2021 BIO PhD Day

Poster abstract book

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1. Alina Malita - Cell and Neurobiology

An intestinal NPF/NPY-mediated homeostatic circuit controls sex difference in nutrient intake

Animals must adapt their food intake and preference towards specific nutrients according to their metabolic needs to ensure homeostasis. This process is important to prevent nutrient depletion by regulation of appetite that allow adjustment of food intake. How nutritional needs are detected at the molecular level and translated into appropriate feeding behavior actions is poorly defined. The gut is a major organ that controls metabolism and appetite, but the mechanism that enable the endocrine gut cells to sense specific nutrients and release feeding-regulating hormones are not well-defined. Here, we show that in response to ChREBP/Mondo-mediated sugar sensing, the enteroendocrine cells (EECs) of the adult *Drosophila* midgut release neuropeptide F (NPF), the ortholog of mammalian NPY. Gut-derived NPF acts via regulation of glucagon-like signaling and the adipose tissue to induces both sugar satiety and promotes consumption of protein-rich food as well as storage of ingested nutrients. Feeding decision are different between sexes, and in Drosophila, mated females have increased preference for dietary protein to support egg production. We show that in females, preference for protein-rich yeast food is mediated by actions of the sex peptide receptor that stimulates NPF release for EECs. Loss of gut *NPF* leads to massive overconsumption of dietary sugar, metabolic dysregulation, and lack of glycemic control. Our findings show a sugar-activated homeostatic mechanism by which a signal from the intestine promotes storage of energy and suppresses sugar appetite after consumption of sugar. These findings contribute to our understanding of the crosstalk between the intestine and systems involved in appetite control underlying state-dependent feeding behaviors that prevents deficiencies or excess nutrient intake.

2. Angela Sanchez Salazar - Microbiology

Conjugative plasmid associated to plant compartments: a possible alternative to plant stress alleviation.

Climate changes is affecting the diversity and distribution of plants and the interactions with other organism such as, bacteria which are pivotal for plant stress tolerance. Conjugative plasmids are important carriers of functional genes (i.e. nitrogen fixation, compounds degradation, among others), that could be the helpers when plants are stressed or growing with nutrient deficiency. However, studies on conjugative plasmids in bacteria associated to plants are scarce, and moreover how plasmid transfer between bacteria can improve plant tolerance. The objective of this research is to determine the occurrence of environmental plasmids in plant compartments and how the drought stress in plants could influence the conjugal gene transfer between rhizosphere and endosphere bacterial community. For this, plasmid DNA was extracted from samples of rhizosphere and endosphere of Carpobrotus aequilaterus and Arabidopsis specimens under drought stress. The screening of replicable and transferable plasmids was done by endpoint PCR using specific primer sets for incompatibility (Inc) groups of plasmids (IncP, IncN, IncQ and IncW) and visualized by agarose electrophoresis. The presence of plasmids was confirmed by amplicon sequencing and quantified by RT qPCR. The preliminary results suggest the occurrence of replicable and transferable environmental plasmids in the rhizosphere and endosphere, particularly IncP and IncN plasmids. Differences in pattern of PCR amplifications also suggest compartmentalization of plasmids. In addition, the quantification of plasmid copies of the gene oriT of IncP plasmid showed significative difference between rhizosphere and endosphere suggesting bacterial communities different. Despite that our results showed the compartmentalized occurrence of replicable and transferable plasmids in C. aequilaterus, their abundance, diversity and role in plant-bacterial interactions under climate change scenario are still unknown so far, and it needs to be elucidated.

3. Anna Cazzola - Cell Biology and Physiology

Skin cancer stem cells and lymphatic vessels crosstalk in skin carcinoma promotion and stemness

Skin squamous cell carcinoma is the second most common non-melanoma skin cancer, and its incidence is increasing over the years. Although most patients have a good prognosis, the tumor can relapse due to the persistence of skin cancer stem cells. Therefore, a better understanding of the cancer stem cells crosstalk with their environment is crucial for identifying potential therapeutic targets. A novel interaction between a lymphatic vascular niche and stem cells has been recently demonstrated to play a pivotal role in the regulation of skin regeneration. However, the contribution of lymphatic vessels in governing cancer stem cell features and behavior is an aspect that has not been investigated yet. We show the existence of a lymphatic vessel niche in the vicinity of both human and mouse cancer stem cells in skin papillomas and squamous cell carcinomas in mouse and human tissues. We aim at elucidating whether lymphatic vessels sustain the maintenance of the cancer stem cell niche and characterizing this interaction, identifying the molecular cues that foster it, by using human and mouse primary tumor samples, in vitro co-culture of lymphatic vessels/stem cell lines, and in vivo mouse models.

