Project Title:

Epigenetic regulation of gene expression during meiosis and oocyte maturation.

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Location of research lab/research center:

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Project will be performed in collaboration with:

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Summary: (1000 characters)

The germ line lineage is immortal with an unlimited proliferative potential and capable of producing the ultimate totipotent cells: the gametes.

The *Drosophila* oocyte has a surprisingly rich and dynamic epigenome, as it reactivates gene expression during meiosis. A highly conserved histone demethylase named KDM5 plays a key role in the regulation of the oocyte epigenome, being rate limiting for meiosis and female fertility.

Multiple evidences suggest that KDM5 is crucial for meiosis and female fertility not only in *Drosophila melanogaster* but also in mouse and humans, For example, in a preliminary screen, mouse KDM5B was identified as a potential interacting partner for the transcriptional modulator CITED2. We recently demonstrated that CITED2 is critical for mouse embryonic stem cells (ESC) self-renewal and survival, at least in part through the positive regulation it exerts on NANOG expression. NANOG is a key transcription factor associated with mammalian ESC pluripotency, also expressed at

high levels in mammalian female primordial germ cells to prevent the premature expression of meiotic genes.

This project aims to use *Drosophila melanogaster* and *in vitro* derived mouse (and potentially human) meiotic cells to study the way KDM5, CITED2, and their interacting proteins regulate meiosis and oocyte maturation.

Bibliographic references:

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2) Kranc KR, Oliveira DV, Armesilla-Diaz A, Pacheco-Leyva I, Matias AC, Escapa AL, Subramani C, Wheadon H, Trindade M, Nichols J, Kaji K, Enver T and **Bragança J** (2015). Acute loss of Cited2 impairs Nanog expression and descreases self-renewal of mouse embryonic stem cells – Stem Cells 33, 699-712.