

Male infertility is up-to-date a burning problem affecting approximately 7% of all males and it is responsible for 40 – 50% of all infertility problems. In 20% of all infertility cases male factor is directly responsible for reduced fertility, while in another 30% it contributes to the fertility disorders. Another major problem within this field is idiopathic infertility, in which the cause of disturbed fertility goes beyond the standard parameters investigated during semen analysis, such as motility, morphology and sperm counts. This creates the need to identify potential causes of male infertility at the molecular level. Both, the exposure to xenoestrogens, compounds which imitate estrogen function, as well as rare examples of estrogen deficiency, have clear negative effect on male fertility. The influence of estrogen-like compounds has become particularly interesting in the context of male fertility, as their presence in the environment can disturb the balance between androgen and estrogen *in vivo*.

Studies indicate that estrogens are essential for the proper development of the male reproductive system, as well as they influence the process of sperm formation and maturation. Our previous research revealed the presence of estrogen receptors in those cells, and not yet published data also confirmed the presence of PELP1 protein, which is involved in estrogen-mediated signal transduction, in the male gametes. As the PELP1 is only one of the proteins involved in estrogen-dependent signal transduction, we would like to check the expression of other components that are involved in this process (estrogen receptors, SRC kinase), not only in germ cells, but also in the human testes and epididymis. Knowledge of the expression of those proteins and their interactions in the male reproductive system may be useful in assessing of the men reproductive potential.

In order to achieve the above objectives of the research we would like to analyze the archival tissue specimens, as well as those obtained from autopsies. Also we would like to study semen samples from patients treated for infertility problems. We plan to assess the expression of PELP1 and other proteins involved in signal transduction associated with estrogen on the level of mRNA and protein expression using quantitative analyses. For the evaluation of gene expression we will use specific primers and fluorescent probes. For the analysis of protein interactions, we will use the Lightning-Link® technology. Analysis of expression of proteins of interest in semen samples obtained from normo- and oligozoospermic men will be carried out using flow cytometry, and compared to different sperm parameters such as motility, morphology, sperm counts and concentration.

We expect that the our investigation will reveal the relationship between the expression of the different elements involved in estrogen dependent signaling in male reproductive system, as well as it will help to understand the mechanisms that may affect the male fertility potential and fertilizing ability of the spermatozoa. This may be valuable in verifying the hypothesis that estrogens control many processes in the male reproductive system using specific proteins, i.e. PELP1, and at the level of gametes – the estrogen's influence depends on the non-genomic mechanism. This, in turn, could allow the search for new diagnosis of male infertility at the molecular level in the future.