4. Bharath Nair - EvoGen

Modelling protein decay using bottom-up proteomics and amino acid racemization

Mass spectrometry is an excellent tool for identifying proteins, but in more degraded ancient samples, only fewer of the queries result in identified peptides. Modelling of protein decay aims at exploring this phenomenon of unidentified fragment scans by degrading a simple model protein, here beta-lactoglobulin (BLG), in acidic (pH 3), basic (pH 11), and neutral (pH 7) conditions and analyzing the decay products by amino acid racemization and mass spectrometric techniques. We sampled the decay products at exponentially increasing time points starting from 0, 0.5, 1, 2, 4, 8, 16, 32, 64, and 128 days. Herein, we use the data generated on decay products at an unprecedented level of detail to understand the underlying mechanisms behind protein degradation across time. High D/L ratios for Ser, Tyr, Phe, and Glx after 16 days particularly in basic conditions, reveal a high extent of degradation at high pH as compared to acidic and neutral conditions. Furthermore, LC-MS2 reveals heavy protein damage in acidic and basic conditions after 64 and 128 days. The low rate of peptide spectrum matches (PSMs) in a single protein system directs towards the integration of multiple experimental and computational proteomics workflows to explore dark proteomes in detail.

5. Bing Xie - Ecology and Evolution

Relationship between vocal communication and social networks: the case of the plains zebra (Equus quagga)

Living in groups results in various conflicts due to the different needs of each individuals. In order to maintain group cohesion, group-living animals thus need to synchronize and coordinate their activities. A notable way to achieve this aim is through auditory signals, which, because of their loudness, conspicuousness and long-range travelling abilities, can be perceived by more than one individual. Though acoustic communication between one signaler and one receiver has been widely studied (e.g. individual recognition, mother-infant interactions), in social groups, communication occurs in a network composed of many potential signalers and receivers. This project aims at filling current knowledge gaps by studying a yet poorly investigated topic: the relationship between vocal communication and social networks.

The project will use the plains zebra as model, for its unique and stable multilevel societies, frequent and multi-meaning calls, migration habits and naturally individually-labeled stripes that for individual identification. In the project, I will construct an acoustic repertoire, test the hypothesis that vocal communication signals facilitate group/herd movement in general and fission-fusion events (when herds split in smaller harems and bachelor groups and later associate again) in plains zebra.

The project is carried out in the wild (Pilanesberg National Park. South Africa). I went to South Africa from December of 2020 to June 2021 to collect data (after several months of delay due to Covid lockdowns). During 7 months of work in the field, I collected video and audio recordings, pictures of individuals for identification, group movements, and social interactions on more than 100 zebra groups, ranging from 1 zebras to more than 50 zebras each.

I am now working on extracting vocalizations from the raw data to construct a vocal repertoire. Furthermore, I will process all pictures for individual recognition, as well as 1-zebra distance and interaction data to construct multiple social networks, to see how social networks differ between seasons, and how vocalization rate or type change accordingly. Later on, I will analyses the videos and extract movement data to investigate the effects of vocalization rate and type on group movement success.

6. Carlotta Porcelli - Computational and RNA Biology

Unveiling the mechanisms of m6A-YTH RNA-binding proteins in Arabidopsis thaliana and their mRNA target identity

Methylation at the N6-position of adenosine (m6A) is a regulatory modification in eukaryotic mRNA. Many important effects of this modification are mediated by YTH-domain proteins, a class of RNA-binding proteins that bind specifically to m6A. In the plant Arabidopsis thaliana, formation of all organs (leaves, roots, stems, flowers, fruits etc) are dependent on m6A-YTH mediated regulation involving the two YTH domain proteins ECT2 and ECT3.

To identify the mRNA targets of ECT2 and ECT3, we applied two transcriptomics methods: iCLIP (individual-nucleotide resolution Cross-Linking and ImmunoPrecipitation) and HyperTRIBE (Targets of RNA-binding proteins Identified By Editing). The combination of the results from iCLIP and HyperTRIBE allowed us to identify high-quality target sets of ECT2. We also found that ECT2 mRNA targets largely overlap those of ECT3, providing a molecular explanation for their redundant functions as revealed by genetics.

