Tight barriers form the major protection for the brain against external insults such as toxins, infectious agents and peripheral blood fluctuations. In her lab, Roosmarijn Vandenbroucke and her team study the role of brain barriers in physiological and pathophysiological conditions, including neurological disorders such as Alzheimer's disease.

These barriers are a central part of the brain homeostasis mechanism and assure a balanced and well-controlled micro-environment in the central nervous system (CNS),» Prof. Vandenbroucke explains. «You can compare it to a firewall. It has to stop potentially toxic substances that might disrupt the functioning of the brain. While the presence of this barrier is essential, our brain also needs specific substances to reach the brain cells. Thereto, the brain barrier contains specialized transporters that decide which molecules can get through the barrier, which, by the way, loses strength as we get older. While very small molecules such as alcohol and e.g. painkillers can penetrate the barrier, most medicines are unable to reach the brain.»

Brain and inflammation

One of the brain barriers is called the blood-cerebrospinal fluid (CSF) barrier, formed by a single layer of choroid plexus epithelial cells. «The main topic of our research is the central role of the blood-CSF interface in the transfer of peripheral inflammation (e.g. sepsis and gut inflammation) to the brain and in the initiation and progression of neuroinflammation (e.g. multiple sclerosis, Parkinson's disease and Alzheimer's disease) and the possible application of this barrier as a gateway for the delivery of drugs to the brain. While curing these diseases might be too ambitious, slowing down the progression of such diseases would already be a major breakthrough.»

«Subtle changes at this blood-brain interface have wide-ranging effects on the brain. Consequently, understanding blood-CSF barrier functionality under physiological and pathophysiological conditions might open up new therapeutic strategies to treat neuroinflammatory diseases,» says Vandenbroucke.

«We focus on tightness of the barrier, leukocyte infiltration, and extracellular vesicle (EV) production. We already identified several alterations at the blood-CSF barrier in both systemic inflammation and neuroinflammatory disorders. For example, we identified a new communication mechanism between blood and brain via the secretion of EVs by the blood-CSF barrier into the CSF, through which a pro-inflammatory message is transmitted from the body to the brain.»

Hijacking a natural transport mechanism

«While the presence of barriers protects our brain, they also hinder therapeutic delivery to the CNS, leading to higher failure rates of CNS drugs in Phase III clinical trials compared to non-CNS drugs. Delivering therapeutic molecules to the brain remains a significant challenge. To address this, we aim to leverage the natural transport mechanisms at the blood-CSF barrier to transport drugs across the blood-CSF barrier into the brain. Currently, this strategy of hijacking these transport mechanisms is being explored with support from my recently granted ERC Consolidator grant.»

Roosmarijn Vandenbroucke was awarded the Baillet Latour Biomedical Award in 2017 for initiating this research.

Stool transplantation

Introducing stool from healthy people through a nasal catheter into Parkinson’s patient’s small intestine can help treat the symptoms of the disease. This is the conclusion of the year-long groundbreaking study Gut-Parfect, conducted by researchers from the Center for Inflammation Research (IRC), Ghent University Hospital and Ghent University, coordinated by Roosmarijn Vandenbroucke, Patrick Santens and Debby Laukens. After twelve months, the participating patients showed a significant improvement in their motor score, the most important measurement for Parkinson’s symptoms. This improvement became more pronounced between the sixth and twelfth month after the transplant of fecal microbiota transplant (FMT), indicating a possible long-term effect. In addition, the participants suffered less from constipation, a common

and troublesome complaint for many people with Parkinson's disease.

Influence of gut bacteria

In Parkinson's disease (PD), the alpha-synuclein protein misfolds and clumps together. Those clumps then damage dopamine-producing nerve cells in the brain, which leads to the typical PD symptoms. Current treatments, primarily medications that replace dopamine, often have side effects and lose effectiveness over time.

"The protein clumps are believed to be formed in the gut wall at a very early stage of the disease, from which they reach the brain cells via the vagus nerve, which connects the gut and the brain. This process can be influenced by gut bacteria. Emerging research suggests a link between PD and the gut microbiome, the trillions of bacteria residing in our intestines. Patients with Parkinson's often have an altered gut microbiome compared to healthy individuals and they often show more (intestinal) inflammation and a disrupted intestinal barrier.

«The clinical study showed that twelve months after the FMT transplant, the actively treated group showed significantly more improvement in motor symptoms compared to the placebo group. Stool transplantation has the potential to improve the quality of life for millions of people worldwide with Parkinson's disease. We will now determine which specific bacteria in the stool give a positive effect, and which patient will be most responsive to this treatment. This could lead to the development of a bacteria pill or other targeted therapy that could replace stool transplantation in the future,» says Prof. Vandenbroucke.

"An important part of our research focusses on the gut-brain axis and how the microbiome can have an impact on the brain and the development of brain diseases," adds Roosmarijn Vandenbroucke. "In light of this, we performed a successful clinical trial on Parkinson patients. Currently, we aim to get a closer look at the mechanisms that might play a role in this gut-brain axis. In the VIB Grand Challenge project, we also plan a new clinical trial on Parkinson patients in collaboration with neurologists at Ghent University and Ghent University Hospital (Profs Patrick Santens and Dr. Arnout Bruggeman), KU Leuven and Leuven University Hospital and Leiden University Medical Center, and together with microbiologist Prof. Jeroen Raes (REGA Institute, VIB and KU Leuven) and gastroenterologist Danny De Looze (Ghent University Hospital).

Roosmarijn Vandenbroucke

In 2008, Roosmarijn Vandenbroucke obtained her PhD in Pharmaceutical Sciences at Ghent University. She then worked for seven years as a postdoctoral fellow in the group of Prof. Claude Libert. In 2015, she became professor at the Faculty of Sciences (Ghent University) and in 2018

group leader at the VIB Center for Inflammation Research (IRC) at the Technology Park of Zwijnaarde (Ghent). Her team includes six postdocs, ten PhD students, four lab technicians, a bioinformatician and an administrative collaborator. Their areas of expertise include blood-brain (BBB) and blood-cerebrospinal fluid (CSF) barriers, gastro-intestinal barriers, the gut-brain axis, sepsis, neuroinflammatory disorders (including Alzheimer, Parkinson and multiple sclerosis) and extracellular vesicles. The entire VIB Center for Inflammation Research has no fewer than 350 employees.

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