ABSTRACT

Reproductive diseases, mainly those resulting in the infertility affect the chances of human being to reproduce. On the contrary, the heart disease, cancer and degenerative diseases currently account for majority of deaths in the world. Usually, these lifestyle diseases need longer lifespan to become the cause of death.

The proteins secreted by cells carry important information about the cell's well-being, as well as about the condition of the tissues formed by these cells. Once secreted, these proteins may also be transferred throughout the body by means of body fluids, many of which are easily accessible for further 'in-depth' studies. Cellular and secreted proteins are often a focus of studies using proteomic means and the revelation of protein alterations can lead us to new ideas about the molecular mechanisms of diseases as well as possible identification of proteins that may be used as new targets for pharmaceutical intervention or molecules that could be used for diagnostic or prognostic purposes.

Taking into consideration the above aspects, this research was undertaken to find proteins that could: (a) characterise the human follicular fluid as microenvironment of the maturing oocyte, to increase understanding of reproductive processes to improve the techniques of assisted reproduction; (b) represent potential diagnostic or prognostic biomarkers in the case of ovarian hyperstimulation syndrome to prevent development of its severe form; (c) have involvement in intercellular communication and regulate growth and aggressiveness of squamous cell carcinomas.

This study identified several interesting key aspects related to hormonal stimulation of women undergoing *in vitro* fertilisation to treat infertility. The levels of several protein components of complement system were different compare to plasma and subsequently the activity of complement system, a part of innate immunity, was found in the follicular fluid to be significantly lower - around 60% of its plasma activity. Studies on the development of ovarian hyperstimulation syndrome revealed connections to changes in concentration levels of many proteins and computer modeling of their interaction network targeted kinin-kallikrein system as the probably key molecular processes behind this disease. In the case of squamous cell carcinomas three cytokines were identified as having a significant role in the disease. Extrapolation of this finding by inhibition of these cytokines using humanised antibodies may increase the differentiation of cancer cells, whilst inhibiting their growth rate and aggressiveness, thus preventing further spread.

The proteins in body fluids offer a rich source for the long awaited disease biomarkers which may be recognised by discovery driven proteomics approach. However, careful validation of the data is absolutely necessary to reach expected selectivity and specificity of such biomarkers for clinical use.