We also used mRNA-seq to characterize gene expression in wild type and mutants defective in function of ECT2, ECT3 and their surrogate ECT4. Analysis of differentially expressed showed that targets tended to be downregulated in the mutant and gave hints as to biological processes of particular importance for m6A-ECT2/3-mediated growth acceleration. In addition, it showed indications of stress response activation upon inactivation of ect2/3/4, an effect that was also clearly visible in the microRNA expression profile.

Finally, we conducted an analysis of sequence motifs enriched around m6A and ECT2 binding sites. This analysis revealed several motifs, some likely to be involved in N6-adenosine methylation while others had properties consistent with an implication in binding of ECT2 to methylated mRNA.

7. Christian Christensen - Cell and Neurobiology

Activin signalling maintains gut homeostasis and intestinal stem cell activity in Drosophila melanogaster.

Adult stem cells maintain organ homeostasis by providing new cells that replace lost ones.
In the intestinal tract; the most proliferative organ in the body, coordination of Intestinal Stem Cell (ISC) activity is dynamically tuned to ensure epithelial integrity at homeostasis and in response to injury. Dysregulation is thought to drive widespread intestinal disease states such as inflammatory bowel disease and gastrointestinal cancers, yet, our understanding of the cellular signals controlling proliferation and differentiation of ISC remain limited. The Drosophila melanogaster gut provides a convenient system to study the homeostatic and stress signals controlling ISC activity and organ homeostasis. Using this, we recently performed a functional genetic screen for secreted peptides released from the ISC niche: the enterocytes, the enteroendocrine cells and the visceral muscle, which control ISC activity and gut homeostasis. We identify the evolutionarily conserved TGF-beta/activin signaling pathway as an important coordinator of ISC activity. We find that ISC niche-derived activins signal directly to the ISC and are involved in supporting regenerative growth and gut homeostasis by controlling aspects of proliferation, differentiation and maturation of the epithelial cells.

8. Daniel Saar - Biomolecular Sciences

Targeting the Yin-Yang of Gastrointestinal Cancer via MTMR7 Interaction

Colorectal cancer is among the most common cancer cases worldwide. The lipid phosphatase myotubularin-related-protein-7 (MTMR7) and an MTMR7-derived mimicking peptide inhibit gastrointestinal cancer growth by interacting with two key proteins of the cancer metabolism through a putative coiled-coil domain, which was not biophysically characterized up to now. We hypothesize that these interactions are competitive and specific to certain isoforms and that they constitute key protein interactions for cancer therapy targeting. To investigate this, the structures and binding behavior of said peptides need to be understood, which is the aim of this very first part of my PhD project. For the first time the coiled-coil character of the peptide and also of the corresponding region in the MTMR7 protein has been confirmed experimentally and its interactions with key players in cancer has been shown, laying the foundation for optimization of said interactions on the way to a peptide-based cancer therapy

9. Diogo Roque - Cell and Neurobiology

Novel Mechanisms of Osmosensation and Systemic Osmoregulation

Animals continuously face harmful changes in ion and water balance as they interact with their environment. Most organisms therefore engage in active osmoregulatory responses that oppose these perturbations in order to survive. These responses involve the coordinated actions of organs with specialized functions, which in turn are modulated by systemic signals communicated by other organs to ensure an appropriate physiological response by the organisms. Molecular osmoreceptors lie at the heart of the central mechanisms coordinating these processes. Yet, the molecular identity of such osmosensitive molecules, and how they modulate the release of known neuroendocrine factors that control systemic osmoregulation, remain unknown. In this project, I will perform an in-vivo RNAi screen to systematically uncover novel osmosensory molecules, which regulate the release of hormonal factors from cells in the brain to control systemic osmoregulation. Follow-up studies on genes of interest will further involve CRISPR-mediated genomic manipulations; live bioimaging of genetic reporters; mass spectrometry analyses; as well as cell and organ assays.

