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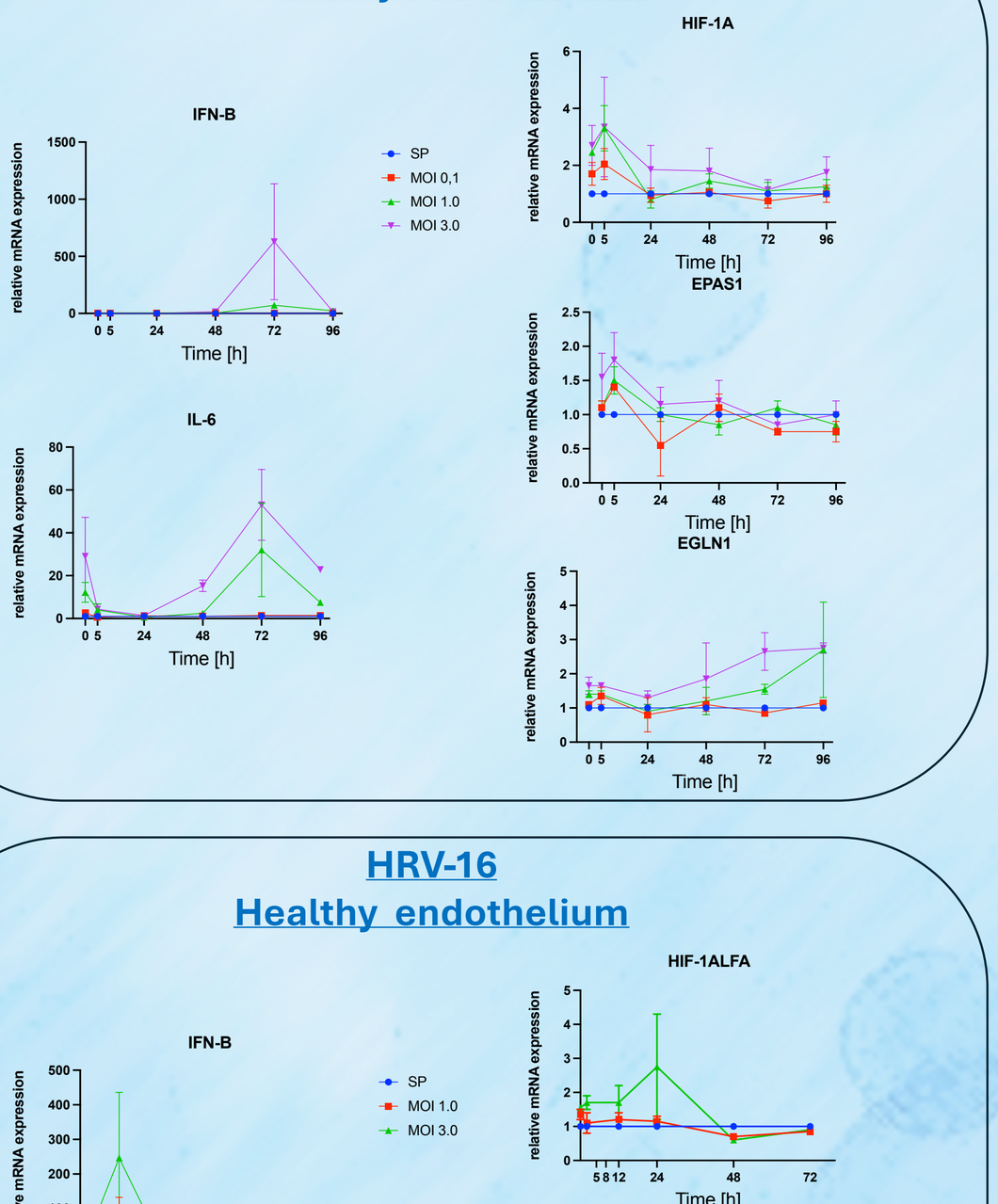
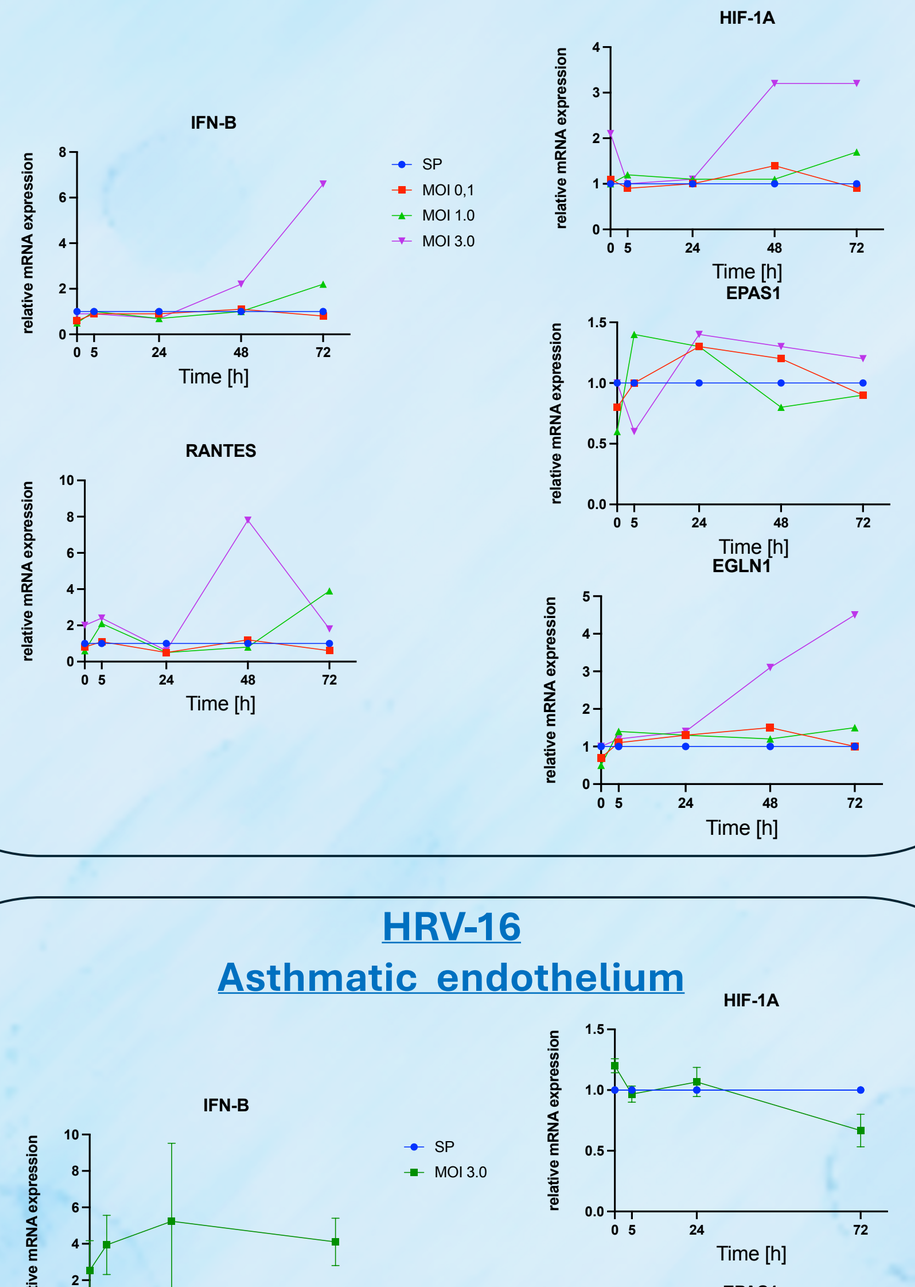
ASSESSMENT OF THE ABILITY OF HUMAN RESPIRATORY VIRUSES HRV-16 AND HCoV-229E TO GENERATE HYPOXIA IN HUMAN LUNG ENDOTHELIAL CELLS

