are powerful tools to reveal microbial function in situ. This talk will focus on how microbes can be studied at the single cell level using molecular methods combined with two powerful chemical imaging tools: nano-scale secondary ion mass spectrometry (NanoSIMS) and Raman microspectroscopy. I will discuss how isotope probing can be used to identify microbes that are utilizers of specific compounds using foraging of secreted mucus by the gut microbiota as an example. In order to identify intestinal mucin- and mucosal-sugar degrading bacteria *in situ*, we developed stable isotope probing and single-cell analysis approaches using NanoSIMS and Raman microspectroscopy coupled to automated microfluidic sorting and post-measurement sequencing. We find that a diverse consortium of bacteria is involved in mucin degradation, including several members of the underexplored "Candidatus Homeothermaceae" family, highlighting both the complexity of this niche and the potential of Raman-based sorting for identifying key players in targeted processes. We then constructed a 5-species cocktail of commensals that reduce colonization levels of the enteropathogen *Clostridioides difficile* by competing for mucosal sugars, suggesting that this may be a promising approach for rational design of bacteriotherapy.

S-07.2-3
Intestinal antibodies in the context of the gut ecosystem

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Secretory IgA ("SIgA") is the only component of the adaptive immune system present in the gut lumen, i.e. in the same physical space as the intestinal microbiota. Whilst the specificity of endogenous SIgA for the microbiota remains a hotly debated topic, it is clear that oral vaccines can induce high-affinity, T-cell dependent SIgA responses specific for vaccine-antigens. These can protect the intestine, predominantly by driving enchained growth and agglutination of bacteria deep in the gut lumen. Large bacterial clumps generated cannot interact with the epithelium and are rapidly cleared in the fecal stream. However, the majority of protective SIgA in fact recognizes bacterial surface glycans such as the O-antigens of lipopolysaccharide. As these are highly repetitive and enzymatically generated, single point mutations are sufficient to generate huge changes in glycan structure, and thus vaccine escape. Given the very large population size of most gut bacterial species, within-host evolution is rapid and inevitable. This has long been seen as the Achilles heel of vaccines targeting bacterial surfaces, but in fact the very inevitability of this evolution can be turned to our advantage: Oral vaccines can be specifically designed to direct bacterial evolution in the gut lumen. We have recently demonstrated this concept to force the evolution of attenuation in *Salmonella typhimurium*. "Evolutionary trap" vaccines therefore have the potential to generate an overlooked form of non-sterilizing herd immunity with major implications in clearing livestock reservoirs of zoonotic and animal pathogens. We could also begin to imagine more subtle applications of this technique for directed evolution of bacteria in the gut lumen. *The authors marked with an asterisk equally contributed to the work.

S-07.2-1
Health effects of microbiota mediated food transformations

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Gut microbiota responds to several environmental factors of which nutrition is certainly among the most relevant. Health effects of nutrients, both beneficial and hazardous, can be modified by microbiota, while specific food components or dietary patterns have the ability to shape microbiota and thereby impact health. Traditionally, food–microbiota interactions are the most thoroughly studied for specific food components, such as probiotics and prebiotics, while systemic health effects of the predominant, beneficial carbohydrates' metabolites – short-chain fatty acids (SCFAs) – have been widely reported. Given the complexity of both microbiota and food, it is clear that the interplay between these two by far exceeds the effects of the predominant metabolites. In contrast to carbohydrates fermentation, protein fermentation yields numerous, diverse, both health-promoting and health-compromising compounds. In that respect, recently two protein metabolites have been assigned to one pathology – type 2 diabetes (T2D), in the opposite direction. In one study an inverse correlation between the risk of T2D development and the abundance of a microbial metabolite of the amino acid tryptophan (indolepropionic acid) was established. Another microbiota metabolite, that is produced starting from another amino acid – histidine (imidazole propionate) – was found in increased levels in subjects suffering from T2D. This metabolite impairs insulin signaling and is produced only in individuals with specific gut microbiota composition. It has been widely shown that individual microbiota signature has a tremendous impact on response to particular foods and, therefore, provides the basis for a personalized approach to nutrition. Today, when technological developments have enabled detailed microbiota assessment, this should be utilized to define nutritional strategies with a beneficial effect on both *Homo sapiens* and microbiota as only such nutrition can confer long term health.

ShT-07.2-2
Microbiota-derived short-chain fatty acids as modulators of intestinal serotonin transporter

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Serotonin is a key neuromodulator of intestinal physiology. Serotonin transporter (SERT) is responsible for serotonin uptake, modulating its availability and consequently, serotonergic signalling. Recently, microbiota has been described to affect intestinal homeostasis through microbiota recognition receptors (TLRs). In fact, TLRs activation seems to regulate intestinal serotonergic system. However, whether intestinal microbiota can modulate SERT by short-chain fatty acids (SCFA) is unknown. Microbiota-derived short-chain fatty acids such as acetate, propionate and butyrate, are important metabolites from non-digestible dietary fibers bacterial fermentation. These metabolites have been shown to maintain intestinal homeostasis through protecting epithelial barrier