10. Elise Nagel Ebstrup - Functional Genomics

Autophagy modulates ARF7 oscillation to authorize root branching

Auxin is a critical hormone for regulation of growth and development in plants. For instance, auxin dictates the root's architecture via auxin response factor (ARF) family of transcription factors, which control primary root growth and lateral roots (LR) formation. In Arabidopsis, ARF7 defines the position of future LRs through an oscillatory mechanism controlling gene expression. In contrast little is known about how proteostasis of ARF7 is regulated and how this impact its function in dictating root architecture.
Here we show that ARF7 turnover is facilitated via selective autophagy, namely through its interaction with cargo receptor NBR1. Additionally, we show that the oscillation of ARF7 insinuates dependency on autophagy as autophagy-deficient plants produce significantly less LRs. These findings supply evidence of a more complex regulation of ARF7 during LR formation and a novel role for selective autophagy in plant development.

11. Emil Thomasen - Biomolecular Sciences

Interplay of folded domains and the disordered low-complexity domain in mediating hnRNPA1 phase separation

Biomolecular liquid-liquid phase separation (LLPS) is a recently uncovered mechanism for compartmentalization in cells. LLPS of proteins is often driven by intrinsically disordered low-complexity domains (LCDs). My poster will present work showing that the LCD-driven LLPS of hnRNPA1 is modulated by the folded domains of the protein. We investigated interactions between the LCD and folded domains of hnRNPA1 by integrating coarse-grained molecular dynamics simulations with experimental small angle X-ray scattering data. Our results show that interactions between disordered LCDs and folded domains can modulate the dependence of LLPS on solution conditions.

12. Felix Kümmerer - Biomolecular Sciences

Fitting side-chain NMR relaxation data using molecular simulations

Proteins display a wealth of dynamical motions that can be probed using both experiments and simulations. Here, we present an approach to integrate side chain NMR relaxation measurements with molecular dynamics simulations to study the structure and dynamics of these motions. The approach, which we term ABSURDer (Average Block Selection Using Relaxation Data with Entropy Restraints) can be used to find a set of trajectories that are in agreement with relaxation kinetics. We apply the method to deuterium relaxation measurements in T4 lysozyme, and show how it can be used to integrate the accuracy of the NMR measurements with the molecular models afforded by the simulations.

13. Genís Garcia-Erill - Computational and RNA Biology

Sequencing the near extinct saola: population genomics sheds light on the evolutionary history of the most recently discovered large mammal

The critically endangered saola is the conservation flagship species of the Annamite Mountains. Thirty years after being first scientifically described, it remains poorly understood; and the fact that it has not been seen for a decade raises doubts on whether there are any saola left alive. Due to habitat fragmentation and overhunting, any extant saola population would also be on the brink of extinction. In addition, its extreme elusiveness, combined with the remoteness of its habitat and its low population size have prevented any description of the saola biology beyond the most rudimentary. Here, we illuminate the saola's evolutionary history using a collection of skin, tissue and bone samples collected throughout its range, from which we generated whole-genome sequencing data for 31 saola samples. After careful quality control of the sequencing data, we identify two highly genetically differentiated lineages that geographically correspond to two discontinuous distribution areas in North and Central Vietnam. The individuals are highly inbred with runs of homozygosity covering much of their genome. Demographic analyses of the genomes indicate saola have had low and declining population sizes in the last million years, with multiple sharp declines and an effective population size below 20 in the last century. While the population decline started prior to human arrival, the timing of the sharp declines coincides with human expansions. This population history is reflected in the low genetic diversity and extensive inbreeding, adding genetic erosion to the list of threats to the survival of any potentially extant saola population.

14. Gerard Arrey - Ecology and Evolution

Genome plasticity through circularization and re-integration of endogenous DNA biosensors in interplay of folded domains and the disordered low-complexity domain in mediating hnRNPA1 phase separation *Saccharomyces cerevisiae*

Circular DNAs generate randomly from the eukaryotic genomes and are responsible for rapid copy number changes and quick adaptive responses that can be conserved in the genome through integrations (Møller et al. 2015, Hull et al. 2019 and Prada-Luengo et al. 2020). rDNA circles have been shown to mainly seggregate to mother cells whereas non-rDNA circles have been reported to segregate unevenly with different frequencies. We have previously proposed that there are two different modes of segregation (Prada-Luengo et al. 2020). Here, we investigate the segregation rate of endogenously generated circular DNAs. In addition, we also calculate the rate of reintegration back into the linear genome and compare it to other Structural Variants (SVs), such as translocations. We suggest that integration of circular DNA can have a great impact on the evolution of genomes by fixing copy number changes, exon shuffling or gene order.

