DOCTORATS INDUSTRIALS

EL PLA DE DOCTORATS INDUSTRIALS

PROJECTE DE DOCTORAT INDUSTRIAL EXPEDIENT 2014 DI 065

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte
Characterization of the human sperm centrosome and its role in fertility
Empresa
EUVITRO S.L.U.
Responsable de l'empresa
Rita Vassena
Universitat
Universitat Pompeu Fabra - Centre de Regulació Genòmica (CRG)
Director/a de tesi
Isabelle Vernos Ruscassier
Treballador/a de l'empresa i doctorand/a
Farners Amargant I Riera

BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

Infertility is a global disease of high prevalence and far reaching personal and social consequences (Zegers-Hochschild et al., 2009). On average, 1 in 7 couples trying to conceive will have some difficulties and most will need assisted reproduction technologies (ART) (Boivin et al., 2007); about 40% of the times infertility is due to a male factor (Hudson, 1987). Recently, there has been a strong research focus on sperm, in part because male infertility continues to be a clinical challenge, and in part due to sperm selection concerns. Although millions of sperms are ejaculated, advanced techniques such as in vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI) make use of just a few sperms for fertilization. ICSI, specifically, results in high fertilization rates, as 80% of the fertilized embryos go through the first mitotic division, however, despite the global expansion of ART, delivery rates after IVF/ICSI cycles rarely exceed 30% (De Mouzon et al., 2012). There is an urgent need to understand the cause and kind of defects occurring during the first developmental stages, and to translate them to the ART clinic, both as reliable diagnostic markers, and as selection tools for improving ART outcomes. In this project, we will focus on getting a useful assay to test sperm functionality focusing on its associated centrosome, an essential component that it provides to the zygote during fertilization.

The centrosome is a non-membranous organelle constituted by a pair of centrioles surrounded by pericentriolar material (PCM). Centrosomes perform essential functions acting as the main microtubule organizing center in most cells and forming the basal body that drives the formation of cilia and flagella (Bettencourt-Dias and Glover, 2007). Animal cells have typically only one centrosome and specific mechanisms control this number as too many or too few centrosomes have deleterious consequences for the cell and the organism. The mechanism that limits the

number of centrosomes to one in the fertilized oocyte involves the loss of centrioles during oogenesis so mature oocytes lack a functional centrosome (Debec et al, 2010). Upon fertilization, in addition to the 23 male chromosomes the sperm provides to the zygote a modified centrosome that formed the basal body of its flagella (Sathananthan, 2013).

Following fertilization, the male centrosome plays important functions favoring the union of the male and female pronuclei as well as efficient spindle assembly and orientation. Interestingly, human parthenotes (embryos derived from activated oocytes in the absence of the male gamete) can go through the first mitotic divisions (Brevini et al, 2012) but they cannot develop further, suggesting that the centrosome plays additional essential functions in early development beyond those mentioned above. It is therefore possible that some of the early development failures occurring after ART are due to functional defects of the paternal centrioles.

In this project we propose to use a heterologous system to characterize the functional properties of the human sperm centrosome and to correlate our results with clinical data on fertilization success and early development. These studies will improve our basic knowledge on centrosome biology and may provide the basis for improving ART by introducing novel sperm selection criteria for IVF/ICSI beyond the morpho-functional aspects (shape, number, motility) currently in use.