Sciences de la Vie et de la Santé
Master BMC, Universités Paris Descartes – Paris Diderot

Parcours : **Biologie et Développement Cellulaires**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : U1050/UMR7241, CIRB, Collège de France **Intitulé Equipe :** Oocyte Mechanics and Morphogenesis **ED d'appartenance :** ED515 Complexité du Vivant **Responsable de l'Equipe :** Marie-Emilie Terret/Marie-Hélène Verlhac	**Responsable du Stage :** Marie-Emilie Terret **Contacts** Adresse : CIRB, Collège de France, 11 place Marcelin Berthelot, 75005 Paris. Email : marie-emilie.terret@college-de-france.fr Tel : 01 44 27 16 92

Titre du projet : Cortical tension, a predictor of oocyte fitness ?

Meiosis produces **oocytes** and spermatozoa, sexual cells of reproduction. In women, it generates a lot of poor-quality oocytes, a trend that increases with age: 20% of oocytes are aneuploid before 35 years, 60% after. This leads to infertility and developmental diseases, such as trisomies. It is a public health problem in industrialized countries where the age of motherhood is increasing, reflecting the investment of women in their professional lives and leading to an increased use of Assisted Reproductive Technologies (ART).
The quality of human oocytes can be predicted by their **rigidity**: if it is aberrant, they do not develop after fertilization. We have shown in the mouse that making oocytes too soft induces defects in **division geometry**[1,2] and **chromosome alignment**[3], potentially describing for the first time a new mode of generation of aneuploidies that could be widespread, 36% of murine and human oocytes being measured as too soft in a normal population.
Our project aims to understand why oocyte **cortical mechanics** predicts their development after fertilization, and how to improve their fitness. To study these aspects, we have developed innovative tools in **imaging**, **biophysical** approaches and **modeling** coupled with **mouse genetics**[1,2,3,4]. Using these tools, we will at short (master 2 project) and long (thesis project) term:
1 / Characterize the oocyte defects induced by a too high cortical tension because until now we mainly analyzed the consequences of a too low cortical tension. For this, we are generating **tools** to force myosin II recruitment at the oocyte cortex and induce an increased cortical tension. We will analyze the phenotypes of these stiff oocytes, and in particular the impact on fertilization and early embryo development.
2 / Measure at the same time cortex tension using **AFM** microscopy and follow meiotic divisions in live on single cells coming from a normal population of oocytes to finely characterize and potentially predict the defects of oocytes naturally bearing an aberrant cortical tension.
3 / Generalize our findings to **human oocytes**, by verifying and predicting defects present in human oocytes depending on the extent of deregulation of their cortical tension. In that case, measure of the rigidity of the oocyte could serve as a minimally invasive technique to evaluate the developmental potential of oocytes in ART, as already explored for tumors.
Our project is ambitious and innovative, requiring a unique interdisciplinary set of skills and collaborations already established. It aims to understand the impact of cortical mechanics on the oocyte fitness and therefore has a high potential for transfer to the society.

Publications de l'équipe, relatives au stage proposé

1. Chaigne A *et al*. A soft cortex is essential for asymmetric spindle positioning in mouse oocytes. *Nat Cell Biol* 15:958-66 (2013).
2. Chaigne A *et al.* A narrow window of cortical tension guides asymmetric spindle positioning in the mouse oocyte. *Nat Commun* 6, 6027 (2015).
3. Bennabi I *et al*. Artificially decreasing cortical tension generates aneuploidy in mouse oocytes. Nat Commun. 2020 Apr 3;11(1):1649.
4. Chaigne A *et al*. F-Actin Mechanics Control Spindle Centring In The Mouse Zygote. *Nat Commun* 7:10253 (2016).