

Tenure-track Assistant Professor in Host-Microbe Biology

Name: Healthy Microbiomes and Food (Gezonde microbiomen en voeding)

Appointment: 1.0 fte

Level: tenure-track Assistant professor

1. Field of research

The envisioned professorship investigates beneficial interactions between bacteria (commensals) and their mammalian hosts and/or between pathogens and their host. The envisioned research group combines expertise in areas such as computational biology, cell biology, immunology, microbiology, functional genomics and/or systems biology to further our understanding of the molecular interactions occurring in the cross-talk between microbes and their mammalian hosts.

2. Vacancy

The vacancy is in the emerging field of Host-Microbe Biology. The candidate complements the expertise in Groningen and elsewhere in the Netherlands on the microbiology of host-microbe interactions. The position has been approved by both the Faculty (letter concept 20/00086, February 12, 2020) and the University Boards, being part of the original Agri/Food program and fitting the University's Healthy Aging spearhead; it also falls within the framework of 'Career Paths in Science 4' ('Bèta's in Banen 4').

3. Selection committee

- Prof. Dirk Slotboom (Scientific Director GBB), chair
- Prof. Sasha Zhernakova (Professor in Systems Genetics; UMCG)
- Prof./Dr. Sahar El Aidy (Adjunct Professor in Host-Microbe Biology)
- Prof. Geert van den Bogaart (Professor in Molecular Immunology and Microbiology)
- Prof. Gert-Jan Euverink (Program director Agri/Food & CCC)
- Prof. Dirk-Jan Scheffers (Director of Education, GBB)
- Prof. Michiel Kleerebezem (Professor in Host-Microbe Biology, Wageningen University)
- Mr/Mrs. Xxxxx (t.b.a. as student member; BSc/MSc level!)

Additional (external) advisors:

- Prof. Oscar Kuipers (Molecular Genetics, GBB)
- Prof. Willem de Vos (Wageningen University)
- Prof. Annick Mercenier (University of Strassbourg)
- Prof. Paul de Vos (University Medical Centre Groningen)
- Mrs. Linda Bosveld-Verburg (Human Resources, FSE)
- Dr. Engel G. Vrieling (Managing Director of GBB), secretary

4. Research area

It is now understood that diet plays an important role in shaping the microbiome, with experiments showing that dietary alterations can induce large microbial shifts. Given this association, there may be significant therapeutic utility in altering microbial composition through diet and/or perturbations by (engineered) microorganisms. However, the complexity of the diet-host-microbe interactions and inter-individual differences hamper an adequate progress in this field.

Computational approaches can help to guide the exploration of the molecular and mechanistic processes of the microbiome by forming hypotheses based on genome-scale metabolic models and testing them in the laboratory. One method that helped elucidating such molecular mechanisms is the constraint-based reconstruction and analysis approach, which has been successfully applied in studies on metabolic pathways, individual species metabolism, and inter- species metabolic interactions. New strategies of modeling the metabolic interactions among the microbiota in response to changes in diet need to be developed in conjunction with experimental work (such as dietary intervention studies in humans and animal models).

A major challenge is to benchmark personalized gut microbiome models, for example based on metagenomics data. This requires a better understanding of the mechanisms underlying the interactions between the different microbial species within the gut milieu. Another attractive possibility is to identify good and bad bugs related to specific disease and modulate the microbiota accordingly by administrating advantageous microbiota (or optimized microorganisms by synthetic biology) that help steering the microbiome in the right direction. Moreover, the approaches and technologies developed via this new position can be leveraged to other ecosystems where microbial communities play a role (e.g. skin, soil, multi-strain fermentation processes).

5. Research group and institute

The position will be embedded in the Groningen Biomolecular Sciences and Biotechnology Institute (GBB) of the Faculty of Science and Engineering (FSE), University of Groningen. The institute GBB has 12 vibrant research groups, targeting biological questions in the two focal areas 'Molecular Mechanisms of Biological Processes' and 'Physiology and Systems Biology'. The molecular and mechanistic signature of the envisioned research well fits the research activities at FSE; particularly that of the GBB groups Molecular Immunology and Microbiology (Sahar El Aidy, Geert van de Bogaart), Molecular Genetics (Jan Kok, Oscar Kuipers), and Molecular Systems Biology (Matthias Heinemann, Andreas Millias). At GBB the position would provide unique opportunities to collaborate with industry and medical centers. The envisioned research also connects to activities at the FSE institute GELIFES (e.g. Gertjan van Dijk, Joana Falcao, Marjon de Vos) and the University Medical Centre Groningen (UMCG), e.g. Systems Genetics (Cisca Wijmenga, Sasha Zhernakova), Pediatrics (Jingyuan Fu, Folkert Kuipers), Gastroenterology (Rinse Weersma, Gerard Dijkstra), Medical Biology (Paul de Vos), Medical Microbiology (Jan Maarten van Dijk, Hermie Harmsen), Internal Medicine (Stephan Bakker), and Neurology (Teus van Laar).

