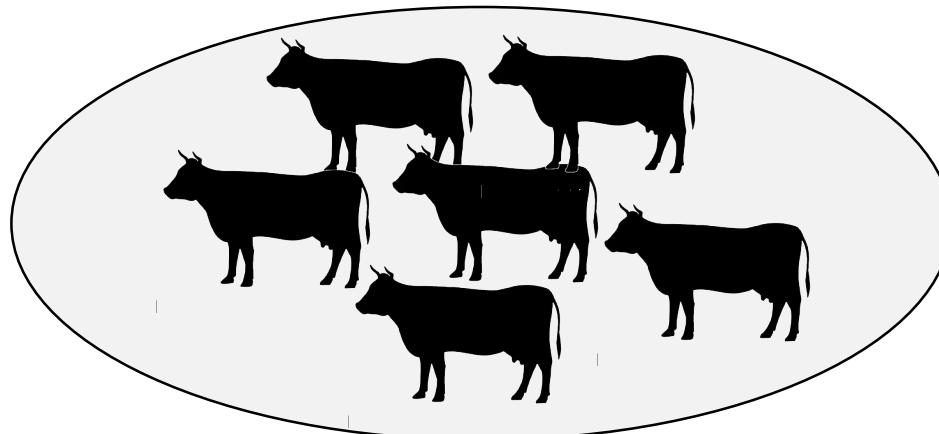


**INRAE**

## ➤ Pluripotent stem cells in livestock: a platform for high throughput phenotyping

A challenge for animal production: phenotyping complex traits and predicting breeding values for those traits

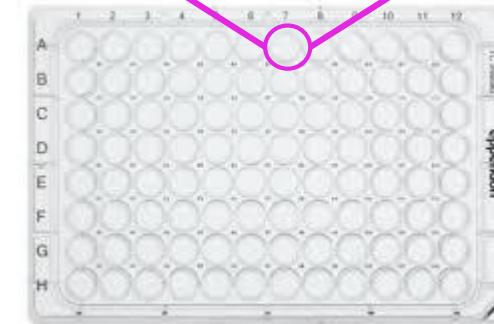
Reference population



**Phenotypes**

Genotypes

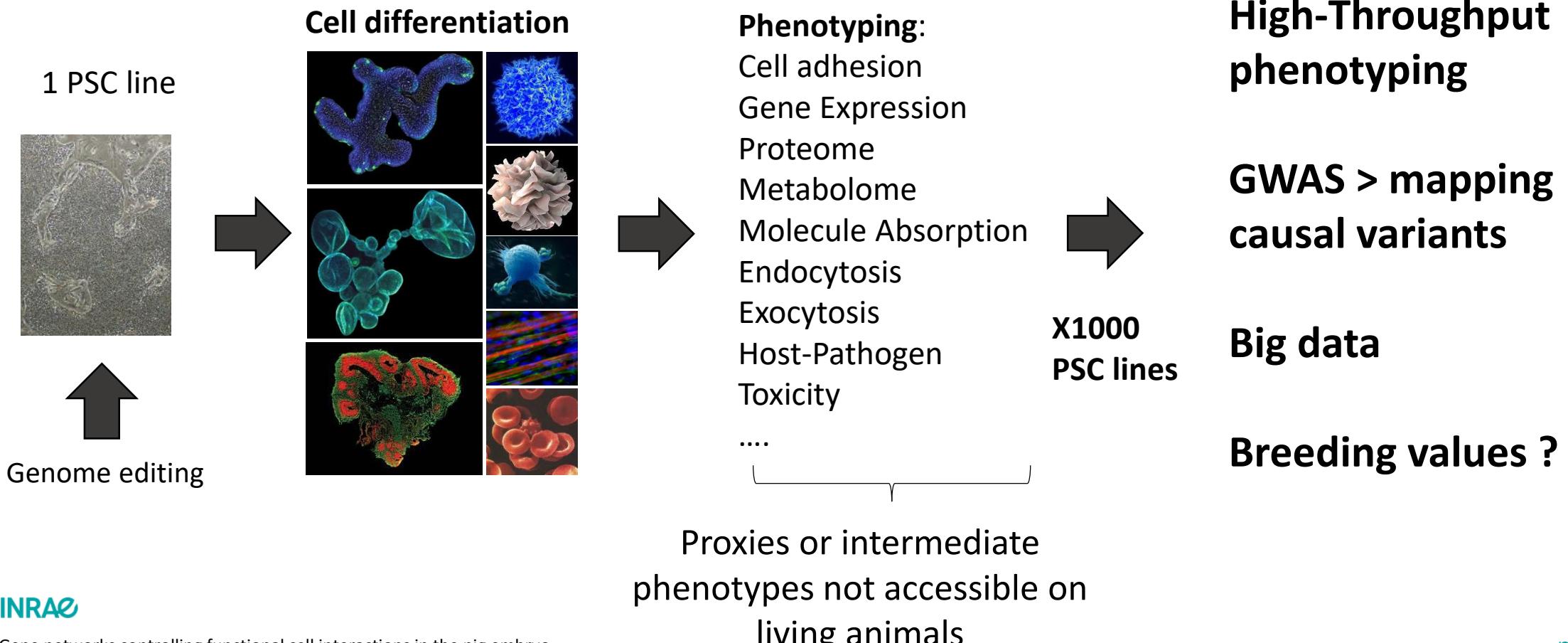
*In vitro* reference population (x1000) cell lines



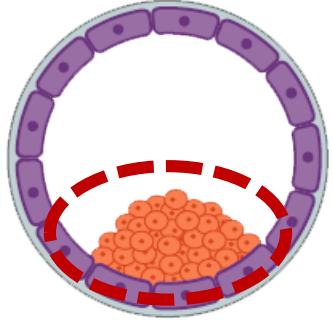
Biobank of pluripotent stem cells

## ➤ Pluripotent stem cells in livestock: a platform for high throughput phenotyping

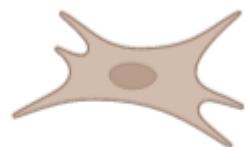
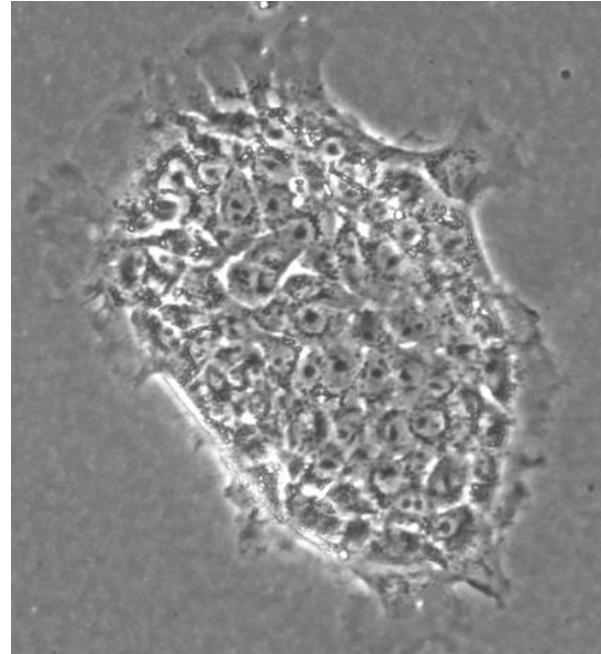
A challenge for animal production: phenotyping complex traits and predicting breeding values for those traits