INTRODUCTION: Under physiological conditions, the lungs provide an oxygen-rich environment, and changes in oxygen availability in the tissues affect physiology and are often associated with pathological conditions. Low blood oxygen levels (hypoxemia) can result from reduced oxygenation, as seen in chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD). Based on literature reports, it is known that certain respiratory viruses are characterised by their ability to generate and effectively exploit local hypoxia conditions to their advantage. Among other things, this enables them to inhibit the production of the main antiviral defence proteins, the interferon (IFN) family. Literature reports indicate that patients with asthma may be characterised by damage to the epithelial cell barrier and reduced ability to produce interferon family proteins. The endothelium is the first layer of cells to encounter the blood and is the first to be exposed to changes in blood oxygen levels. Hypoxia and hypoxia-inducible factor (HIF)-mediated signal induction significantly impact endothelial function and biology at hypoxic sites. In addition, as shown by studies by a team from the Department of Immunology and Allergy at the Medical University of Lodz, pulmonary vascular endothelial cells have a broad spectrum of functions during respiratory virus infection: from the ability to constitutively secrete high concentrations of inflammatory cytokines, to possess a range of antiviral response mechanisms (e.g. IFN-β), to the surface presence of entry receptors for low- and high-pathogenic respiratory viruses.

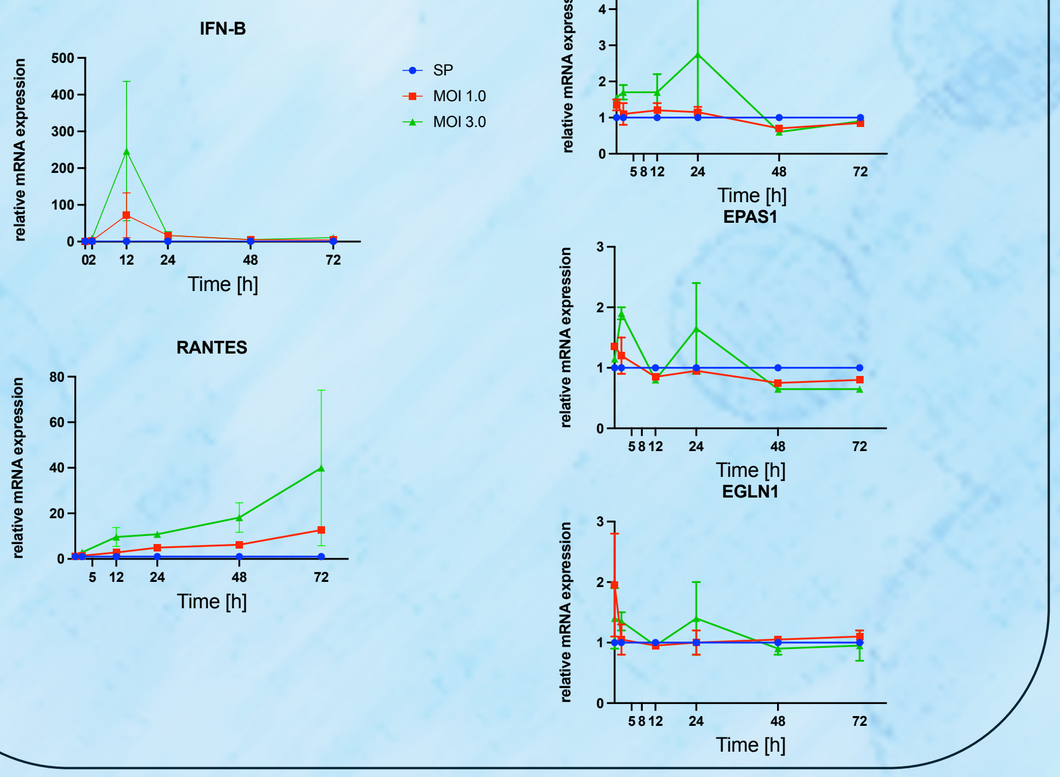
HCoV-229E
Healthy endothelium



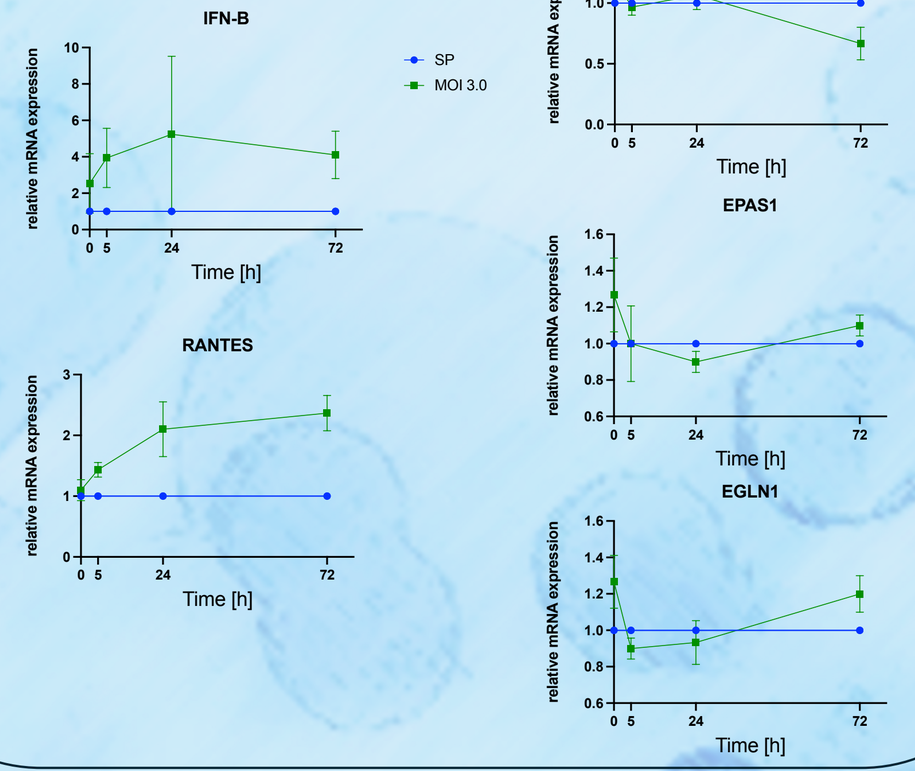
HCoV-229E
Asthmatic endothelium



HRV-16
Healthy endothelium



HRV-16
Asthmatic endothelium



CONCLUSION: Induction of hypoxia-inducible factors such as HIF-1α and EPAS1 (HIF2α) occurred at a very early stage of HCoV-229E infection (5hpi), which may contribute to the attenuation of the antiviral cellular response, according to previous studies, is characterised by a delayed phase relative to the replicating pathogen. We observed that HCoV-229E virus infection of pulmonary vascular endothelial cells from a patient with asthma induces increases in mRNA suppression of hypoxia-inducible factors (HIF1α and EGLN1). Interestingly, when cells were induced with HRV-16, increases in mRNA expression of the same factors occurred at later time points (24hpi), even though the dynamics of replication and induction of inflammatory and antiviral responses differ significantly between the viruses used in the study and, in the case of HRV-16, occur at earlier time points.