Abstract for the general public

Harnessing gut microbiota-derived metabolites to combat acute respiratory distress syndrome

The gut microbiota is a collection of microbes, including bacteria, archaea, fungi, viruses, and protozoa, which inhabit our intestines. It is becoming apparent that the interactions between these microorganisms and human cells are central to maintain health, and become dysregulated in disease.

Despite this, one major question remains unanswered: how does the gut microbiota influence immune function in distal body organs, such as the lungs?

Our preliminary research identified thirteen gut microbiota-derived metabolites, which associate with the protection against allergic inflammation. Furthermore, we tested a causative effect of one such metabolite, p-cresol sulfate, in a mouse model of asthma. P-cresol sulfate was transported from the gut to the lungs via the bloodstream. In the airways, it acted upon lung cells to inhibit the production of a dendritic cell chemoattractant, CCL20, and reduced the severity of allergic responses. Given that CCL20 production precedes the initiation of various inflammatory responses, not just allergic reactions, we hypothesize that its blockade might be efficacious in disease models other than asthma.

In this project, we aim to test p-cresol sulfate, along with other identified metabolites, in a mouse model of acute respiratory distress syndrome (ARDS). ARDS is a major cause of death in patients suffering from severe respiratory infections. In addition, ARDS survivors experience a long-term decrease in life quality, caused by physical dysfunctions (resulting from persistent weakness) and mental impairments (e.g. due to multiple life challenges, including job loss, social isolation, sexual dysfunction, and financial difficulties).

It is currently unknown if lung metabolites contribute to the acute and chronic disease outcomes, or if any relevant metabolic pathways may provide the basis for a therapeutic approach to alter the disease course.

This project aims to test this relationship and design novel approaches for ARDS treatment. This strategy may pave the way to harnessing microbial metabolites for human health benefits.