## ➤ Producing standardized true PSCs for livestock species is still challenging



Amplification of **Epiblast cells**



**Chemically defined medium**

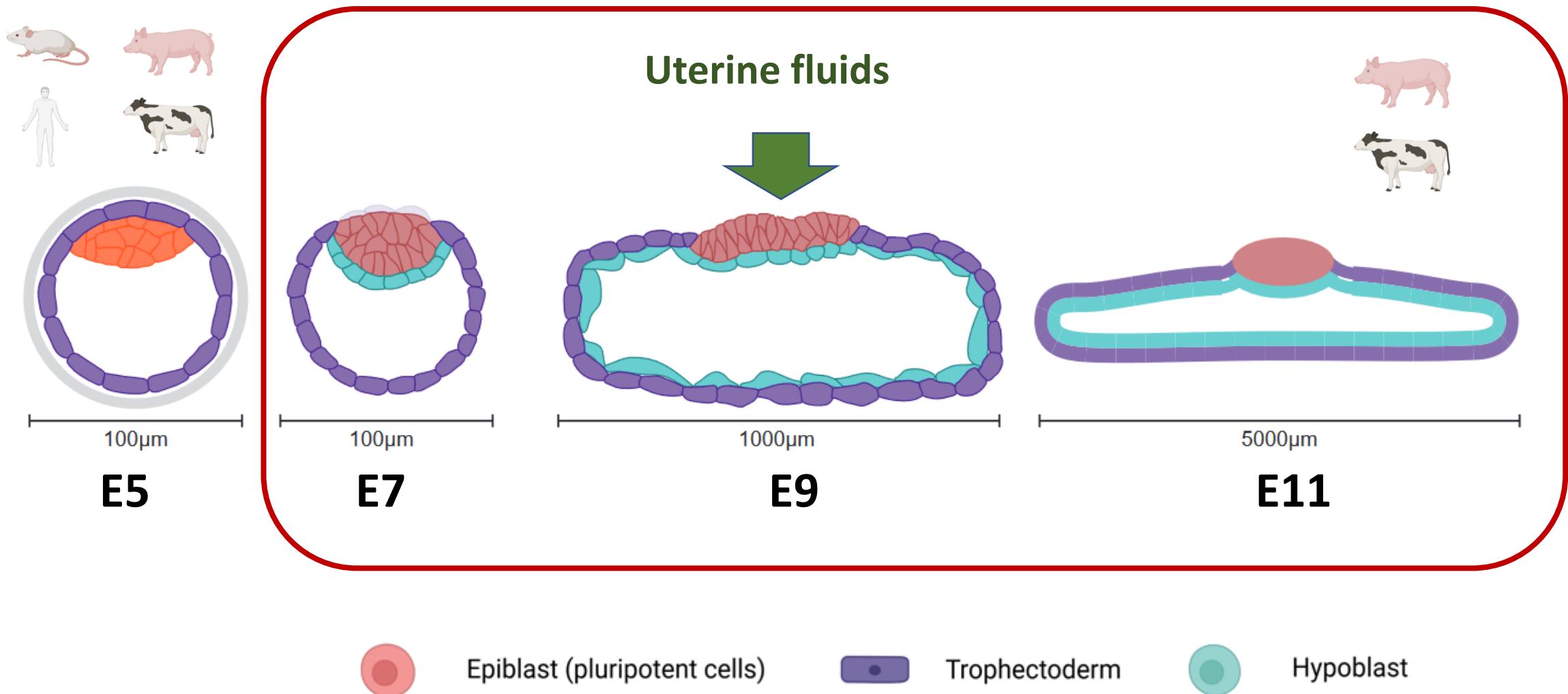


Reprogramming cocktail  
(OCT4, SOX2, KLF4, MYC)

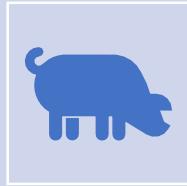


Heterogeneity ?  
Stability overtime ?  
Differentiation potential ?

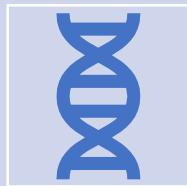
## What can we learn from the embryo ?



## > Working hypothesis

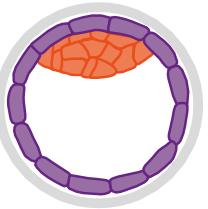


Paracrine regulations specific to pig embryonic development are not taken into consideration for the establishment of pig's pluripotent lines

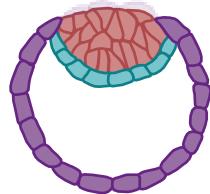


Embryonic regulatory networks are not necessarily conserved in mammals

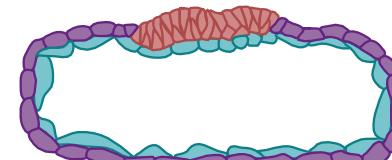
## > Methods



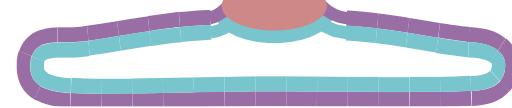
Early blastocyst E5



Hatched blastocyst E7



Spherical blastocyst E9



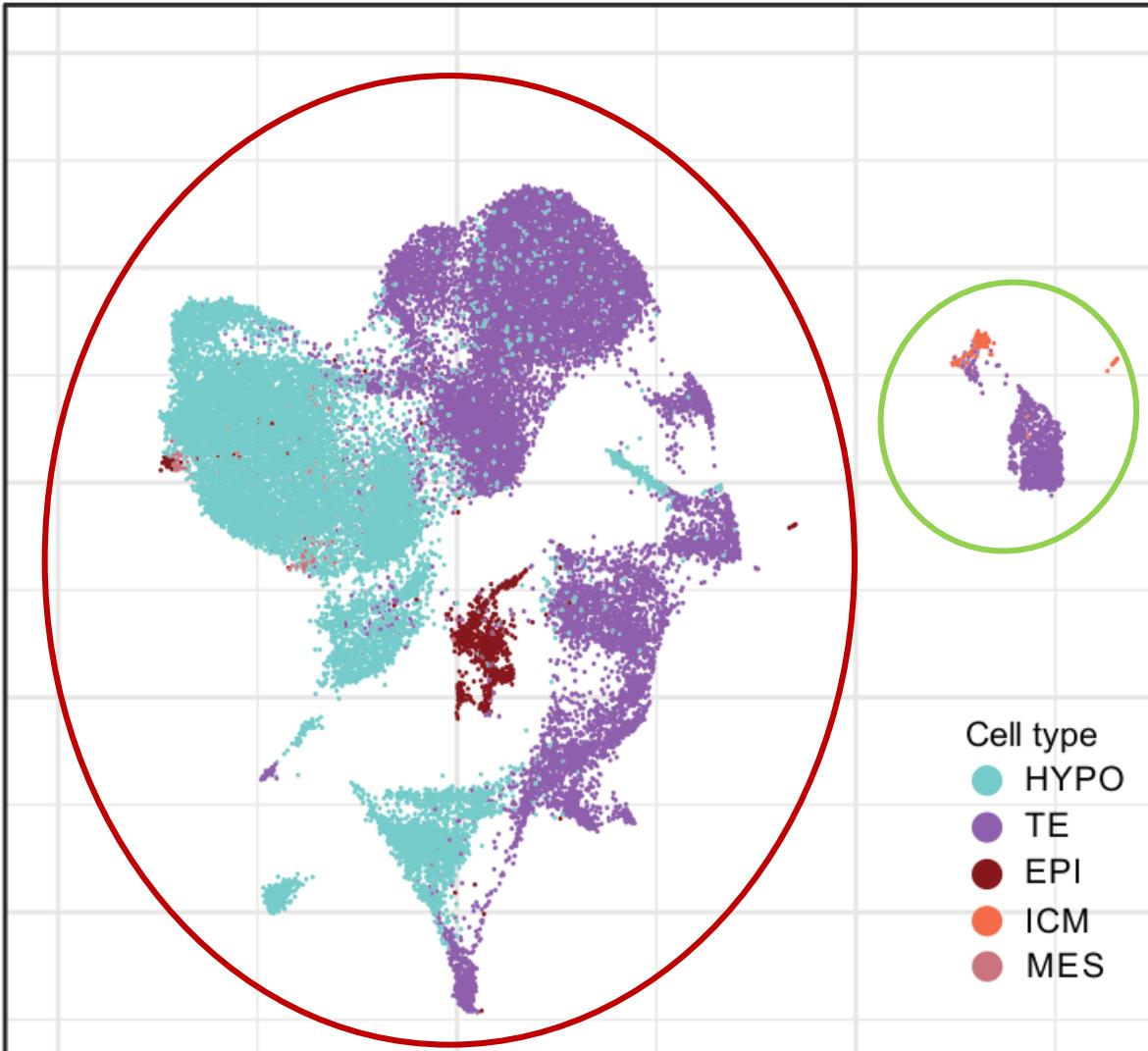
Ovoid blastocyst E11

Single-cell RNAseq	2 libraries (~2000 cells each)	4 libraries (~1000 cells each)	4 libraries (~3000 cells each)	2 libraries (~6000 cells each)
Uterine fluids	8 sows	4 sows	3 sows	3 sows
Single-cell multiomics (scATAC-seq + scRNA-seq)	0	1 library (~2000 cell's nucleus)	2 libraries (~4000 cell's nucleus)	4 libraries (~8000 cell's nucleus)

