2020-2022 Projects

SALMINT: Metabolic interactions in Atlantic salmon gut microbiotas and their effects on community structure

Abstract

Gut microbiotas consist of microbes that perform the multitude of functions encoded in the gut microbiome. In humans, they have been widely studied and associated with changes in development, environment, diet, and health, but the factors that govern their establishment, maintenance, and function in marine animals such as fish remain largely unknown. In Atlantic salmon, Norway's major livestock species with an annual generated revenue of several billion dollars, gut microbiota composition varies with diet in young freshwater fish and across the transition from freshwater to saltwater as they approach adulthood, after which a novel and likely mutualistic strain of Mycoplasma dominates. In the SALMINT project, we aim to clarify the connection between salmon gut microbiota composition and environmental factors such as diet or water salinity. In particular, we seek to explain Mycoplasma dominance after transition to saltwater, which we hypothesize to have protective effects for the salmon. We use a combination of experiments and spatiotemporal metabolic modeling, and our primary objective is to find mechanistic explanations of salmon gut microbiota compositions in terms of metabolite exchange between gut microbes and the host.

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Early-life experiences – a lifetime of ovine microbiota?

Abstract:

Worldwide, most mortalities and diseases of sheep are associated with the lambing period. Infectious diseases of the peri- parturient ewe and neonatal lamb have a large impact on lamb growth, health and welfare. Disease early in life or "a bad start" is considered to have a long-term negative effect on animal immunity, resilience to disease, growth rates and mortalities which can have a large impact on farm productivity and economics.

Neonatal disease is often associated with bacterial infection e.g. with Escherichia coli, and thus treated with antibiotics. Ideally, sheep flocks would be pre-emptively managed to mitigate the risks of neonatal lamb disease and death, such as preventive vaccination and improved nutrition of the pregnant ewe. Knowledge into the widespread methods and details of sheep flock management in the peri- and neo-natal period in Minnesota and Norway are currently lacking. Evidence on the impacts of early life events including development of a healthy gut bacterial population (microbiome), and impacts of common management strategies e.g. providing non-sheep (cow) colostrum, oral probiotics or antibiotics and their effects on development of the gut microbiome and antimicrobial resistance (AMR) are lacking.

Greater knowledge into development of the gut microbiome together with research to understand common practices of farmers will be combined to inform best practice risk-based flock management and disease control strategies. This is key to reducing antimicrobial usage, particularly targeting any unnecessary and non-prudent use of antibiotics and maintaining the sustainability, safety and health of lamb meat, and reducing the selection of AMR.

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Fungal wood decay mechanisms in a global perspective

Abstract:

Basidiomycete wood decay fungi are the primary decomposers of deadwood in Earth's largest biome, the Boreal. The two main fungal wood decay types, brown and white rot, are mechanistically different. White rot fungi remove a barrier in wood, lignin, to access and eat wood sugars. Brown rot fungi access sugars without removing lignin as a requirement, thus leaving more carbon behind in lignin-rich residues for long term storage in soils. In our project, we will assess environmental factors affecting distribution of fungi with different wood decay mechanisms and their tolerance for change. We hypothesize that brown rot fungi use nutrients more efficiently, requiring less nitrogen and phosphorous to decompose wood. We will study which factors correlate most strongly to wood decay distribution and whether this is primarily driven by nutrient availability, climate or vegetation. Secondly, we will correlate decay types and soil nutrients using field collected samples. Finally, we will test differences in nutrient level tolerance between brown and white rot fungi using in vitro experiments. We hypothesize that climate shifts, supplying more nitrogen and phosphorous at higher latitudes and in areas with higher nitrogen and phosphorous pollution-derived deposition, will favor white rot fungi. This would have an immediate global implication in increasing CO2 release, a greenhouse gas, to the atmosphere, perhaps 'tipping' the balance for emissions of carbon from boreal forests. The project will also help build a logical new US-Norway collaboration bridging institutions and cultures with distinct approaches to these questions but a shared need to answer them.

