The infertility is a social disease concerning about 10-18% of couples. It is estimated that male factor determines 40-60% of all couples infertility cases. It became clear that numerous factors, that can be reciprocally related between each other and which disturbances are being observed in males with reproductive failures, pays attention to the complexity of the problem. Beside of a variety of known molecular and environmental factors, such as: genetic mutations, chromosomal abnormalities, bad habits (low-quality food, smoking, alcohol, etc.), work in heavy/toxic conditions, also the light should be shed on so-called epigenetic factors, which are in some kind a make-up for genetics. Among them, the methylation of sperm DNA, and methylation/acetylation of the sperm histones (a protein component needed for DNA packaging in a cell) seems to play crucial role in proper embryo development. Another epigenetic factor is the positioning of chromosomes within sperm nucleus, what means the defined localization of particular chromosomes. Spermatozoa characterizes unique nuclear packaging of the chromatin, thus the chromosomes' positions are also specific. It is known that in men with various disturbances of fertility, the nuclear organization is changed. Disturbances in those epigenetic elements are connected to male infertility. There are evidences that epigenetic changes are prone both to: genetics, as well as for environmental factors. What is interesting, relative interaction between them may work as a cause or a reason of disturbances in male fertility.

The MAIN PURPOSE of the Project is to determine how THE POSITIONS OF THE CHROMOSOMES within human sperm nucleus may be altered depending on: the state of fertility, karyotype, chromatin integrity status, epigenetic variations within DNA or histones, and between male members of the same family, incl. various fractions of sperm cells, according to their quality. The NOVELTY of the Project is that all analyses will be done sequentially on the same individual sperm cells, which means that the positioning of the chromosomes will be prepared in particular single spermatozoa, cell by cell, with known and documented: genetic content, chromatin integrity state, and epigenetic marks level/change. Positioning of chromosomes will be performed in 2D and 3D manners.

Tests will be performed in males with normal karyotype (control, fertile vs. infertile from the same family, i.e. brothers), and with chromosomal abnormalities but phenotypically normal (reciprocal translocation carriers RCT, Robertsonian translocation carriers Rob – two mostly observed rearrangement types in live newborns: 1/500-700; other aberrations), pointing out the possible role of chromosomal characteristics in nucleus spatial organization. All tests will be performed in various sperm fractions: cells with good movement, with mature chromatin, and checked fertilization potential.

The COMPLEMENTARY AIM is TO DELINEATE THE ALGORITHM of multi-level diagnosis of genetic risk for male carriers with reproductive failures, of newly found chromosomal rearrangements (CR), following the complex analytical panel of well-established tests evaluating the genetic and epigenetic factors listed above.

The proposed experimental panel will underline also the role of: carriership of chromosomal rearrangements (CR), and positioning of chromosomes within sperm nuclei. It has to be mentioned, that frequency of chromosome aberrations is higher in infertile men (about 5% of all chromosomal factors). CRs can be called: a 'hidden biological bomb', because CRs very frequently do not affect phenotype (in about 40% of RCTs the sperm parameters are normal), contrary to its negative influence on the sperm production. CR carriers may be at risk for abnormal pregnancy and/or offspring with developmental disabilities, because of the production of genetically unbalanced sperm cells during improper meiotic segregation. It is important, especially in the context of IVF techniques, where only visual evaluation of sperm motility and morphology is performed, when selecting sperm cell for IVF procedure.