➤ scRNAseq allows the identification of cell populations constituting the embryo

UMAP of 34,888 cells

INRAe



Gene networks controlling functional cell interactions in the pig embryo  
29 August 2023 / EAAP meeting / Hervé Acloque

Dufour et al. submitted; <https://doi.org/10.1101/2023.05.30.542847>

E5

E7

E9

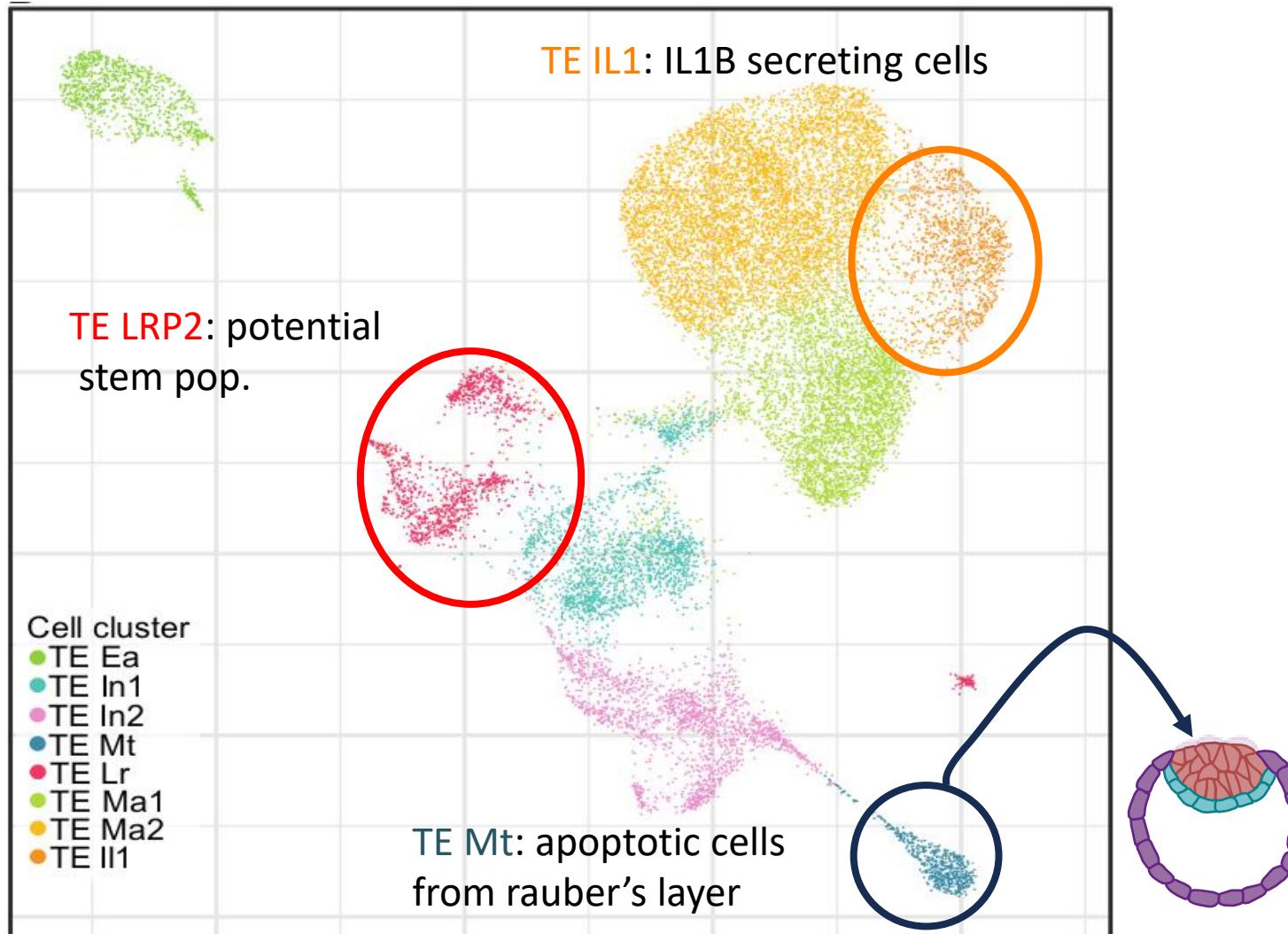
E11

p. 8

- scRNAseq data provide cues to better understand the biology of the pig embryo

