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THE INFLAMMATORY GUT-BRAIN AXIS

The term gut-brain axis refers to the communication between the gastrointestinal (GI) tract and the brain, linking intestinal functions including the microbiota composition, with emotional and cognitive functionality of the brain. While both human and rodent data support that the GI tract affects the health of the central nervous system, not much is known about the mechanisms of this gut-brain axis communication. Moreover, unraveling the disturbance of the gut-brain axis in gut inflammation associated neurological disorders, might result in the identification of innovative therapeutics for these diseases.

Leading scientists:

Faculty of Sciences: Prof. Roos Vandenbroucke (Department of Biomedical Molecular Biology, Barriers in Inflammation); Prof. Peter Vandamme (Department of Biochemistry and Microbiology, Laboratory of Microbiology); Prof. Claude Libert (Department of Biomedical Molecular Biology, Mouse Genetics in Inflammation)

Faculty of Medicine and Health Sciences: Prof. Patrick Santens (Department of Neurology); Prof. Martine De Vos & Dr. Pieter Hindryckx (Department of Gastroenterology); Prof. Luc Leybaert (Department of Basic Medical Sciences, Physiology Group);

Faculty of Veterinary Sciences: Prof. Freddy Haesebrouck, Prof. Richard Ducatelle and Prof. Filip Van Immerseel (Department of Pathology, Bacteriology and Avian Diseases); Prof. Lynn Vanhaecke (Laboratory of Chemical Analysis)

Faculty of Bioscience Engineering: Prof. Wim Van Criekinge (Laboratory for computational genomics and bioinformatics & NXTGNT); Prof. Tom Van de Wiele (Center for Microbial Ecology and Technology (CMET)).

Faculty of Psychology and Educational Sciences: Prof. Ernst Koster (Psychopathology and affective neuroscience (PAN) lab)

Faculty of Pharmaceutical Sciences: Prof. Dieter Deforce & Prof. Filip Van Nieuwerburgh (Laboratory of Pharmaceutical Biotechnology); Prof. Sarah De Saeger (Laboratory of Food Analysis)

 # new professorships: 2

Project description

The human gut contains more than 100 trillion microorganisms that perform a variety of essential functions such as digestion, preserving tolerance and immunity and protecting the host from pathogen colonization. A broad range of high-throughput and culture-independent '-omics' analyses are nowadays available to study complex microbial communities, including their function and interaction with the host. These '-omics' techniques complement each other in revealing the impact of the intestinal microbiota on human health. Over the past decade, the importance of the gut microbiome in health and disease has become increasingly recognized. The discovery that an imbalanced microbiome composition influences behavior and cognition, resulted in the establishment of the well-accepted concept of **the gut-brain axis**, referring to the complex communication network between the gastrointestinal (GI) tract and the central nervous system (CNS) and *vice versa*, and includes immune, vagal and metabolic pathways. Dysregulation of the gut microbial composition and function, typically associated with low-grade inflammation (*e.g.* as observed in *Helicobacter* infection), or overt chronic inflammatory conditions of the GI tract (*e.g.* as observed in inflammatory bowel diseases; IBD) increase the risk or contribute to the pathogenesis of extra-intestinal diseases like neuropsychiatric and neurological anomalies. Importantly, for most of these inflammatory CNS disorders there are at present no preventive or causal treatments.

The microbiome is highly subjected to host genetics and environmental factors, including diet and lifestyle. The latter is called the exposome, i.e. the cumulative measure of environmental influences and biological responses throughout an individual's

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lifespan. Understanding the changes in microbiome composition and function through the analysis of multi-omics data, how this relates to GI inflammation and the exposome, and how these alterations feed-forward to brain function, will **increase our understanding of the pathogenesis of neuro-inflammatory disorders** such as inflammation-associated fatigue, depression, Alzheimer's and Parkinson's disease. Moreover, the integration of microbiome, metagenome, metabolome, transcriptome, translatome and proteome data from feces, blood and GI and brain tissue, called integromics, and their linking to the patient's exposome and pathology will **allow the identification of novel therapeutic pathways and interventions to treat complex neuro-inflammatory disorders**.

Based on existing expertise and established collaborations in this field at UGent, two full time ZAP positions are available to further consolidate this innovative area of the 'Inflammatory gut-brain axis'.

Proposed impact

CNS disorders such as inflammation-associated fatigue, depression, Alzheimer's and Parkinson's disease, are among the most disabling disorders, not only in terms of their impact on quality of life, but also in terms of societal and economic impact. Many of these CNS disorders lack a causal treatment, a treatment that prevents progression and a preventive action plan altogether. Such a preventive action plan is now considered one of the top priorities in societal action programs for neurological disorders. In recent years, we have witnessed the rise of the gut microbiota as a major topic of research interest in (bio)medical research. The emerging concept of a microbiota–gut–brain axis indicates that modulation of the gut microbiota may be a tractable strategy for developing novel therapeutics for complex CNS disorders. In addition, one of the most effective parameters eligible to microbial modulation is diet, an upcoming field of research that is linked with a widespread societal interest. Food sciences and their relation to overall well-being and health is of major interest to the general public. Unfortunately, research in this field has long been considered as a 'soft science', in which poorly validated common knowledge and public media have played a major role. Especially, the improved knowledge and well-controlled pre-clinical studies in which the role of nutritional habits on the intestinal microbiome composition, metabolic processes and its role in immune-regulation are addressed, will boost this intriguing area to scientifically solid interpretation. In addition, the development of novel microbiome-based therapeutics and preventive products is currently gaining attention not only within an academic setting, but also within several pharmaceutical companies. This 'inflammatory gut-brain axis' consortium will feed into new therapeutic and preventive strategies and form the basis for the creation of economic value of microbiome-based therapeutics.