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integrity, promoting IgA production and regulating T-cell differentiation. In this study human enterocyte-like Caco-2/TC7 cells were used as intestinal epithelial cells model, which expresses serotonin transporter. Caco-2/TC7 cells were treated for 24 h with different concentrations of acetate, propionate and butyrate and then, and 5-HT uptake was measured. SERT molecular expression was analysed by measuring both, mRNA levels by real-time PCR and protein expression by western blotting. Our results show that the treatment with SCFA modulates SERT function and expression, in a different way for each fatty acid. Consequently, a different production of SCFA by microbiota could differently modulate SERT and affect to serotonergic signalling and intestinal physiology. Our study contributes to growing evidence about the key role of microbiota on host physiology regulation, and it opens a cutting-edge opportunity of microbiota modulation to balance serotonergic signalling alterations.

ShT-07.2-1
Effect of per oral administration of the ŽP strain, a new potential probiotic, on intestinal microbiota and immune status of rat and chicken

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The spread of pathogenic antibiotic resistant bacteria in poultry farms triggered the development of novel methods for maintaining poultry health during its industrial production. The use of probiotics in this field is promising. A new antimicrobial agent, the ŽP strain, was constructed: the bacteriocin ColE7 immunity gene was inserted into the chromosome of the *Escherichia coli* probiotic strain Nissle 1917 and a conjugative plasmid carrying the colicin ColE7 activity gene was introduced into the strain (Starčič Erjavec et al., 2015). The effect of ŽP strain on 4 weeks old rat (Wistar line), as well as on one-day old chicken (cross ROSS 308) animal model systems after oral administration in the drinking water at a dose of 5×10^8 and 5×10^{10} cell/ml/head was studied. Intestinal microbiota, histology of the intestine, spleen and Peyer's patches, blood biochemistry, hematology, microbicidal activity of leukocytes and macrophages, as well as body weight were analyzed. Our results showed that the ŽP strain effectively colonized rat and chicken intestinal tract and remained in the host animals at ~$1–5 \times 10^7$ cell /g feces for 21 days. Further, our results showed that in the intestinal microbiota, the number of beneficial bacteria (lactic acid bacteria and bifidobacteria) increased, while the number of pathogenic microbes (staphylococci, pseudomonas, clostridia and fungi) decreased, compared to controls with no ŽP strain in the diet. In addition, evidence was obtained that the ŽP strain administered in the drinking water was safe, exhibited a positive effect on local and non-specific immune response of animals and led to weight gain of rats. Thus, due to these beneficial effects revealed by the used rat and chicken animal models the ŽP strain may be considered an efficient potential probiotic for farm animals. The study was carried out in the framework of the project No. C-26/792 supported financially by the Government of Perm Krai. *The authors marked with an asterisk equally contributed to the work.

Tuesday 6 July
16:00–18:00, Povodni mož Hall

Bioinformatics and computational biology

S-06.5-1
Evolution of small RNA pathways in rodents

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Small RNA pathways are found in most eukaryotes and serve multitutude roles. Mammals utilize three small RNA pathways: PIWI-associated small RNA (piRNA) pathway, RNA interference (RNAi) pathway and microRNA (miRNA) pathway. All three pathways co-exist in mouse oocytes, which offer a unique model for understanding their function and evolution. The piRNA pathway functions in the germline where it recognizes and suppresses mobile elements. It employs entirely different protein factors than the other two pathways and is non-essential in the mouse female germline. RNAi is an ancient eukaryotic defense mechanism against viruses and mobile elements. In mammals, RNAi became a vestigial pathway, being surpassed during vertebrate evolution by other innate and acquired immunity mechanisms. The molecular mechanism for RNAi remains essentially intact, but it used by the microRNA pathway, which regulates endogenous gene expression. In mouse oocytes, RNAi evolved into an essential mechanism thanks to a long terminal repeat (LTR) insertion in a gene encoding Dicer, a factor producing small RNAs acting in RNAi. This insertion occured in the common ancestor of mice and hamsters and represents a great example how LTRs remodeled gene expression and its control in the mouse germline during evolution. In fact, evolution of the RNAi pathway in mice accommodated effects of dozens of such insertions. The last pathway, the miRNA pathway, is involved in control of gene expression. Genetic analysis showed that maternal miRNAs are non-essential for oocyte growth and development. This is apparently because unique constraints existing in the oocyte. My presentation will summarize our latest results concerning mechanistical and functional overlaps of the three pathways and will provide a revised insight into their (in) significance in the female germline and beyond it.

S-06.5-3
Exascale biology: from genome to climate with a few stops along the way

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The cost of generating biological data is dropping exponentially, resulting in increased data that has far outstripped the predictive growth in computational power from Moore's Law. This flood of data has opened a new era of systems biology in which there are unprecedented opportunities to gain insights into complex biological systems. Integrated biological models need to capture the higher order complexity of the interactions among cellular components. Solving such complex combinatorial problems will give us extraordinary levels of understanding of biological systems. These exponentially increasing volumes of data, combined with the desire