## Identify new subpopulations

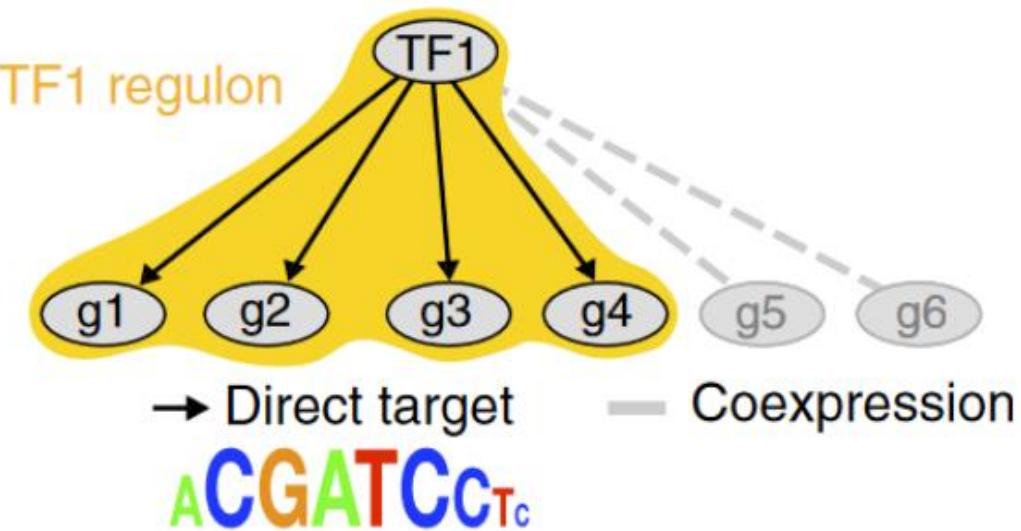
UMAP of 18,239 TE cells



- scRNAseq data provide cues to better understand the biology of the pig embryo

## Identify modules of gene regulation

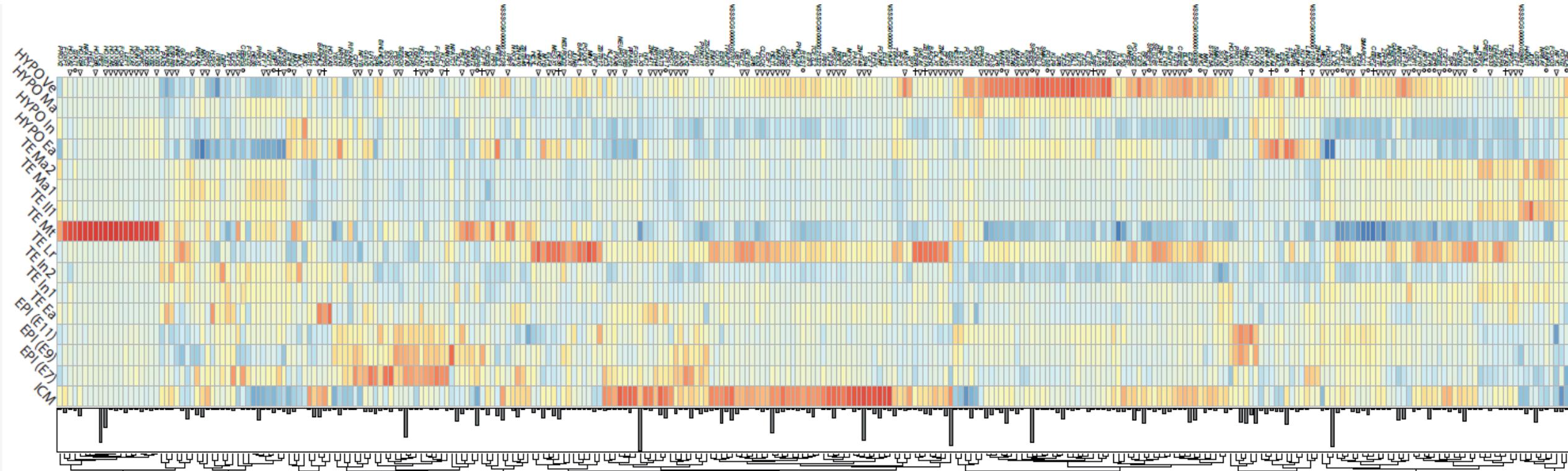
### Regulons (gene regulatory network)



Aibar et al. 2017

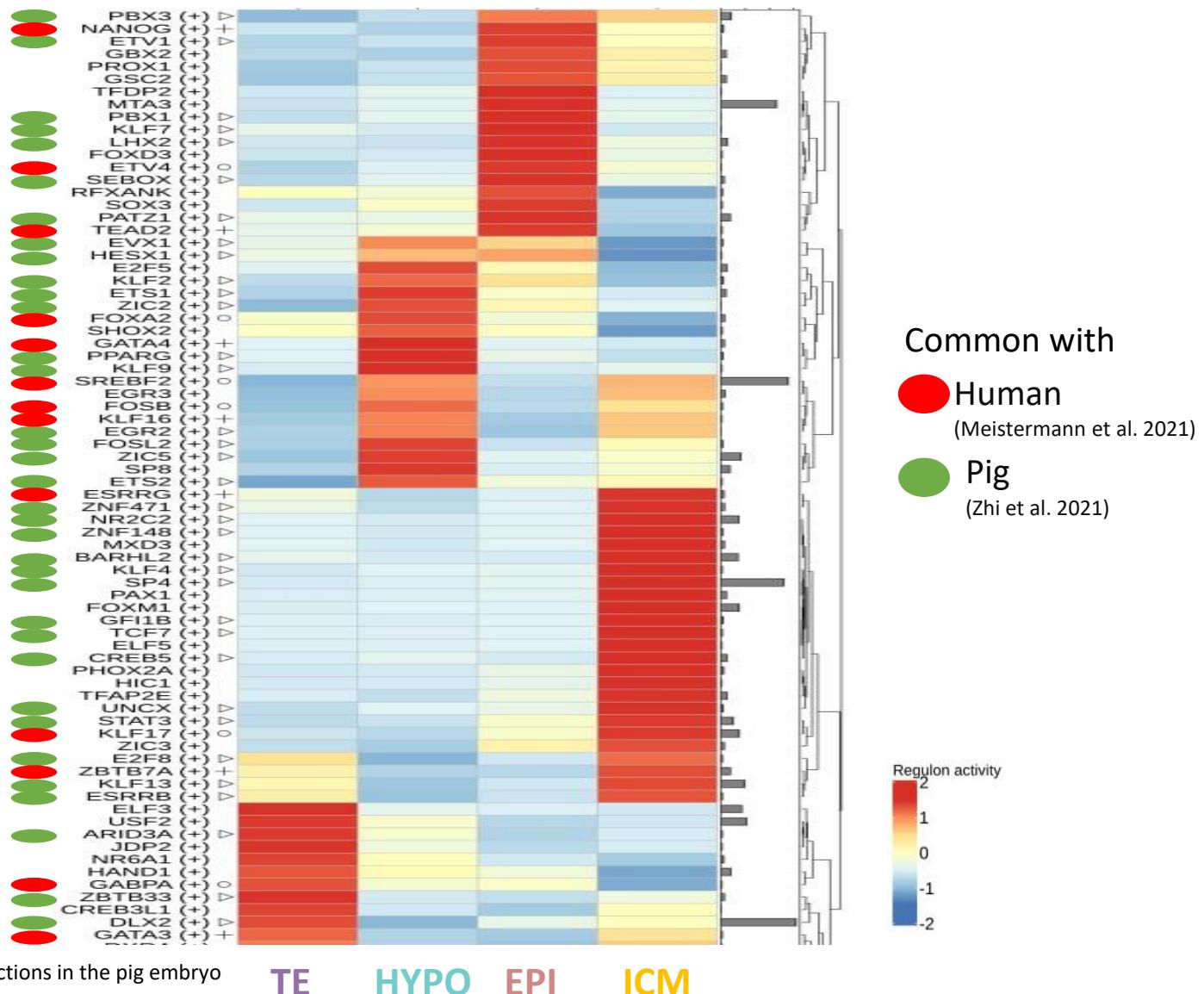
- scRNAseq data provide cues to better understand the biology of the pig embryo

