UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2024-2025

Title : *Stem cells in the embryo: analysis of novel factors important for preimplantation in mice.*

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Summary : Our team analyzes the genetic mechanisms of cell lineage differentiation in the mouse embryo during pre-implantation. We are particularly interested in the differentiation between epiblast cells (Epi) and primitive endoderm cells (PrE), which takes place during the first 3 days in mice, corresponding to the first 6 days in humans.
Epiblast cells will produce all the cells of the future individual and its descendants. Epi is also the source of the famous ES pluripotent stem cells ("Embryonic Stem cells, Nobel Prize 2007 by Evans, Smithies, Capecchi) or similar to iPS reprogrammed cells ("induced Pluripotent Stem cells, Nobel Prize 2012 by Yamanaka). These cells can give rise to any embryonic or adult cell type, and therefore have great potential for cell therapy.
In the course of our recent single-cell RNAseq analyses, we have discovered new factors potentially involved in epiblast or PrE differentiation. The student will characterize the expression of these new factors by various techniques such as immunofluorescence and fluorescent in situ hybridization (smFISH), protein interactions (Proximity ligation assay) or transcriptomic analyses. Functional analyses (RNAi or CRISPR/CAS9) will then be carried out in the embryo or in *in vitro* models of differentiation such as ES stem cells.
Understanding the mechanisms underlying this "developmental program" is of paramount importance both from a fundamental point of view and for therapeutic applications aimed at using stem cells in regenerative medicine or improving in vitro fertilization techniques.

Methodologies (key words) : The project will potentially involve various techniques: embryo culture and electroporation, gene expression analysis (RTqPCR, immunofluorescence, FISH, PLA), single-cell analysis, confocal microscopy (fixed tissue and live-imaging), transgenesis, cell culture, RNAi, CRISPR/CAS9...

Publications of the research group on the proposed topic (3 max.)

- Allègre N, Chauveau S, Dennis C, Renaud Y, Meistermann D, Valverde Estrella L, Pouchin P, Cohen-Tannoudji M, David L and Chazaud C (2022). A Nanog-dependent gene cluster initiates early embryonic lineage segregation. ***Nature Communications*** 13, 3550. doi: 10.1038/s41467-022-30858-8. IF: 15.
- Huyghe A, Furlan G, Ozmadenci D, Galonska C., Charlton J., Gaume X., Combémorel N., Allègre N., Zhang J.Y., Wajda P., Rama N., Vieugué P., Durand I., Brevet M., Gadot N., Merrill B.J., Koch M., Mehlen P., Chazaud C. , Meissner A. and F. Lavial (2020). Control of naive pluripotency by the netrin-1/Neo1/Unc5B signalling axis. ***Nature Cell Biology*** 22:389-400. IF: 17
- Azami T*, Bassalert C*, Allègre N, Valverde Estrella L, Pouchin P, Ema M and Chazaud C (2019). Regulation of ERK signalling pathway in the developing mouse blastocyst. ***Development*** 146: dev177139. * equal contribution IF: 6