LITHUANIAN UNIVERSITY OF HEALTH SCIENCES

International Summer School Practice

Associations of SERPINA1 Gene Single-Nucleotide Variants with Pituitary Neuroendocrine Tumors

Pituitary neuroendocrine tumors (PitNETs) are neoplasms originating from the neuroendocrine cells of the anterior pituitary gland. Although most PitNETs exhibit slow growth and relatively favorable clinical outcomes, some demonstrate invasive behavior, increased proliferative activity, resistance to treatment, and recurrence. The biological mechanisms responsible for these differences remain incompletely understood. Therefore, identifying genetic factors associated with PitNET development and biological behavior is important for improving our understanding of tumor pathogenesis and identifying potential prognostic biomarkers.

The SERPINA1 gene encodes alpha-1 antitrypsin (AAT), a serine protease inhibitor involved in the regulation of proteolytic activity, inflammatory responses, and tissue homeostasis. Alterations in SERPINA1 expression and function have been investigated in various pathological conditions, including malignancies. Previous studies have suggested that SERPINA1 expression may be associated with tumor progression, invasion, and interactions within the tumor microenvironment. However, the potential contribution of SERPINA1 genetic variability to the development and biological characteristics of PitNETs remains insufficiently investigated.

Single-nucleotide variants (SNVs) may influence gene expression, protein function, and susceptibility to disease. Two well-characterized SERPINA1 variants, rs28929474 and rs17580, are associated with altered alpha-1 antitrypsin function and circulating protein levels. Another variant, rs1243168, will be investigated to explore potential associations between genetic variability within the SERPINA1 locus and PitNET characteristics. Investigating these variants may provide additional insights into the possible involvement of SERPINA1 in PitNET pathogenesis.

The aim of this project is to investigate the associations of SERPINA1 gene single-nucleotide variants (rs28929474, rs17580, and rs1243168) with pituitary neuroendocrine tumors and their clinical and morphological characteristics.

The objectives of the project:

To determine the genotype and allele frequencies of SERPINA1 rs28929474, rs17580, and rs1243168 variants in patients with PitNETs.

To evaluate the associations between the investigated SERPINA1 variants and PitNET occurrence,.

To investigate potential associations between SERPINA1 variants and PitNET characteristics, including size, invasiveness, and proliferative activity.

Research methodology. The study will involve DNA samples obtained from patients diagnosed with PitNETs. Genotyping of the selected SERPINA1 variants will be performed using Real time polymerase chain reaction (RT-PCR). Genotype and allele frequencies will be calculated, and statistical analyses will be conducted to evaluate potential associations with available clinical and morphological data.

Expected results and scientific significance. This study is expected to provide preliminary data on the distribution of selected SERPINA1 variants among patients with PitNETs and their potential associations with tumor characteristics. The findings may contribute to a better understanding of the genetic factors involved in PitNET development and biological behavior. Given the limited evidence concerning the role of SERPINA1 genetic variants in PitNETs, the project may provide a foundation for further investigations involving larger patient cohorts and complementary molecular analyses.