15. Johan Emil Kjær - Freshwater Biology

Supporting climate and biodiversity by rewetting low-lying areas

Drained low-lying areas are hotspots for greenhouse gas (GHG) emissions and converting them into lakes and wetlands would substantially reduce GHG emissions, sequester carbon, and increase nature areas. The conversion of these areas is a tool that may both help mitigate climate change and support biodiversity. The specific outcome of rewetting concerning climate mitigation and biodiversity depend on the actions and the starting conditions of the designated areas. Although land conversion is generally favourable for both climate and biodiversity, some solutions are optimal for carbon sequestration while others are better for biodiversity. Our research aims to clarify synergies and conflicts between climate mitigation and biodiversity across gradients in hydrology, nutrient status, soil carbon stock, and extant biodiversity. Specifically, we measure GHG emissions using novel cost-efficient sensors and monitor plant biodiversity in wetlands across Denmark. We aim to construct a predictive framework to identify scenarios that entail synergy between climate mitigation and biodiversity.

16. Kira Devantier - Biomolecular Sciences

Decomposing the Structural Behaviour of Small Single-Pass Viroporins

Viroporins constitute a family of small, virally encoded, integral membrane proteins found in many viruses. Through their capability of homo-oligomerisation, viroporins can form ion channels, which by modifying the intracellular ion gradient concentrations during viral infection can perform functions in multiple steps of the viral life cycle. Host cell rearrangement is an important element in a productive virus infection, and viroporins are generally known to be virulence factors, adding to the effectiveness of the virus. Viroporins could therefor constitute a currently overlooked class of antiviral drug targets.

One of the major barriers in rational drug-design of antivirals targeting viroporins is the lack of structural knowledge about viroporins. Therefore, the aim of this project is to characterize the structures of multiple single-pass viroporins. This would enable the determination of commonalities between viroporin structures and possibly mapping the binding of small molecule inhibitors to these novel viroporin structures.

The early stages of this PhD-project will focus on viroporins from (re)emerging viruses such as the small hydrophobic (SH) protein from the mumps virus and the possible novel viroporins from SARS-COV-2, the causing virus of the current covid-19 pandemic, open reading frame (ORF)7b and ORF10. This work will include optimization of purification schemes for several viroporins in order to perform structural characterization. Hereafter, multiple biophysical techniques for structure determination will be employed to obtain structural data of the viroporins, both in the presence and absence of small molecule inhibitors. Furthermore, the effects of mutations on viroporin structure, oligomerization and drug binding will be investigated.

17. Lara Magni - Cell Biology and Physiology

The role of P2X7 receptor in the interplay between pancreatic stellate and cancer cells

In pancreatic ductal adenocarcinoma (PDAC), cancer cells and pancreatic stellate cells (PSCs) help each other to promote PDAC progression. The tumor microenvironment (TME) contains extracellular ATP (eATP) and both cell types express the purinergic P2X7 receptor (P2X7R), which is involved in the regulation of cell survival, migration and collagen release. Several factors, i.e. growth factors, cytokines and nucleotides/sides contribute to the cellular interplay. Our hypothesis is that the P2X7R in PSCs in involved in this interplay possibly by influencing cytokine (IL-6) release.

First, P2X7R activation has been studied monitoring calcium signalling and pore formation after stimulation with ATP-agonist BzATP and high concentration of ATP, respectively. Further, we measured ATP released from both cell types in response to mechanical stimulation and osmotic and metabolic stimulation in PANC-1. In PSCs, P2X7R activation/inhibition influenced IL-6 release. Conditioned media experiments revealed that P2X7R stimulation of hPSCs caused IL-6 release and this in turn activated JAK/STAT3 pathway in PANC-1. As a further confirmation of IL-6 signalling, addition of Tocilizumab (specific monoclonal antibody against IL-6 receptor) to the conditioned media and directly to PANC-1 cells significantly reduced pSTAT3 levels in PANC-1 cells.

Our data shows that both PANC-1 and hPSCs release ATP and express P2X7R that acts as an ion channel and a pore. The activation of P2X7R in PSCs leads to IL-6 release and activation of STAT3 in PANC-1. This cascade can be interrupted with Tocilizumab. To conclude, both P2X7R and IL-6R may be considered as potential therapeutic targets in PDAC.