# Identify modules of gene regulation

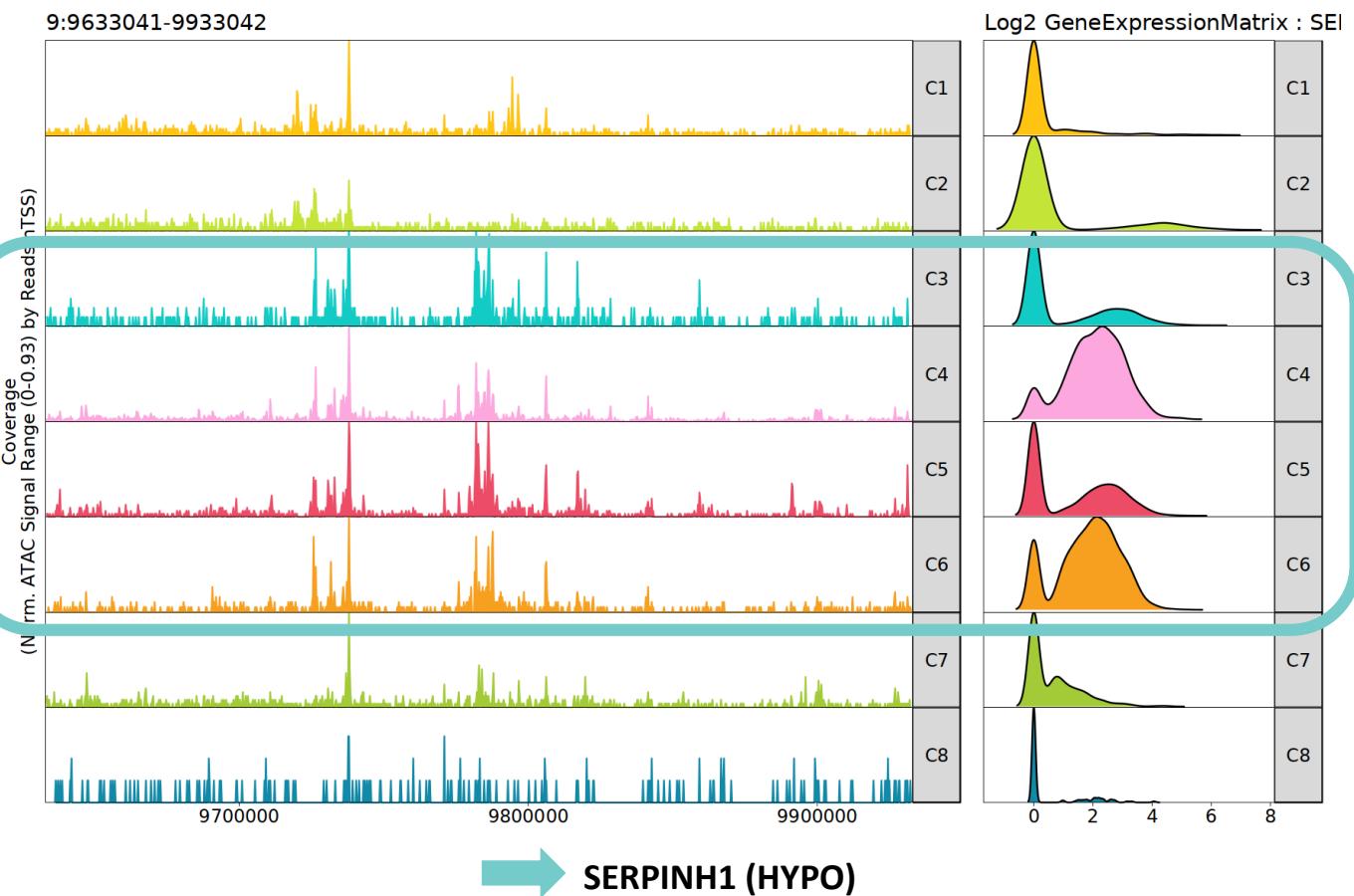
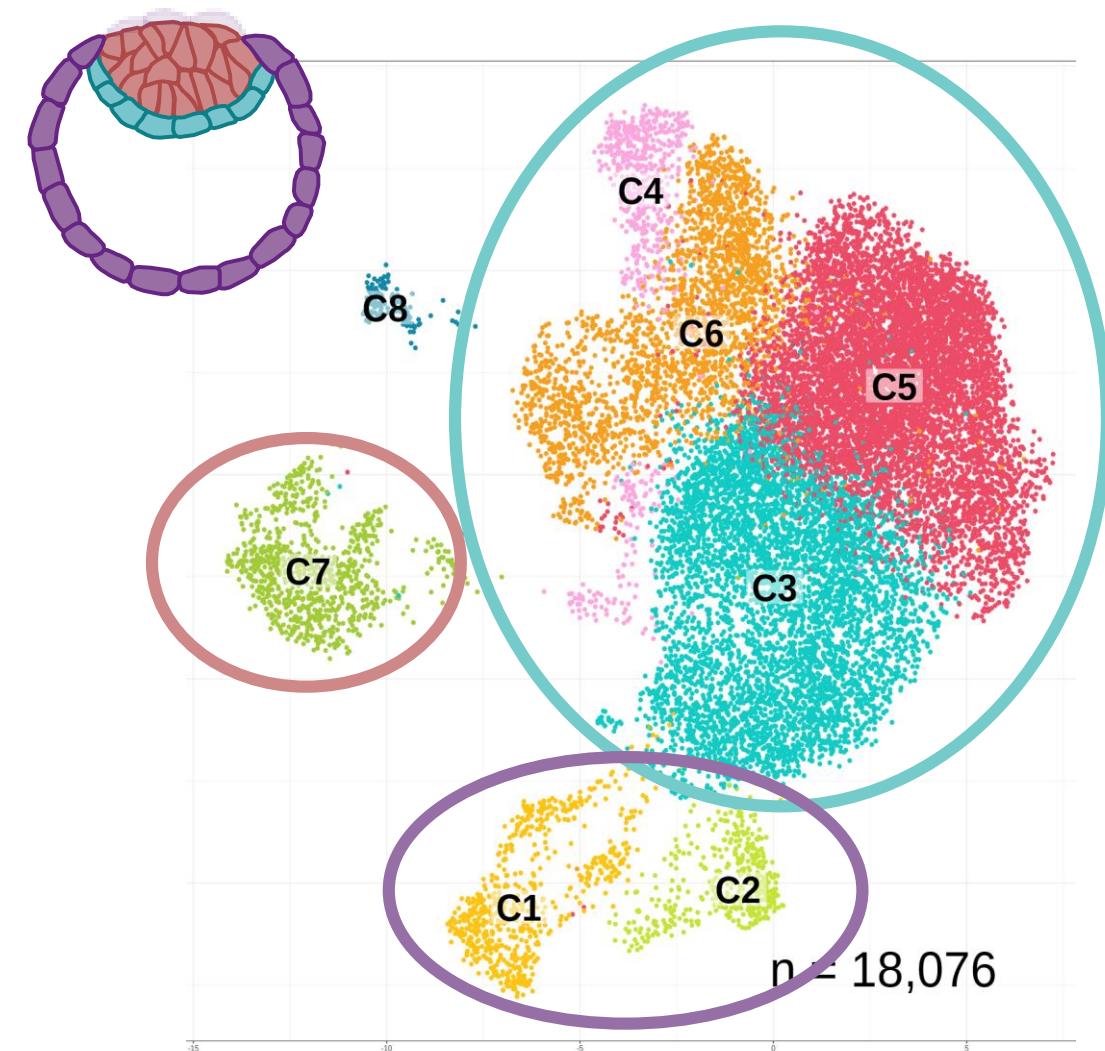


- scRNAseq data provide cues to better understand the biology of the pig embryo

