DESCRIPTION FOR THE GENERAL PUBLIC

Autophagy is pro survival cellular mechanism activated in mammalian cells in response a very diverse set of death stimuli and only in critical condition leads to cell death. A previous study by our group show that autophagy is up-regulated in the placentae of embryos having only paternal genome while down regulated in the placentae of embryos having only maternal genome. Based on this I hypothesize that paternal genome positively regulates the activation of autophagy while the maternal one tends to inhibit it. To verify this hypothesis I will study the occurrence of autophagy during Embryonic Diapause (ED). ED is reversible arrest of the embryos development while waiting for uterine receptivity signal. The survival of embryos during diapause has been related to high level of autophagy. Therefore, the **general objective** of this project **is to verify the regulation of autophagy by paternal and maternal genome during Embryonic Diapause.** To this aim, first I will investigate the viability of diapaused mouse embryo having only paternal (androgenotes) or only maternal genome (parthenogenotes). (***Specific Aim 1- Evaluation of the viability of androgenetic and parthenogenetic embryo during Embryonic Diapause***). Second, I will investigate the activation/progression of autophagy in androgenetic and parthenogenetic embryos during ED (***Specific Aim 2 - Role of parental genome on the occurrence of autophagy during embryonic diapause***).

Androgenotes, parthenogenotes and control embryos will be produced on a mouse model as ED can be easily induced in mice. Androgenotes will be in vitro produced by the fertilization of enucleated mature oocytes by two spermatozoa. Parthenogenotes will be produced by chemical activation of mature oocytes that simulate the fertilization process under non-sperm condition. Control embryos will be collected from the oviduct of females after natural mating. All embryos will be in vitro cultured and transferred into recipient females. To induce the Embryonic Diapause on those embryos, ovaries will be removed to avoid the estrogens stimulus to implantation and a daily injection of progesterone will be performed until the day before embryo collection. Embryo will be collected from the recipient females every two days from the induction of Embryonic Diapause until viable embryos will be found. Autophagic activity in those embryos will be analyzed by transmission electron microscopy, immunostaing of common markers of autophagy and by expression level of genes involved in autophagy.

Results from this study will prove whether cell death mechanisms are regulated by parental genome and their occurrence in physiological mechanism such as ED. This is a pioneering project as the role of parental genome on the regulation of embryo survival during ED has never been studied before. Our hypothesis, if confirmed, would have a great impact on the understanding of autophagy, opening up a fertile new investigation into the benefits or otherwise of cell death mechanisms in general.