OC03 - **The choroid plexus epithelium as a novel player in the gut-brain axis**

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Background: The healthy human gut microbiome consists of 100 trillion commensal bacteria. Shifts in gut microbiota, caused by a variety of triggers, have been linked to human health problems, including neurological disorders. Brain homeostasis is secured by the presence of several tight brain barriers, such as the blood-brain and blood-cerebrospinal fluid (CSF) barrier. The latter is formed by a single layer of tightly connected epithelial cells of the choroid plexus, a highly vascularized tissue hanging in the ventricles of the brain, and plays an important role in the development, repair and homeostasis of the central nervous system (CNS). We previously showed that both peripheral and central inflammation have a negative impact on blood-CSF barrier integrity. With its unique position between blood and brain, the choroid plexus possibly plays a role in the communication between the periphery and the brain.

Objective: In this study, we aimed at elucidating whether specific changes in microbiota have an impact on brain homeostasis, via the blood-CSF barrier.

Methodology: C57BL/6 mice were infected with *H. suis*, a gram-negative, spiral-shaped bacterium colonizing the stomach, and one month later, blood, stomach and brain were analysed using immunostainings, bioplex analysis, qPCR and behavioural tests.

Results: One month after infection with *H. suis* we observed increased inflammation in both the stomach and brain. This lead to disruption of brain homeostasis, reflected by increased microgliosis and cognitive decline. While the blood-brain barrier remained functional, disruption of the blood-CSF barrier was detected. This was associated with decreased expression of tight junction proteins at the choroid plexus. Moreover, the gastrointestinal barrier becomes leaky, resulting in low-grade systemic inflammation and the presence of toll-like receptor 4 (TLR4) ligands in the blood of *H. suis* infected mice.

Conclusion and future plans: Our results show that *H. suis* infection results in leakage of the gastrointestinal barrier, with subsequent systemic inflammation. This leads to the loss of blood-CSF barrier integrity, causing disruption of brain homeostasis.

As a next step, we are currently studying the influence of an *H. suis* infection on the development and progression of Alzheimer's disease. To this purpose we are infecting Alzheimer's disease mice with *H. suis* infection and analysing the impact on disease development.