UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

# Track « Integrative Biology, Physiopathologies »

**Proposal for a Master 2 internship** – 2023-2024

***Title*** : Stem cells origin in the embryo: investivating novel factors important for mouse preimplantation development.


***Laboratory*** : Institut GReD (CNRS/INSERM/UCA)
***Laboratory director*** : K. Jagla
***Address*** : UFR Médecine, 28 place Dunant, 63000 Clermont-Fd

***Internship tutor*** : Claire CHAZAUD, Directrice de Recherche INSERM
***Tel*** : 04 73 17 83 83
***e-mail*** : claire.chazaud@uca.fr



***Summary*** : On the third day of development, the mouse embryo consists of three distinct cell types: trophectoderm, epiblast and primitive endoderm (PrE) cells. Epiblast cells are the stem cells of the embryo and will, through sequential differentiation programmes, produce all the cells of the body. They are also the source of the so-called ES cells, which are used for cell therapy purposes. The cells of the trophectoderm and the primitive endoderm are involved in the development of appendages such as the placenta and the yolk sac.
Our team is analysing the genetic mechanisms of the differentiation of cells into epiblasts or PrE. We have shown that this differentiation depends on the antagonistic interactions of two transcription factors, Nanog and Gata6, as well as on the Fgf signalling pathway. Indeed, without Nanog or under the action of Fgf, all cells become PrE cells and conversely without Gata6 or by inhibiting the Fgf signalling pathway all cells adopt an epiblast identity.
In our recent analyses, including single-cell RNAseq, we have discovered new factors that are potentially involved in epiblast or PrE differentiation. The student will characterize the expression of these new factors by different techniques such as immunofluorescence and fluorescent in situ hybridization or transcriptomic analyses. Functional analyses (RNAi or CRISPR/CAS9) will then be carried out in the embryo or in *in vitro* differentiation models such as ES cells.
Understanding the mechanisms underlying this "developmental programme" 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 fertilisation techniques.


***Methodologies (key words) :*** The project will potentially lead to different techniques: embryo culture and electroporation, gene expression analysis (RTqPCR, fluorescent in situ hybridization, western, immunofluorescence), 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: 17.
- 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:7