6. Local and (inter)national position

Current state in the Netherlands: Research on various aspects of the interactions among the healthy and pathogenic microbial communities and of those communities with the (human) host is performed at different universities and medical centres in the Netherlands, including the University of Groningen and the UMCG.

At the Groningen Biomolecular Sciences and Biotechnology Institute (GBB), Sahar El Aidy aims to unravel the mechanisms and function of microbial neurochemicals in the gut microbiota-host dialogue. Geert van de Bogaart studies membrane trafficking in immune cells, including effects induced by microbiome metabolites. Matthias Heinemann and Andreas Millias investigate the cellular metabolism of microbes and integrate experimental research with computational and modelling approaches. Oscar Kuiper and Jan Kok focus on Gram-positive bacteria (mainly lactic acid bacteria and pathogens) to unravel molecular processes that guide homogeneity, competence, persistence and virulence.

At UMCG various research groups study the gastro-intestinal track (GIT) microbes. For instance, Prof. dr. Paul de Vos investigates the role of gut microbiota composition on metabolism and cardiovascular disease, and Prof. dr. Jan-Maarten van Dijk addresses the dynamics of the human gut microbiota and the interactions between bacteria, not only in relation to disease but also in response to interventions with antibiotics or prebiotics and probiotics. Microbiome research at Systems Genetics (e.g. Ciska Wijmenga, Sasha Zhernakova) and Pediatrics (e.g. Jingyuan Fu) target on functional genomics the GIT microbiome related to diseases and make use of samples obtained from a large population in the northern Netherlands (i.e. the Lifelines program).

At Wageningen University, Prof. dr. Jeremy Wells and Prof. dr. Michiel Kleerebezem both focus on innate defence mechanisms in the small intestine, probiotic interactions with dendritic cells, and virulence factors of *Streptococcus suis* and disease pathogenesis. Also, at Wageningen University (and formerly jointly with Helsinki University), Prof. dr. Willem de Vos aims at a fundamental understanding of the diversity/function of GIT microbes, with a focus on mucus-binding bacteria that are either indigenous or ingested as part of the diet. Generally, 'omics' technologies, including high-throughput functional (meta)genomics approaches, and systems biology are used to investigate host-microbe interactions. Other relevant studies on host-microbe interactions different from the GIT are pursued for instance at: i) UMC Utrecht (Prof. Jos van Strijp), regarding the question on how bacteria escape the immune system, ii) the Amsterdam Institute for Molecules, Medicines and Systems (Prof. Willem Bitter), addressing mycobacterial virulence, and iii) Erasmus University Rotterdam (Prof. Willem van Wamel), targeting host-pathogen interactions.

International: Several (recent) initiatives exist on research of the human (GIT) microbiome, underpinning the importance of the field. Examples are:

- *MetaGenoPolis (MGP), France.* A demonstration project funded by the French initiative Investissement d'avenir, aiming at establishing the impact of the human gut microbiota on health and disease. MGP integrates the technology and the expertise to explore this complex field of research. Major research themes are nutrition and medical interventions.
- *NGBI - Örebro University, Sweden.* The Nutrition-Gut-Brain Interactions program was established in 2012 as a multidisciplinary research- and innovation center. Major questions are related to how (e.g. by diet or administration of pre- and probiotics), when and in whom gut function can be improved by modification of diet and/or composition of the intestinal microbiota. Specific focus is on common intestinal disorders such as irritable and inflammatory bowel syndrome, and decreased gut function associated with ageing.
- *The NIH Human Microbiome Project* is one of several international efforts designed to take advantage of large-scale, high-throughput multi-omics analyses to study the microbiome in human health.
- *Genome Institute of Singapore (GIS) and Nutricia Research NL* (Prof. dr. Jan Knol) investigate the health benefits of prebiotics, probiotics and synbiotics and seek to understand how nutrition supports microbiome in early life and can help prevent disease later in life.

7. Expected contribution to research

The research tasks entail (i) fundamental scientific studies that result in publications of high impact, appearing in internationally renowned scientific journals, and (ii) the supervision of PhD students and postdoctoral fellows in their research. External fund raising is essential to accomplish the aforementioned tasks. The research activities should further result in the

strengthening of the international position of GBB in (microbial) physiology and systems biology in general.

8. Expected contribution to teaching

The successful candidate contributes to the relevant teaching programs of the bachelor, master and PhD programs of the Faculty of Science and Engineering, appropriate to the career stage. The requirements for the University Teaching Qualification will have to be fulfilled. Teaching is affiliated to the curricula of the majors Molecular Life Sciences, Biomedical Sciences, Behavioural and Neurosciences at the bachelor level and the ensuing respective Masters' programs.

9. Expected contribution to the organisation

It is expected that the candidate will play an active role in the general organization of research at national and international levels and within the research group Molecular Immunology and Microbiology, the institute GBB, the UMCG, the Carbohydrate Competence Center (CCC), and overarching activities within the FSE theme Molecular Life and Health.