Aspirin-exacerbated respiratory disease (AERD) is a distinct phenotype of asthma. AERD is an important clinical issue because it is characterized by sensitivity to aspirin, nasal polyps and rhino-sinusitis, overproduction of cysteinyl leukotrienes (cys-LTs) and mast cell activation. Nasal polyps from patients with AERD contain significantly more extravascular leucocytes with adherent platelets than polyps from aspirin-tolerant control subjects *(Blood 2012;119:3790-8)*. Moreover, the percentages of circulating neutrophils, eosinophils, and monocytes with adherent platelets were markedly higher in blood of patients with AERD than in aspirin-tolerant control subjects *(Blood 2012;119:3790-8)*, and adherent platelets lead to an increased production of leukotrienes (LTs), which contributes to the features of persistent respiratory tract inflammation and LTs overproduction *(J Allergy Clin Immunol. 2014;133:1692-701).*

There are a number of biomarkers that are used to evaluate platelet activation, many of which are likely to be relevant in patients with asthma such as broncho-constricting agents eg, thromboxane A2 and platelet-activating factor (PAF) as well as eosinophil chemotactic factors eg, PAF and platelet factor 4.

Adenosine diphosphate (ADP)–reactive purinergic (P2Y12) receptors play a pivotal role in platelet activation and aggregation through a complex cascade of actions. Several drugs targeting the P2Y12 receptor have been introduced to therapy, that selectively and irreversibly inhibit P2Y12 receptor. It has been speculated that P2Y12 receptor inhibitors (eg, clopidogrel) could be efficacious as treatments for acute aspirin-induced respiratory reactions and chronic inflammatory state in patients with AERD, because 1) P2Y12 receptor inhibitors reduce the formation of platelet-leukocyte aggregates, and 2) P2Y12 receptors are essential for the platelet-dependent pro-inflammatory effects of cys-LTs.

The results of this study on aspirin-sensitive asthma will set new objectives and research hypotheses: 1) Oral administration of clopidogrel will decrease the percentage of circulating platelet-adherent leukocytes; 2) Oral administration of clopidogrel will reduce systemic (measured in urine and blood) and local biosynthesis (measured in induced sputum supernatant) of platelets activity biomarker in patients with AERD; We assume that the inflammatory mediators measured in induced sputum supernatant would reflect the inflammation process in the bronchial tree *in vivo*. 3) Oral administration of clopidogrel will reduce systemic and local biosynthesis of cys-LTs in patients with AERD; 4) pretreatment with clopidogrel will cause prevention against acute bronchial aspirin-induced reactions during aspirin challenge in patients with AERD.

The aim of this study is to answer the following questions: Does oral administration of clopidogrel 1. Decrease the percentages of circulating leucocytes with adherent platelets, 2) affect the levels of circulating platelet-adherent leukocytes and platelets bioactive mediators [thromboxane B2 (TXB2), sP-selectin (soluble P-selectin), platelet factor 4 (PF4/CXCL4) and sCD40L (soluble CD40 ligand)] as well as cys-LTs measured in induced sputum (bronchial derived material) and in urine ? 2. What is the relationship between platelets bioactive mediators, cys-LTs levels in induced sputum supernatants and the provocative dose of aspirin (PD20 – the dose of aspirin cause 20% fall of FEV1) ? 3. Does pretreatment with clopidogrel prevent against acute aspirin-induced reactions?

This *in vivo* study will shed new light on the role of platelets in asthma patients hypersensitive to aspirin. This first-time study can lead to new possibilities for antiplatelet treatment in patients with AERD. In the future, we will need to further study the assessment of long response (eg, 1-year) therapeutic efficacy of platelet inhibitors on chronic bronchial inflammatory state in patients with AERD.