Dottorato di Ricerca in "Medicina Molecolare"
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In the second year of my PhD in Molecular Medicine, I investigated the possible role of taste receptors (TAS) in human fertility, focusing on sperm-oocyte attraction and recognition that represents an important step in the fertilization process.

Taste receptors are G-protein-coupled receptors responsible for the primary sensory transmission process of taste perception, which can be stimulated by many diverse natural or synthetic ligands. Recent reports described their extra-oral expression; interestingly, the G-protein α-subunit gustducin was also found to be expressed in mammalian spermatozoa, suggesting the possibility that taste receptors may act as molecular sensors during the sperm passage through the female reproductive tract. To our knowledge, no data are available on the possible role of these receptors in the oocyte as well as in the somatic cells surrounding the female gamete. Follicular cells are known to play a key role in the oocyte metabolism, maturation, competence acquiring and finally in the fertilization process. To this regard, it has been recently demonstrated that cumulus cells are fundamental in sperm-oocyte attraction and recognition by synthesizing and secreting progesterone. Since ethical issues do not allow us to study female gametes, and considering the just described intimated relationship between oocyte and follicular somatic cells, I focused my attention on the expression of taste receptors genes in granulosa and cumulus cells, in order to highlight their contribution to the sperm-oocyte attraction and recognition process.

To this end, I have studied selected *TAS* mRNA expression in both granulosa and cumulus cells collected from patients who underwent *in vitro* fertilization at the Centre for Diagnosis and Treatment of Couple Sterility, Obstetrics and Gynecology Unit, University Hospital in Siena. mRNA was extracted from each sample and analyzed by Droplet Digital PCR, an innovative precise, accurate and reproducible technique, sensitive enough to detect as little as few molecule/samples. The most

innovative characteristics of ddPCR are the distribution of the PCR reaction into thousands of individual reactions before the amplification and the acquisition of data at reaction end point. Moreover, the quantification procedure in ddPCR data is precise due to the digital nature of the assay and the fact that no standard curve is required. For this reasons, ddPCR technology can be used for extreme low-target quantitation.

In this preliminary study I measured by ddPCR the mRNA levels of the most representative gene of *TAS2Rs* family (*TAS2R3*, *TAS2R4*, *TAS2R14*, *TAS2R19* and *TAS2R43*) in granulosa and cumulus cells, in order to establish if these receptors are expressed in the follicular microenvironment.

Our data demonstrate that all gene belonging to the *TAS2Rs* family I investigated are expressed and significantly modulated in both granulosa and cumulus cells, even if at low levels. *TAS2R14* results the most expressed, with a significant statistical difference if compared with the others *TAS2Rs* genes, suggesting its possible key role. To our knowledge, no data are available on the role of this gene in granulosa and cumulus cells. Recently our research group demonstrated that *TAS2R14* is also expressed in the testis and in spermatozoa, and that polymorphisms on this gene have been associated to sperm motility, suggesting possible implications for human fertility (Gentiluomo *et al*, 2017).

Comparing the genes expression of taste receptors among granulosa and cumulus cells, I don't highlight a significant statistical difference between these two cell types. We can explain this comparable *TAS2Rs* fingerprint profile due to the characteristic development of somatic follicular cells, since it is known that cumulus cells differentiate from the granulosa cells during the folliculogenesis.

Poster:

- 35rd Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), 23 - 26 June 2019.
  Organoids of human endometrium: is this a powerful 3D culture model in replicating the endometrial glandular epithelium?
  Pavone V., Ietta F., Luddi A., Marrocco C., Semplici B., Luisi S., Piomboni P.

Partecipazione a congressi:

- 35th Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), 23 - 26 June 2019.

- 2nd Congresso Internazionale Fondazione PMA Italia, 21-22 March 2019.

- Droplet Digital™ PCR Scientific Conference 2019, 21 May 2019.

- "L'unione Europea e la salute dei suoi cittadini. Parliamo dei tumori.", 5 February 2019.

Pubblicazioni:

Increased expression of neurogenic factors in uterine fibroids
Luddi A., Marrocco C., Governini L., Semplici B., Pavone V., Capaldo A., Tosti C., Greco S., Luisi S., Ciarmela P., Petraglia F., Piomboni P.
Accepted by Human Reproduction

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