

Master 2 internship project proposition :

Study of the molecular mechanism of follicular dormancy from Drosophila to humans

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Summary :

Human ovarian development represents one of the most spectacular examples of homeostatic control in the living world. Indeed, after the definition of a large stock of primordial follicles during development, these can be kept dormant for decades while only one can escape this dormancy to enter the steroid phase leading to the formation of a mature oocyte. The mechanisms explaining, 1) this dormancy and 2) the escape from this dormancy, remain very poorly understood. Drosophila is considered to have a different reproductive strategy with the continuous production of large numbers of mature follicles. However, we have defined physiological conditions, which can be genetically mimicked, in which females accumulate the mature steroidogenic stages without laying them. This accumulation causes early follicle dormancy similar to mammals. Using transcriptomic studies and the genetic potency of Drosophila we have identified a paracrine factor produced by mature stages and which inhibits the growth of young stages. The purpose of this internship will therefore be to study 1) the control of the expression of this factor 2) to confirm its impact on the dormancy of the follicles 3) to define the signaling pathway explaining the dormancy. Since this factor is conserved in humans, where it is also expressed in the follicular cells of mature stages, this work will be done, in parallel and in collaboration, on human follicles in culture, with the aim to solve an important enigma of animal physiology.

Methodologies (key words) : *Cell imaging, CRISPR genome editing, tissue culture, Drosophila genetics*

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

Venugopal P, Veyssière H, Couderc JL, Richard G, Vachias C, Mirouse V. Multiple functions of the scaffold protein Discs large 5 in the control of growth, cell polarity and cell adhesion in Drosophila melanogaster. *BMC Dev Biol.* 2020 Jun 18;20(1):10

Vachias C, Fritsch C, Pouchin P, Bardot O, Mirouse V. Tight coordination of growth and differentiation between germline and soma provides robustness for drosophila egg development. *Cell Reports.* 2014 Oct 23;9(2):531-41.

Vachias C, Tournalias C, Grelee L, Gueguen N, Renaud Y, Venugopal P, Richard G, Brassat E, Mirouse V. Promotion of germ cell growth by gap junction-dependent amino acid transfer. *BioRxiv* 2023.