18. Long Lin - Computational and RNA Biology

Analysis of a large cohort of admixed Greenlandic siblings shows that genetic load of metabolic phenotypes differs between Inuit and Europeans

Different human populations have different genetic load meaning that they will have a different mean phenotype due solely to genetics. Genetic load is important to understand different populations' disease prevalence, relative heritability and fitness in evolution. However, genetic load cannot be directly estimated because the environment also differs between populations.

We propose a new unique way to estimate genetic load by using full siblings who are admixed with both Inuit and European ancestry. Admixed siblings have slightly different fractions of ancestry due to random recombination. We propose to use regression to correlate their difference in ancestry with their difference in phenotypes. The regression slope will be an estimate of genetic load. This design has the strength that it is robust to differences in environment.

Using genotype genome data for 4,607 Greenlandic individuals we infer 1,339 admixed full siblings with both Inuit and European ancestry. We analysed 112 metabolic traits and found 12 with significant genetic load difference between European and Inuit ancestry. Most of these were differences in body composition, where Inuit had a higher genetic load. This includes weight (0.4 kg per % inuit), waist (0.3 cm per % Inuit) as well as hip, fatty acids and lean mass. Thus the observed difference in body composition between Greenlanders and Europeans is partly explained by their genetics.

This is the first time difference in genetic load has been shown for human populations using a method which is not confounded by possible differences in environmental factors.

19. Lys Sanz Moreta - Computational and RNA Biology

Ancestral protein sequence reconstruction using a deep probabilistic model

Ancestral Sequence Resurrection (ASR) methods reconstruct the sequences of the ancestors of the proteins that exist today. ASR is widely used in protein engineering, understanding the evolution of pathogens and tumours, vaccine design and so on. Currently, most ASR methods are based on overly simple evolutionary models to keep the problem computationally tractable. We explore the use of modern machine learning methods, including deep probabilistic programming and representation learning, to improve on conventional ASR methods.

20. Matilde Knapkøien Nordentoft - Biomolecular Sciences

Using fluorescence size exclusion chromatography (FSEC) to optimize structural homogeneity of membrane proteins -from project start to finish

The human sweet receptor (T1R2/T1R3) is a heterodimer of class C G-protein coupled receptors (GPCR) and as of yet the structure has not been experimentally confirmed. It is involved in the perception of taste but also exhibit extragustatory function through expression in tissues that are not associated with taste perception. These functions are not well characterized today. Neither is the way this receptor is able to interact with a pletora of various ligands ranging from small sugars or arteficial sweeteners up to large sweet proteins.

In my project we aim to determine the activation mechanism through functional ex vivo and in vivo studies combined with structural studies mainly applying single particle cryo electron microscopy (cryo-EM).

At present we are recording our first cryo-EM micrographs and starting to do initial functional characterization. My poster will focus mostly on the methods that have aided in the initial parts of the project, the expression and purification and just maybe, possibly an initial low resolution structure.

21. Mette Lassen - Cell and Neurobiology

Cholesterol: Organismal and Cellular Growth Control by Hormonal and Nutritional Signals

Growth control is fundamentally important for normal biological development. Nutrient availability is a key factor in regulating cellular and systemic growth and timing of maturation (including mammalian puberty and insect metamorphosis). Cholesterol, an essential nutrient, and its metabolites are important as a substrate for steroid hormone synthesis and as a structural component of cell membranes. Emerging evidence indicates that cholesterol is also an important regulator of cell growth and thereby plays a critical role in health and disease. In fact, cholesterol has recently been identified as a driver of cancer development and as a clinically important therapeutic target in some of the most common cancers. Despite this biological and clinical importance, the mechanism by which cholesterol regulates both normal cell growth and cancer development remains poorly understood. Our goal is to uncover the role and mechanism of cholesterol and as a nutritional signal that promotes growth. Since growth control is a fundamental process during development, the signaling pathways that regulate growth have been conserved between flies and humans. Using Drosophila as a model organism, we have found that cholesterols influence on systemic and cellular growth acts primarily through a novel mechanism of the highly conserved nutrient sensor Target of Rapamycin (TOR) and the superimposed insulin/IGF signaling system. This research is an area of great scientific and medical interest, since it will provide a basis for understanding the link between cholesterol, hormonal signaling, and growth control in development, cancer, and metabolic disorders.

22. Miguel Ángel Salinas García - Microbiology

Extremophiles, atmospheres and alien life.

