**New approaches to determination pathophysiological changes in patients with cystic fibrosis**

Cystic fibrosis (CF) is a life-limiting disease caused by mutation in the cystic fibrosis transmembrane regulator (CFTR) gene. To date, more than 2,000 mutations in the CFTR gene have been described, of which only 360 are directly related to CF. In a group of patients carrying mutations of unknown or variable clinical significance, it may be difficult not only to diagnose CF but also to facilitate clinical studies to determine the efficacy of new low - molecular weight compounds targeting disrupted CFTR protein. These so-called CFTR modulators have opened a new era in causal treatment of CF. To maximize the effect of these new therapies, not only the patient's genotype, but also the individual rate of response is crucial. In recent years, intestinal organoids have been used as an *ex vivo* model to determine the degree of CFTR function and at the same time to predict the therapeutic response to available therapeutic molecules. In our project, using the patient's native tissue and cultures of intestinal organoids derived from this tissue, we demonstrated varying degrees of CFTR residual function in a total of 14 patients with CF (0–39.7% of healthy control function). We characterized de novo mutation of the CFTR gene in a patient whose diagnosis has not been confirmed using available standard diagnostic methods. Based on *ex vivo* prediction, we identified potential responders to available CFTR modulators in 8 cases and non-responders in 5 cases. Translation of this research into clinical practice becomes, in accordance with the principle of theranostics, the basis for personalized care for all patients with CF.

**Keywords: cystic fibrosis, CFTR modulators, intestinal organoids, personalized treatment**