SUMMARY

Infertility involves ca. 15% - 20% of couples at reproductive age, among which a male factor can account for a half of these cases. Despite of a progress in medicine, still high percentage of idiopathic male infertility is being reported. Therefore, in recent years molecular background has been intensively studied, also at the protein level. Proteomic studies on male infertility have started more than 20 years ago, and current progress in this field makes proteomic research very useful. The present work includes a set of three publications (one review and two original articles) which aimed to identify molecular basis of male infertility by using proteomic tools. Two types of male infertility were included in the study: immunological infertility and asthenozoospermia.

The study included: 1) the identification of sperm antigens by the use of ASA-positive blood sera from infertile women and men, 2) the identification of sperm antigens by the use of ASA-negative blood sera from healthy and fertile controls, 2) the identification of metabolic pathways involved in isolated asthenozoospermia and 4) the determination of status of sperm mitochondria on the basis of sperm mitochondrial membrane potential, and detection of produced by them reactive oxygen species (ROS). Additionally, in both cases of infertility the data obtained were validated by Western immunoblotting, and additionally the immunostaining of sperm cells was also performed in asthenozoospermia cases.

The identified immunoreactive sperm proteins have been divided into 3 groups of antigens: 1) antigens recognized specifically by ASA-positive blood sera (32 antigens), 2) antigens recognized by both ASA-positive and ASA-negative blood sera (35 antigens) and 3) antigens recognized only by ASA-negative control blood sera. Among sperm antigens specifically recognized by ASA-positive blood sera there were 12 proteins already known for their role in fertilization. Moreover, there were three proteins specifically recognized by ASA-positive female. Two of them (ARSA, TCP1-theta) were involved in sperm-oocyte interaction, the third one (ARRDC5) was a sperm-specific protein but its role in fertilization is yet not known.

In the study on isolated asthenozoospermia there were identified 25 sperm proteins displaying altered expression. Most of them were down-regulated and were connected with

metabolic pathways responsible for energy production. There was also indicated the low sperm mitochondrial membrane potential in the group of asthenozoospermic males what confirms the dysfunction of sperm mitochondria. Moreover, the high levels of ROS in asthenozoospermic serum indicates that oxidative stress plays an important role in aetiology of this type of infertility. Among proteins with altered expression there were detected three proteins of epididymal origin. The expression of two of them (LTF, DJ-1) was conversely correlated with the level of oxidative stress, what suggests that isolated asthenozoospermia can be evoked by high levels of ROS in epididymis and perhaps even in testes.

Summing up, the published reports included in this study contribute to better understanding of two types of male infertility: immunological infertility and asthenozoospermia. The data obtained indicate that some of ASA reactions with sperm can be treated as the natural ones, but in specific conditions they can evolve into reactions directed towards spermatozoa. Moreover, the presented data indicated that antigens recognized by ASA can play an important role in fertilization but were developed in immunological reactions in females being specifically directed to sperm cells. In the study on isolated asthenozoospermia the data obtained clearly indicated that this sperm pathology can be a result of oxidative stress present in the male reproductive tract. It seems that ROS damage of sperm mitochondria may lead to their dysfunction and inefficient energy production which is required for normal sperm movement.