

Infertility worldwide demonstrates the amount of 1/5 of married couples aiming to conceive. Beside numerous factors appearing as a result of so-called expanding civilization (change in a life style, contamination of air, water and soil. Appearance of new chemical/toxic substances affecting hormonal network and/or gene expression must be noted. Recognition of male infertility reasons is still very poor and there is a huge number of so-called idiopathic infertility (approx. 50 % in males) which is understandable when accounting more than 2,000 genes taking part in spermatogenesis alone. Still little is known about the genetic causes of infertility, which until recently, due to the technical limitations and lack of knowledge cannot uncover mechanisms leading to impaired spermatogenesis. This leads very often to non-treatable syndromes (azoospermia) and extensive use of assisted reproduction techniques. Furthermore, non identified reasons of infertility hamper new therapeutic options that may arise from genetic engineering and/or genomic editing. Meanwhile, azoospermia cases rose up to 1% of male population which makes the situation epidemic. In the presented Project, we propose the use of all available methods of system biology (including: whole genome sequencing, analysis of the rare variants and the coding and regulatory regions of genome, as well as transcriptome) after previous recruitment of infertile male individuals from extended and often related families, which enables especially fruitful analysis due to the accumulation of negative genetics features predisposing to infertility. Identified variants within this Project will form the basis for a diagnostic molecular platform effective for determination of infertility. It may envisage the high possibility of application of such platform for use both: by public and private clinics dealing with infertility diagnosis and treatment. As cumulation of genetic errors might be suspected in consanguineous families, often due to arrange marriages, we propose to use systemic biology tools for thorough genomic analysis as the Whole Genome Sequencing, analysis of so-called rare variants, putting attention on both: coding and noncoding elements together with evaluation of gene expression library.