POPULARNONAUKOWE STRESZCZENIE PROJEKTU (W JĘZYKU ANGIELSKIM)

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women in reproductive age. Additionally, the increased frequency of Hashimoto thyroiditis (HT), the principal autoimmune thyroid disease, has been observed in this group of patients, in comparison to healthy persons. Both PCOS and HT may result in a wide range of metabolic disorders, such as dyslipidemia, insulin resistance, hiperinsulinemia and impaired glucose tolerance, leading to obesity, metabolic syndrome, diabetes and cardiovascular pathologies, as a long-term consequences. What is more, women suffering from these diseases are at higher risk of procreation difficulties as spontaneous abortions, miscarriages, preterm deliveries and infertility which are considered a growing medical problem nowadays, connected with strong emotional consequences and large socioeconomic costs. Not surprisingly, both diseases predispose to the presence of depression episodes and self-acceptance disorders.

The association between PCOS and HT is rather beyond doubts. More importantly, joint occurrence of both diseases is associated with higher risk and higher severity of metabolic and reproductive consequences than in PCOS or HT alone, and the severity of the disease symptoms depends on the duration of the thyroid dysfunctions. Although, high impact of the genetic factor to the development of these two diseases is well documented, genetic variants associated with PCOS or HT as well as variants that predispose to their joint occurrence are still uncertain.

The whole-exome sequencing (WES) is a relatively new, comprehensive approach for the identification of the disease susceptibility genetic variants. So far, WES was not applied in regard to the susceptibility to PCOS or HT development. Thus, the principal aim of our study will be to **undercover new genetic variants associated with the development of both PCOS and HT, and predisposing to joint occurrence of these two diseases**, using WES application. We want to answer the following specified questions: (1) which genetic variants are uniquely associated with the susceptibility to PCOS or HT development? - and (2) are there any new, so far unknown, genetic variants that predispose to joint occurrence of both diseases?

The study will included two stages of genetic testing. In the first stage, 210 patients divided into three groups (70 women each) will be recruited upon the diagnosis: (1) with PCOS, (2) with HT and (3) with joint PCOS and HT. Diagnosis will be made based on comprehensive clinical evaluation, USG examination and serum level measurements of several biochemical-hormonal parameters and antibodies. Genomic DNA will be isolated from peripheral blood and used for WES. Genetic variants identified by WES, associated with PCOS or/and HT development, will be validated in the second stages' genotyping by TaqMan allele discrimination method, performed on at least 300 unrelated women with PCOS, HT or joint PCOS and HT occurrence. We believe that the results of our study will enable identification of the patients who are at the higher risk of more severe disease symptoms and will allow to more effectively prevent their long-term medical consequences.