

## **15-oxo-eicosatetraenoic acid (15-oxo-ETE) as a potential diagnostic biomarker of aspirin-exacerbated respiratory disease.**

Aspirin-exacerbated respiratory disease (AERD) is characterized by the presence of asthma, chronic rhinosinusitis with nasal polyposis, and acute respiratory reactions induced by aspirin and other cyclooxygenase-1 inhibitors. The key feature of AERD is the dysregulation of arachidonic acid (AA) metabolism pathways. Despite a relatively broad knowledge on the pathophysiology of AERD, only a few *in vitro* diagnostic tests have been proposed, but none of them can be recommended for the purpose of diagnosing AERD. In clinical practice, the most reliable diagnostic method is an aspirin provocation tests. However, oral provocation test, which is a gold standard, is time-consuming and carries a risk of severe hypersensitivity reactions. Therefore, we are going to propose an AA metabolite- 15-oxo-eicosatetraenoic acid (15-Oxo-ETE) for *in vitro* diagnosis of aspirin hypersensitivity.

Previous studies have shown that epithelial and mast cell interactions, leading to the synthesis of local 15-Oxo-ETE, may contribute to the dysregulation of AA metabolism in patients with AERD. This indicates a possible role of global (blood and urine) level of a 15-Oxo-ETE as a diagnostic predictor for aspirin hypersensitivity. It might be a safe *in vitro* method during SARS-CoV-2 pandemic that could facilitate the diagnosis of AERD.

The study will use a prospective database of 70 patients with AERD, 70 aspirin-tolerant asthma patients and 70 healthy subjects. The evaluation of 15-Oxo-ETE will be performed in plasma and urine. In each patient two samples of blood and urine will be collected in order to investigate the repeatability of measurements. The main aim of the study will be the assessment and validation of both plasma and urine 15-Oxo-ETE levels as the diagnostic index for aspirin hypersensitivity. Additionally, we will try to find the cut-off point of blood and urine 15-Oxo-ETE levels in the healthy group.

We believe that our data will demonstrate that global 15-Oxo-ETE production is a specific and sensitive test for the identification of aspirin-sensitive asthma patients.