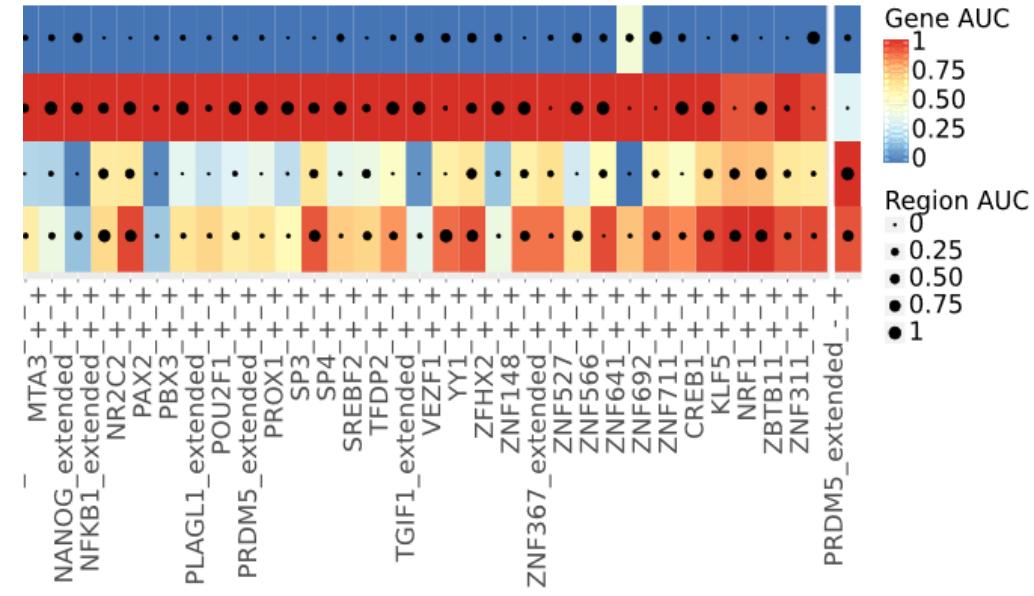
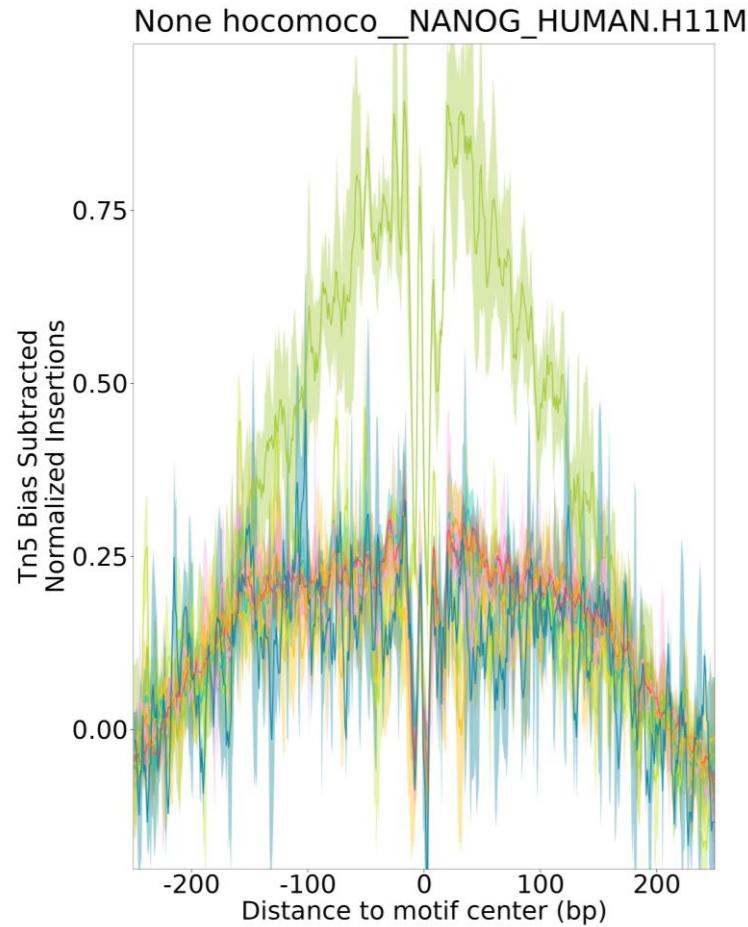
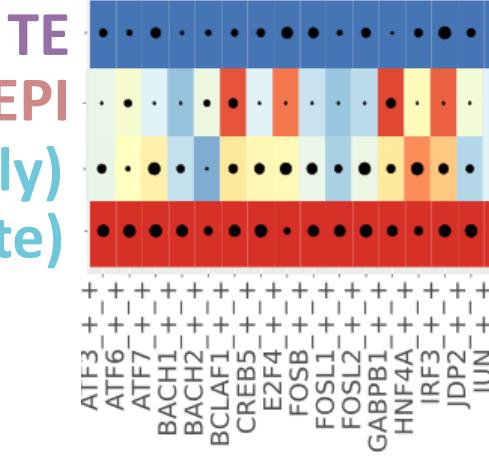
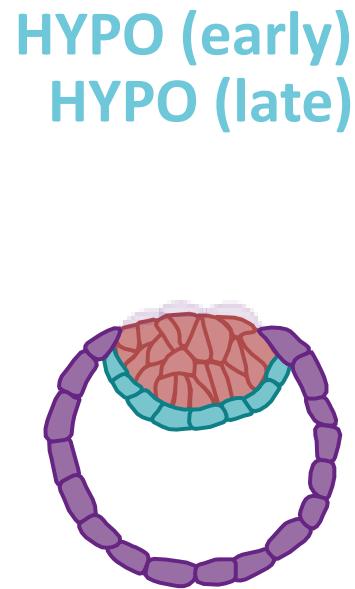
## Identify modules of gene regulation



