Projects from Molecular Pneumology Research Group, Department of Respiratory Medicine, MHH.

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We need support from highly motivated and ambitious life sciences and/or medical students to pursue scientific research at the highest level in the projects listed below.
Translational research projects, together with clinical studies, are the core of our group. Our aim is to build a bridge between basic and clinical research. Our general interest is to study the mechanisms involved in acute and chronic inflammation, with particular focus on the diverse roles of acute-phase proteins in lung and liver diseases, and in cancer. More specifically we are interested in native and post-translationally modified forms of α1-antitrypsin (AAT), one of the major human protease inhibitors having broad immunomodulatory properties.
Researchers have a considerable interest in AAT because about 1-3% of Caucasians have severe inherited AAT deficiency, which is a high-risk factor for developing early onset emphysema and at any age liver diseases, such as steatosis, fibrosis, cirrhosis, and even hepatocellular carcinoma. In some cases, individuals with severe deficiency of AAT can also develop skin diseases and inflammatory bowel diseases. Therefore, purified human plasma AAT is used as an augmentation therapy.
Our first project focuses on the effects of AAT therapy on lung and liver disease development and progression.
Currently, companies in patient cohorts are testing novel approaches, one of which is to silence in the liver the production of the mutant misfolded AAT protein (causing the deficiency of AAT in the circulation).
Our second project aims to investigate the consequences of AAT elimination in vitro and in vivo.
There is ample evidence for the involvement of AAT in the development, growth, and metastasis of various types of cancer, including lung cancer. Our results from lung cancer cell lines *in vitro* and findings from lung cancer patient cohorts suggest that AAT is a modulator of cancer cell proliferation, colony formation, invasiveness, and responses to chemotherapies. Moreover, the effects of AAT seem to depend on its molecular form, cancer cell properties, specifically lipid metabolism, and the microenvironment of cancer cells.
Our third project focuses on the mechanisms involved in AAT effects on cancer cells and cancer tissues in vitro, and in biological samples from lung cancer patient cohorts.

Current findings provide evidence that AAT regulates the entry of the SARS-CoV-2 coronavirus into cells and that higher plasma levels of AAT have a positive effect in patients with COVID-19. The positive impact of AAT therapy was documented in small cohorts of COVID-19 patients.
Our fourth project focuses on the biological effects of recombinant spike proteins on human blood cells, on human primary bronchial epithelial and lung endothelial cells *in vitro*.

Projects involve all modern methods for experiments in vitro and in patient materials ex vivo.

End of application: 31th Okt, 2023