Infertility is a growing global health issue of the 21st century, currently affecting approximately 15% of all couples worldwide. Nearly half of its cases are related to male factors. Diagnostic methods routinely used in seminological laboratories are usually limited to basic semen analysis, which does not provide information on possible causes of deteriorating semen quality. A particular challenge is idiopathic male infertility, where parameters related to semen quality are proper, making it difficult to locate the cause of reproductive failures. Therefore, new parameters are still being searched for, the introduction of which into routine diagnostics would translate into faster and more effective diagnosis, and consequently, the implementation of appropriate prevention/therapy for couples struggling with the problem of infertility. However, the last decades have resulted in the discovery of the potential of seminal plasma components as a source of information on possible causes leading to male fertility decline and markers whose changes could reflect the spermatozoa's ability to fertilize the egg. Among them, polyunsaturated fatty acids (PUFAs), their derivatives (prostaglandins (PGs), isoprostanes (IsoPs)), and components of the antioxidant system such as glutathione peroxidase 1 (GPX_1), superoxide dismutase (SOD), and nitric oxide synthase 1 (NOS_1) can be distinguished.

Omega-3 and omega-6 fatty acids are among the most important representatives of polyunsaturated fatty acids (PUFAs). Their role in maintaining proper organ and cellular function is invaluable, as they are structural components of cell membranes and are responsible for maintaining their fluidity and integrity. This is particularly important for spermatozoa, which must possess the appropriate characteristics for free and smooth movement toward the egg cell in order to fulfill their biological function. However, there are many environmental factors, including improper diet, that negatively impact male reproductive potential. They often lead to the development of oxidative stress in the male reproductive system, which results in an imbalance between oxidative and antioxidative mechanisms and the formation of toxic reactive oxygen species (ROS) that enter the environment of spermatozoa. ROS may lead to damage of the spermatozoa cell membrane, the release of fatty acids into seminal plasma, and the formation of pro-inflammatory prostaglandins, which negatively affect male reproductive potential, as well as isoprostanes, the quantity of which depends on the intensity of oxidative stress and can be an indicator of the degree of disruption of the oxidative-antioxidative balance. Seminal plasma also contains enzymes that are responsible for eliminating ROS and protecting sperm cells from damage. However, researchers have shown that in the semen of infertile men, ROS levels are significantly lower than in fertile men, which, combined with sperm membrane damage, fatty acid release, and prostaglandin formation, may not only potentially explain the mechanisms leading to the deterioration of semen quality, but also be a source of markers that could be used in the diagnosis of male infertility and therapeutic molecular targets, the modification (e.g., pharmacological) of which could result in improved male reproductive potential.

The aim of this project is to analyze the levels of polyunsaturated fatty acids, with particular emphasis on docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), also known as omega-3 fatty acids, arachidonic acid (AA), representing omega-6 fatty acids, linoleic acid, alpha and gamma-linolenic acid, expression of selected derivatives of arachidonic acid (including prostaglandin PGE_2, the stable metabolite of PGI_2 – 6-keto-$PGF_{1\alpha}$, as well as F_2-isoprostane), and markers of oxidative stress (GPX_1, SOD, and NOS_1) in the seminal plasma of infertile patients (n=220-250) with abnormalities in sperm count, morphology, and/or motility, divided into groups according to the WHO 2021 criteria for male infertility, normozoospermic infertile patients ($n \geq 15$) as well as fertile men ($n \geq 17$) with proven fertility. The measurements of levels of selected parameters will be performed using advanced analytical methods (including gas chromatography with mass spectrometry and immunoenzymatic ELISA tests used in routine diagnostics of many other diseases) and statistical methods. This will enable the identification of at least one marker differentiating studied groups of men and the determination of correlations between parameters, which may be the starting point for understanding many unknown mechanisms leading to decreased male fertility and new therapeutic targets. In addition, the assessment of the possibility of using attenuated total reflection infrared spectroscopy (ATR-IR) in non-invasive differential diagnostics will be verified. In this project, the diagnostic usefulness of multivariate models and discriminatory analysis will be verified, making it possible to distinguish individual disorders from each other and from a control group of fertile men. The assumed goal will be achieved through the use of ATR spectra obtained for seminal plasmas from all study groups, in conjunction with parameters studied in this project - as far as we know it is the first such attempt. The obtained results will allow for a better understanding of the diagnostic potential of selected biomarkers in the pathogenesis of male infertility, including idiopathic infertility, and may be used to develop more effective diagnostics, prevention, and/or therapy.