## ► scOMICS: adding a layer of information to refine module of gene regulation

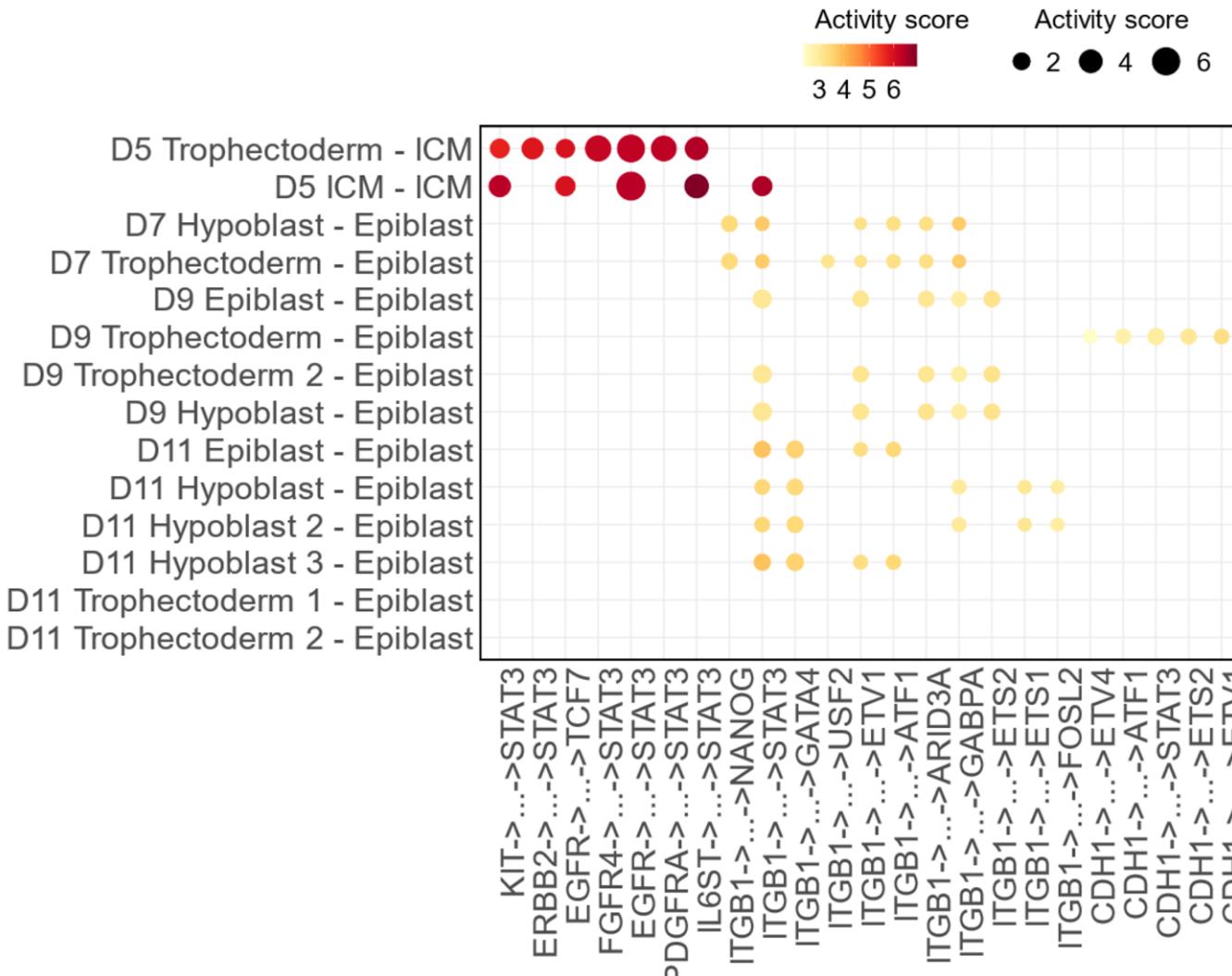


# ➤ Added value of omics data: selection of active regulons

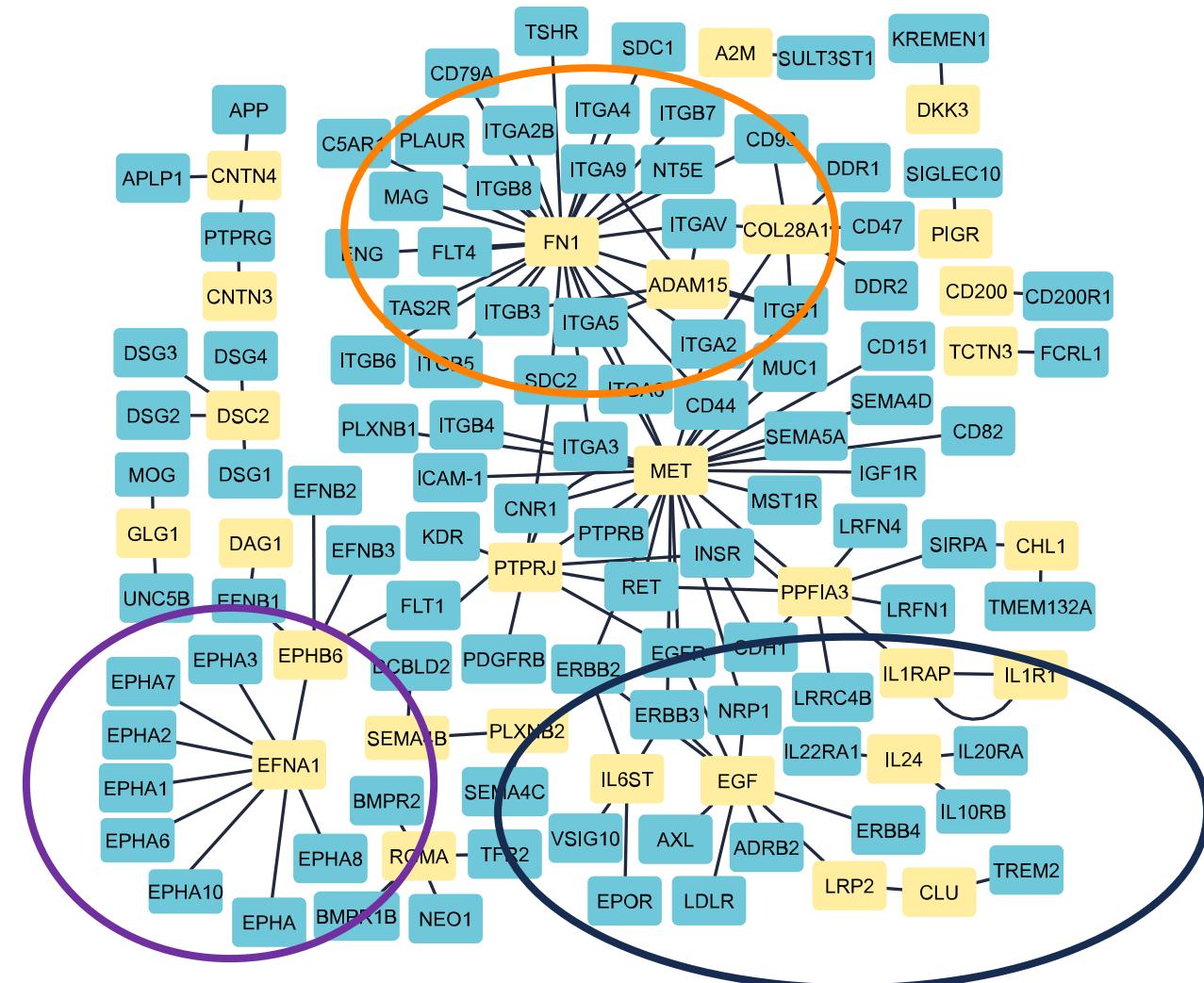
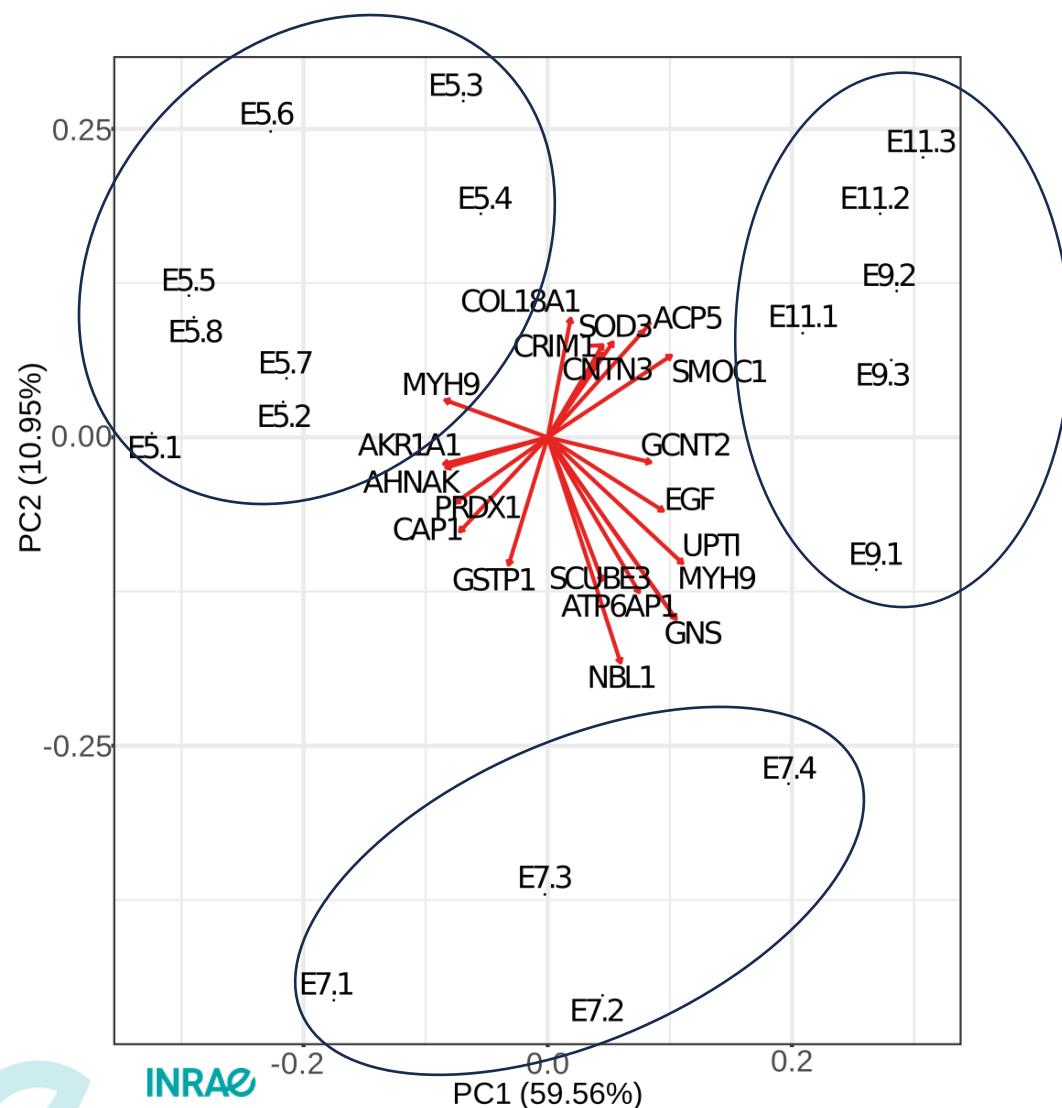


