Al collegio docenti del Dottorato in Medicina Molecolare

Dr.ssa. Francesca Paola Luongo

Ciclo XXVI Tutor prof Alice Luddi

Attività scientifica svolta nel 1°anno di Dottorato, Anno Accademico 2020/2021

Introduction:
Effective and reliable embryo implantation modeling is necessary to mimic the molecular event cascade that occurs *in vivo*.
Human Endometrial Organoids (EOs) are considered a new step forward precision medicine as tool for the study of endometrial biology, associated diseases (i.e. endometriosis) and to understand the complex mechanism surrounding endometrium-embryo cross talk.
In my project the main objective is to establish a reliable and complete human 3D model using both stromal and epithelial endometrial cells. Once obtained a solid model that resemble all molecular and morphological changes occurring *in vivo* during the woman cycle, co-culture EOs with embryos culture Media obtained from day 5-6 of Embryo culture and to characterize the secretome released.
Methods:
EOs are usually obtained from endometrial biopsy, in my project a less invasive approach is explored.
Epithelial endometrial cells can be obtained from menstrual blood of donors using a green option: the menstrual cup. Menstrual blood obtained from donors was processed to isolate these cells.
Samples were processed and isolated cells were resuspended in ice cold Matrigel, allowed to set at 37 °C and overlaid with organoid expansion culture medium. Organoids cultures have been exposed to hormonal treatments to mimic the endometrial hormonal milieu typical of the proliferative and mid secretory phase of the menstrual cycle. In particular, in order to mimic the proliferative phase, the expansion medium has been supplemented with 10^{-8} M E2, while, to mimic the mid secretory phase, the expansion medium has been supplemented with 10^{-8} M E2 + 10^{-6} M P4 and 50 mM cAMP. Treated organoids have been cultured for 4 days; after that, organoids have been washed with PBS, detached from the well and centrifuged. Cultures of human endometrial organoids were fixed for 2 h at 4 °C in cold Karnovsky's fixative. The samples were cut to expose the internal surface and coated with 20 nm gold/palladium and observed in a Quanta 400 (FEI) scanning electron microscope.
Results:
The luminal surface of EOs in proliferative phase is characterized by the presence of large apical cytoplasmic protrusions traditionally called "pinopodes". Their presence is reported to be a specific marker of the implantation window. In conclusion this model so far can respond to stimuli.

Abstracts

-A Luddi, B Semplici, F P Luongo, L Governini, R Ponchia, G Morgante, V De Leo, P Piomboni, O-217 Bitter Taste Receptors expression in human follicular cells: new perspectives in female fertility, *Human Reproduction*, Volume 36, Issue Supplement_1, ESHRE congress July 2021, deab128.028, https://doi.org/10.1093/humrep/deab128.028 (Oral presentation performed by Luddi A.)

-Francesca Paola Luongo [1], Alice Luddi [1], Adele Boccuto [1], Filippo Dragoni [1], Ilaria Vincenti [1], Mariangela Gentile [1], Maurizio Zazzi [1], Paola Piomboni [1]
SARS-COV2 in human somatic ovarian cells: possible impact on female fertility (Fertility Conference Liverpool 5-7 January 2022)(Accepted for Poster Presentation)

Pubblications:

-Laura Governini, Francesca P. Luongo, Alesandro Haxhiu , Paola Piomboni , Alice Luddi
Main actors behind the endometrial receptivity and successful implantation. Review .*Tissue and Cell (In press 2021)*