

Role of TP53 mutations in corticotroph pituitary tumors

Pituitary tumors are one of the most commonly diagnosed intracranial tumors in adults. They can develop from different types of cells forming pituitary gland. Corticotroph tumors may develop from pituitary cells that secrete adrenocorticotrophic hormone (ACTH). These tumors most often cause excessive secretion of ACTH and, as a consequence, specific endocrine symptoms - Cushing's disease.

In recent years, the results of few studies focused on identification of genomic mutations that cause tumor transformation of corticotrophic pituitary cells were published. Few genes with changed DNA sequence changes have been identified in tumor samples from patients. In the most recent of these studies, a significant proportion of patients revealed mutations in *TP53* gene. This gene encodes for TP53 protein, which is one of the most important tumor suppressors, a factor inhibiting the process of neoplastic transformation. Mutations in *TP53* gene are observed in approximately 50% of human cancers. The discovery of the *TP53* mutation in a significant number of patients with corticotrophic tumors was surprising because earlier studies on TP53, although burdened with various technical imperfections, indicated rather the lack of this gene mutation in this type of tumors.

Importantly, the mentioned results and the few literature case reports on *TP53* mutations patients with corticotrophic adenomas suggest that mutations in this gene occur in patients with those subtypes of corticotrophic adenomas that are characterized by unfavorable prognosis and a greater risk of tumor regrowth after surgical tumor removal, which is the basic therapy method.

In the proposed study, we are going to determine the presence of mutations in *TP53* gene in 144 patients with corticotrophic pituitary adenomas. Mutations will be identified using a modern method of DNA sequence analysis - the so-called next-generation sequencing.

In addition to *TP53* mutations we will determine the occurrence of several other selected mutations typical for corticotrophic adenomas to determine the possible co-occurrence or mutual exclusion of various mutations.

Using clinical information on the occurrence of tumor regrowth in patients included in the study, we will verify the possible usefulness of assessing the *TP53* mutation in evaluating the risk of recurrence of the disease. Finding new prognostic factors in patients with pituitary adenomas is of special importance because patients at higher risk could benefit from more frequent check-ups or receive additional adjuvant treatment after tumor removal, which is the primary treatment method.