Respiratory viruses may infect airway epithelium of upper and lower airways and cause mild infections as well as serious life-threatening pneumonias and severe acute respiratory syndromes (SARS). They are the major cause of asthma and chronic obstructive pulmonary disease (COPD) exacerbations. Respiratory viruses such as HRV (*Picornaviridae*), HCoV (*Coronaviridae*) and RSV (*Paramyxoviridae*) are single stranded RNA viruses eliciting innate and adaptive immune response. We observed and published that HRV16 may *in vitro* infect the lung vascular endothelium and induce antiviral and inflammatory response. In preliminary studies, we confirmed the infection of lung endothelium with human low-pathogenic coronavirus HCoV229E.

In this project we stand the hypothesis that the lung vascular endothelium may be infected with respiratory viruses during airway viral infections. Being a source of antiviral and inflammatory mediators, it may actively participate in the generation antiviral immunity. Chronic inflammatory conditions, inc. asthma and COPD, may determine the ability of the lung vascular endothelium to generate antiviral immunity against respiratory viruses. The main aim is to confirm this hypothesis. Second aim is to assess if chronic hypoxic airway conditions may affect antiviral immunity of the lung vascular endothelium.

Why the lung vascular endothelium may generate antiviral immunity? Because it: (1) expresses entry receptors for respiratory viruses (HRV, CoVs, RSV); (2) has pattern recognition receptors (TLR, RLR, NLR) capable of sensing viral RNA; (3) generates mechanisms responsible for IFN-dependent antiviral immunity; (4) is a potent source of cytokines and inflammatory mediators and it can interact with cells of the host tissues and immune cells; (5) may professionally present the antigen to Th cells, thus shaping the acquired immunity.

The study will be performed on lung tissues and vascular endothelium isolated from lung tissues obtained during thoracoscopy or lung surgery from patients due to diagnostic/therapeutic reasons. Individuals with allergic asthma, COPD and patients without chronic inflammatory airway diseases will be included to the study. In a set of experiments analysis of susceptibility of the lung vascular endothelium to respiratory viruses such as HRV16, HCoV229E and RSV and its potential for generation of antiviral and inflammatory response will be analyzed. Additionally, set of experiments will be done in hypoxic conditions reflecting chronic hypoxia that may occur in asthma and COPD patients.

Possible impact of the project on research and knowledge: (1) It may initiate the revision of understanding the virus effect on the generation of antiviral responses during airway viral infections. It may redefine the knowledge about the differences of antiviral immunity in chronic inflammatory condition focused on the vascular endothelium. (2) By further understanding the endothelial immunopathology, the development of endothelial-specific preventive approach for chronic inflammatory airway conditions might arise. (3) It opens the discovery of innovatory approach of airway viral infections treatment based on the endothelium-focused therapies in healthy individuals, asthma and COPD patients.