- scRNAseq data provide cues to better understand the biology of the pig embryo

## From ligand/receptor interactions to modules of gene regulation



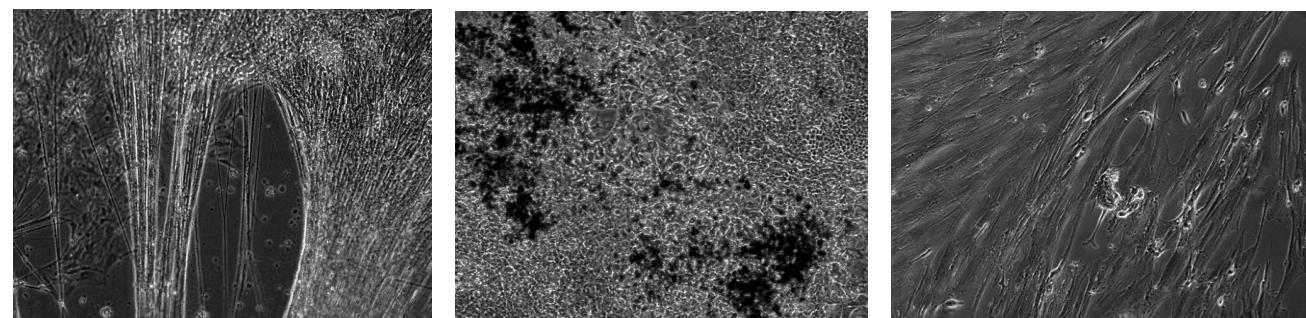
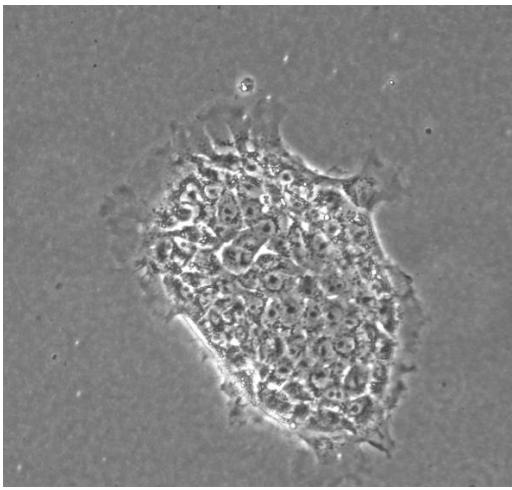
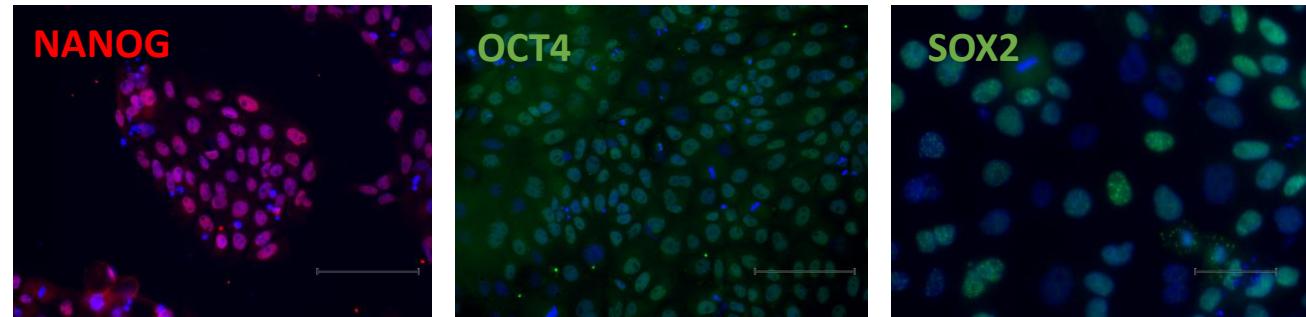
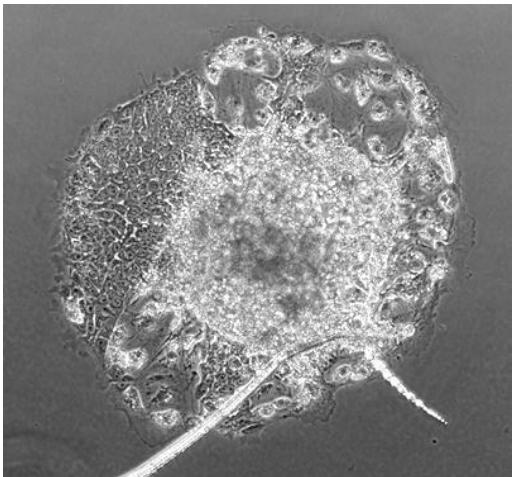
## Adding the fourth dimension: input from uterine fluids proteomics



Interactions between **uterine fluid ligands** and **trophectoderm receptors (E9/E11)**

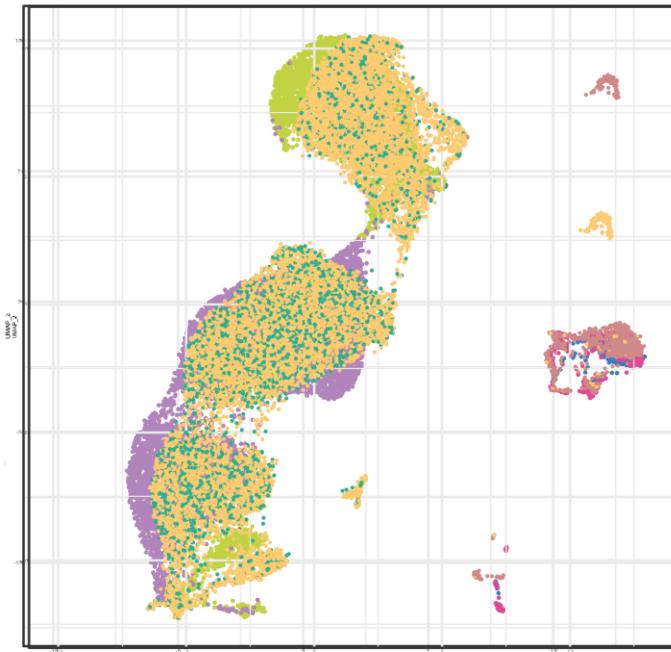
## ➤ Omics plus-value: detection of poised states in pig ESCs

Pig ESCs

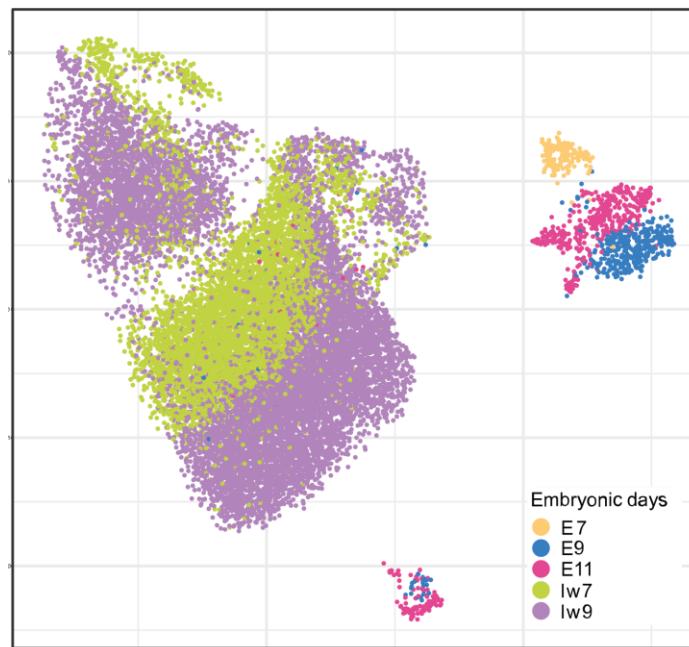


## Omics plus-value: detection of poised states in pig ESCs

- E7
- E9
- E11
- pESC\_1
- pESC\_2

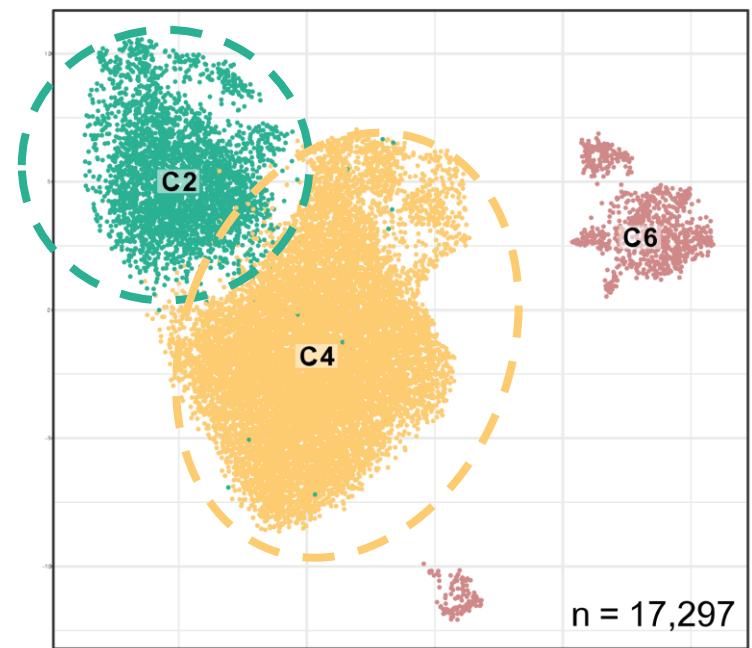


scRNAseq



scOMICS

Cells poised toward a neural fate



Cells poised toward non neural  
ectoderm & mesendoderm fate

## ➤ Conclusions

### **Added values of omics vs gene expression:**

- Identification of potential molecular interactions between embryonic cells and uterine fluids
- Better characterisation of gene regulatory networks at work in embryonic cells
- Validation of candidate regulons with motif footprints
- Detection of cell states not detectable by looking at gene expression only

## > Acknowledgements

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