UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title

Environmental factors impairing fertility outcome: treatment approaches for sperm cells in patients candidate to assisted reproduction techniques

2) Abstract (max 500 words)

Sub-fertility represents one of the major health concerns in developed countries, with the male factor accounting for 40-60% of all the causes of infertility. It is increasingly clear that most of the causes of male infertility are associated with the direct exposure of sperm cells to environmental factors detectable in semen, that directly affect the gamete function. Biological factors such as bacteria, viruses causative of sexually transmitted diseases, together with pollutants such as heavy metals or chemical additives widely used in the production of plastic materials, are among the acknowledged agents detected in human semen. Excessive semen levels of these factors are frequently associated with altered sperm parameters and in turn to sub-fertility conditions.

The mechanisms by which the aforementioned factors interfere with sperm cell function mainly rely on the interaction with cell membrane since spermatozoa are nucleated cells characterized by transcriptional and translational inactivity, together with an essential lack of cytoplasm. Accordingly, most of the functional variations in sperm cells rely on the modification of the properties of plasma membrane such as: increased permebility to Ca^{2+} ions at the inlet and H^{+} at the outlet, removal of membrane cholesterol with correspondent increased fluidity of plasmalemma and activation of membrane receptors involved in chemo-, thermo- and rheotaxis. All these processes are prodromal to the gain of motility within female genitalia and subsequent fusion and fertilization of the oocyte. Environmental factors of infertility are known to interact with or accumulate into sperm membrane, altering the precise time-course of membrane modification aimed at achieving fertilization. Alternatively, sperm cells represent possible carriers of these factors into the oocyte at the time of fertilization, altering the subsequent phases of embryo development. Taken together, these events result in an overall reduction of the fertility pattern, in a potential risk for embryo development and in a possible hazard for the health of childbirth.

In natural fertility, because of the functional anatomical features of the lower female sexual organs, the sperms undergo to a strict selection allowing only the best quality cells to proceed towards the

fertilization site. However, this natural selection is largely violated by the use of assisted reproduction techniques (ART). During ART, and even more during the intra-cytoplasmatic sperm injection (ICSI), the isolated oocyte is put in contact with poorly selected sperm cells in *in vitro* conditions in order to increase the probability of fusion between the two gametes. If on one hand ART increase the rate of fertilization, the lack of sperm selection associates with increased risk of exposure to disrupting environmental factors by the embryo, leading to possible developmental impairment.

The aim of this 3 years PhD project is the identification of specific washing procedures to be used in ART processes, able to reduce the sperm load of contaminants without affecting major cell function. The clinical efficacy of these procedures in terms of fertility outcome will also be tested in qualified centers for assisted reproduction. In addition to the wide of clinical use, the expected results of this project are innovative and patentable with possible economic and commercial implications.