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Dirt against colon cancer: Does a microbially diverse environment infer cancer protection through epigenetic reprogramming of immune cells?

Abstract:

While the house mouse is the no.1 model animal in medical research, this ground-living rodent is almost exclusively studied under ultra-hygienic conditions in the research lab. Two of the collaborating groups (NMBU and UMN) have made independent exceptional studies of house mouse immunology when living under more natural conditions: By co-housing lab mice with wild-caught or pet store mice, or by rearing mice in farmyard-type habitats. The latter unique housing system at NMBU contains microbes from farm animals, soil and open space, close to living conditions the house mouse adapted to during evolution.

We have found that such environmental cues protect mice against colorectal cancer (CRC), and that immune traits in "dirty mice" approach those of an adult human being. The gut microbiota is likely to cause many of these differences, but clear mechanisms remain to be deciphered. With the strong expertise on epigenetics in the third group (UiO), we will here investigate how environmental conditions may infer immune cell reprogramming in cancer-protective ways. Combined with the UMN team's leading expertise on key tissue-resident immune cells in cancer, and the housing model and innate and comparative immunology experience of the NMBU team, this consortium is ideally positioned to investigate potential immune mechanisms behind the observed CRC protection. Potential impact includes lifestyle measures for cancer prevention, adjunctures for checkpoint inhibition therapy, as well as refinement of animal disease models. The project will provide networking events, support a PhD and a postdoctoral fellow, and build a basis to seek joint further funding.

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Robust predictive model for patient outcome following anterior cruciate ligament surgery (ACL) using the Norwegian Knee Ligament Registry (NLKR) and Machine Learning

Abstract:

Artificial intelligence has become ubiquitous in society and has already made significant contributions to the field of medicine. However, orthopaedic surgery, specifically sports medicine, has been slow to integrate this new technology into clinical practice. Machine learning is a subset of artificial intelligence commonly used for interpreting large amounts of data - finding patterns and associations that can be used to predict outcome. This study will use machine learning to analyze data contained within the Norwegian Knee Ligament Registry, a database containing the pre-operative, intra- operative, and outcome data on over 20,000 patients who underwent anterior cruciate ligament reconstruction since 2004. The specific goals will be to identify which factors influence outcome following surgery, which patients are at highest risk of experiencing a poor outcome, and to create an in-clinic calculator which can be used to accurately predict the probability of failure on a patient- specific level. While certain factors and high-risk populations have been identified in the past, the hypothesis is that the machine learning algorithm will predict failure more accurately than has been possible until now. This technology can influence decision making and holds the potential to greatly improve patient outcome.

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Computational approaches for personalized cancer therapy

Abstract:

Recent technological advances have generated a lot of interest in personalized drug screening (PDS) in cancer. In PDS, small samples of patient's tumor cells are tested for responsiveness to a large library of approved drugs; the results of these screenings have the potential to rapidly identify the most effective therapeutics for each individual cancer patient. However, these results are usually confounded by the high levels of cellular heterogeneity found in tumors 1–3. Indeed, tumors are often comprised of many different subpopulations or clones, each of which may respond to drug in a different manner. Many of these subpopulations may contain drug-resistant cells which then drive drug resistance and treatment failure, thus posing a central challenge to personalized drug screening approaches.

In this project we aim to develop novel computational approaches to address the problem of heterogeneity in personalized cancer therapy. In particular, we will first utilize mathematical models of cell population evolution in combination with machine learning methods to develop a computational tool to infer a tumor's heterogeneity profile from standard PDS data. Although this tool can be utilized across cancer types, we will parametrize and validate our computational model using experimental drug screening studies in multiple myeloma, a complex disease which has been shown to exhibit high levels of heterogeneity and evolutionary diversification.

Second, we will develop a mathematical model of clonal evolutionary dynamics in multiple myeloma, that can aid in predicting optimal combination or sequential therapy choices for patients with heterogeneous tumor burdens

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