Microorganisms, despite their size, have a great effect on the Earth's atmosphere. They produce Biogenic Organic Volatile Compounds (BVOC) and seed clouds. The aim of my project is to measure the production and consumption of BVOCs by halophiles and psychrophiles via gas chromatography, and to use this data to create atmospheric models that we will use to model the atmospheres of exoplanets. This will give us hints on how to look for life on them. This information will become especially important once the James Webb telescope goes online and we can look at exoplanets with higher resolutions. For my project, I will use both extremophiles that I am isolating from samples from Greenland, as well as commercial strains, with a special focus on Ice Nucleating Protein producing strains; these proteins play an important role in cloud formation here on Earth. Additionally, I will perform simulation experiments with a custom-built Martian Simulation Chamber, to test the survival capability of my selected bacteria under Martian conditions, i.e., low temperature, pressure, water activity, and presence of toxic perchlorates. I will also genetically modify some of them to enhance their survival capability under these conditions. The information that I will gather will not only be relevant for astrobiology, but it may also have biotechnological applications (such as the discovery of industrially relevant extremozymes), and it may be useful for the eventual colonisation of Mars.

23. Mojtaba Khani - Microbiology

Investigation of biofouling on RO-membranes and new strategies to control membrane biofilm formation in a novel RO laboratory set-up

Biofouling on reverse osmosis membranes is a phenomenon whereby microorganisms are attached to the membrane surface and begin to grow and aggregate by secreting extracellular polymeric substances (EPS). Biofilm formation causes many problems for RO membranes, including blocking and clogging of the membrane, reducing permeate flux and quality of treated water, and increasing energy consumption by RO pumps. This research seeks to find a scientific connection between the quality of feed water and membrane biofouling along with the analysis of biofilm composition. The results can propose a biological-chemical treatment approach for the membrane that is clogging. Whereby, the main purpose of this research is the development of a side stream containing chemical (biocide) and biological (enzyme) materials for degrading extracellular polymeric substances (EPS) matrix comprised of polysaccharides, proteins, lipids (phospholipids), and extracellular DNA. Industrial enzymes and enzyme solutions are applicable as eco-friendly agents for this purpose. Also, the applied path of the effects of chemicals and enzymes will be determined and verified, depending on their type and expected reaction for maximum utilization. On the other hand, based on the data and biofilm growth models on the membrane surface, a protocol is to be proposed to prevent or inhibit biofouling formation. A combination of molecular and microscopic techniques will be applied to analyse the abundance, composition, architecture, and three-dimensional structure of biofilm communities. Physical and mechanical tests will be done to evaluate RO performance on a novel semi-real RO platform test similar to an authentic RO system. It is intended that the output of this research be an effective way to exploit or maintain the membrane desalination industry.

24. Muriel Leandra Schicketanz - Functional Genomics

Molecular regulation of SpoT in the stringent response

Given the rising antibiotic resistance and tolerance (persistence), it is an urgent necessity to further understand the underlying mechanisms, such as the stringent response (SR). The SR is a universal bacterial stress response, which is induced during bacterial stress, e.g., during antibiotic treatment, or infection resulting in the production of the signaling molecules (p)ppGpp. In gram-negative bacteria, there are two proteins involved in the (p)ppGpp production, the (p)ppGpp synthase RelA, and SpoT, which has a weak synthase activity, as well as a strong hydrolase activity for (p)ppGpp. Interestingly, it has been shown that SpoT, instead of RelA, is essential for virulence and antibiotic tolerance in pathogenic bacteria. Whereas RelA has been extensively studied, the complex regulation of SpoT remains to be elucidated.

Thus, this study aims to investigate the molecular regulation of SpoT. So far, SpoT was recalcitrant to full-length purification, yet we developed a method to purify full-length and active SpoT enabling structural insights and in vitro studies. Furthermore, we identified essential residues for surviving stress conditions and found evidence that undetectable basal levels of (p)ppGpp produced by SpoT seem to finetune the SR. We will confirm our theory by in vitro studies and investigate which domains of SpoT are involved in the intra-molecular regulation. Moreover, we also started characterizing the binding of known protein regulators, and we aim to identify and characterize novel protein regulators as these could be promising drug targets. Overall, interfering with the regulation of SpoT seems to be a promising strategy for antimicrobial development.

