Dottorato di Ricerca in "Medicina Molecolare"
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In the first year of my PhD in Molecular Medicine, I concentrated my attention in the role of taste receptors (TAS) in human fertility, focusing on sperm-oocyte attraction and recognition that represented a central point of fertilization process, so that the molecular mechanisms involved in fertilization may be triggered.

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, and tasting proteins. Recent reports described their extra-oral expression, moreover, 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.

For this reason, we have studied selected *TAS* mRNA expression in spermatozoa collected from patients who performed analysis of seminal fluid at the Centre for Diagnosis and Treatment of Couple Sterility, Obstetrics and Gynecology Unit, University Hospital in Siena, and also in both granulosa and cumulus cells collected from patients who underwent *in vitro* fertilization. mRNA was extracted from each sample and analyzed by qRT-PCR.

1. *The expression analysis of TAS in human spermatozoa*

The gene expression analysis carried out in human spermatozoa demonstrated that receptors belonging to the TAS2s family, that mediates the primary sensory transmission process of bitter taste perception, are expressed in this cell type. Immunofluorescence on human ejaculated sperm allowed us not only to proper localize these receptors, but also to demonstrate that the capacitation process induce a significant redistribution of these receptors on sperm membranes.

Our data lead us to speculate that TAS2s may play an important role in the capacitation process and, as a consequence, in the acquisition of hyper-activated motility spermatozoa, suggesting their involvement in the fertilization process. The interesting hypothesis that would involve taste receptors in perception of chemical variations present in the microenvironment, modifying their direction and their status of activation, should be further investigated.

2. *The expression analysis of TAS in granulosa and cumulus cells*

The granulosa and cumulus cells are involved in the metabolism of the oocyte, its maturation, competence acquiring and fertilization. For example, recently, it has been demonstrated that cumulus cells play a key role in sperm-oocyte attraction and recognition by synthesizing and secreting progesterone. Based on these findings, we focused our attention on the possible role of taste receptors in mediating sperm-oocyte attraction and recognition, investigating their expression in both granulosa and cumulus cells.

To this end, we performed a deep gene expression analysis by investigating the mRNA levels of the most representative genes involved in the taste perception process: *CAMKK1*, *GATA1*, *GCM1*, *GNAT1*, *GNAT3*, *MZF1*, *PDE4A*, *PLCB2*, *TAS1R1*, *TAS1R2*, *TAS1R3*, *TAS2R14*.

As regard the G-protein coupled with taste receptors, the first data we have obtained is that *GNAT3* is not expressed in both granulosa and cumulus cells, whereas *GNAT1* is expressed only in cumulus cells. suggesting a possible role of taste receptors in cumulus cells in the process of sperm-oocyte attraction and recognition. In regard to the *TAS* genes family, we showed that *TAS2R14* is significantly more expressed than *TAS1R3*, whereas *TAS1R1* and *TAS1R2* were not expressed at all. When we compared the relative expression of these genes in cumulus *vs.* granulosa cells we observed a statistically significant modulation of several of them, with *CAMKK1*, *GCM1* more expressed in cumulus than in granulosa cells. About *TAS* genes family, *TAS1R3* and *TAS2R14* resulted to be significantly more expressed in cumulus compared to granulosa, suggesting a possible role of these receptors in these cells, due to their extreme specialization.

Poster:

- 5th Annual Meeting of the Society of Endometriosis and Uterine Disorders (SEUD), 25 - 28 April 2018.
  Endometrial receptivity: Expression profile of candidate genes in endometriosis.
  Pavone V., Luddi A., Governini L., Marrocco C., Semplici B., Capaldo A., Boschi L., Luisi S., Petraglia F., Piomboni P.

- 34rd Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), 2 - 5 July 2018.
  Taste receptors expression in human sperm: possible chemosensors for sperm-oocyte attraction.
  Alice Luddi, Camilla Marrocco, Laura Governini, Angela Capaldo, Bianca Semplici, Valentina Pavone, Letizia Boschi, Vincenzo De Leo, Paola Piomboni.

Partecipazione a congressi:

- 5th Annual Meeting of the Society of Endometriosis and Uterine Disorders (SEUD), 25 - 28 April 2018.
- 34rd Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), 2 - 5 July 2018.
- "Generiamo il futuro". Conferenza sulla ricerca nelle Scienze della Vita in Toscana, 14 - 15 September 2018.

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