25. Nadja Ahrentløv - Cell and Neurobiology

Endocrine signals from the gut that regulate metabolism

Metabolic homeostasis requires coordinated interorgan communication between different tissues, mediated by endocrine signals. Organs with specialized functions sense changes in internal and external nutrient availability and release various factors to other tissues to coordinate energy intake and expenditure in order to regulate metabolism (Droujinine & Perriomon, 2016; Kim, 2016). The gut, the first organ that register recently eaten food, is a source of some of these signals (Capo et al., 2019). Although some gut-derived factors have already been characterized (Nauck & Meier, 2018; Prasad-Reddy & Isaacs, 2015) are thousands of proteins predicted to be secreted, and the function of most of these are largely unknown. This gap in our knowledge of regulation of food intake and metabolism represents a significant unexploited resource for the discovery of new therapeutic interventions for treatments of metabolic disorders, such as diabetes and obesity. There is a high degree of conservation between humans and the model organism Drosophila melanogaster, in terms of both anatomical structures as well as signaling pathways. Human organs have fly equivalents, such as the gut, making it a prime model to study gastrointestinal function (Droujinine & Perriomon, 2016; Padmanabha & Baker, 2014; Trinh & Boulianne, 2013). The aim of this project is to take advantage of this conservation and the genetic tools that are available in Drosophila (Hales et al., 2015; Kennerdell & Carthew, 2000; Yamaguchi, 2018), to screen and characterize the gut "secretome" using tissue-specific gene knockdowns in adult flies - with the goal of identifying intestinal hormones that regulate food intake and metabolism, based on phenotypic readouts. Identified factors of interest will be investigated further through various assays to establish target tissue(s) and mode of action, to identify novel gut-to-organ connections and possible targets for treatment of metabolic diseases.

26. Oscar Alberto Rojas Castillo - Freshwater Biology

The impacts of oil palm plantations on aquatic biodiversity and ecosystem functions in Guatemala

Oil palm has increased 96% of its territory in the last two decades with expectations of expanding furthermore in the tropics known for their role as biodiversity hotspots. This has caused species loss, freshwater pollution, and decreased ecosystem functions. Assessing these impacts in the tropics is imperative, but in this regard, most studies have focused on terrestrial species, while freshwater biota has been dramatically less studied. In Guatemala, the palm-oil industry has been accused of serious deterioration on freshwater ecosystems. However, little research has focused on it. We aimed to evaluate these impacts by contrasting freshwater ecosystem functions (litter-decomposition, biomass, water quality, water temperature, and silica's transportation) and biodiversity (macroinvertebrates, periphyton, and bacteria) in streams from forests, grasslands, and oil palm plantations in Guatemala (6th world's greatest palm-oil producer). Litter-decomposition will be assessed through litter bags (by macroinvertebrates) and tea-bags (by bacteria), periphyton biomass by measuring chlorophyll in rocks and the substrate in the streams, water quality (physical and chemical parameters), temperature (data-loggers), silica content (silica transportation) and biodiversity (direct sampling and bacteria metabarcoding) in strategic points in the streams. We expect to detect and describe important differences in the biota and ecosystem function based on land use. Moreover, we expect to find solutions to mitigate the impacts of this agriculture.

27. Qinqin Wang - Microbiology

Cooperative antibiotic resistance facilitates horizontal gene transfer

The rise of β-lactam resistance among pathogenic bacteria, due to horizontal transfer of plasmid encoded β-lactamases, is a current global health crisis. Markedly, β-lactam hydrolyzation by β-lactamases, not only protects the producing cells but also sensitive neighboring cells cooperatively. How such cooperative traits effect plasmid transmission and maintenance is currently poorly understood. Here we experimentally show that β-lactamase expression and extracellular activity was higher when encoded on plasmids compared with chromosomes, resulting in elevated rescue of sensitive non-producers. This facilitated efficient plasmid transfer to the rescued non-producers and expanded the potential plasmid recipient pool and the probability of plasmid transfer to new genotypes. Social conversion of non-producers by conjugation was efficient yet not absolute. Our results suggest that cooperative antibiotic resistance especially promotes the fitness of replicons that transfer horizontally such as conjugative plasmids.

28. Rocio Espinosa - Biomolecular Sciences

Protein synthesis regulation under phosphate starvation in *Escherichia coli*

During exponential growth, Escherichia coli uses the resources available to maximize its growth rate. This is accomplished through a tightly regulated allocation of resources for production of the protein synthesis machinery (ribosomes mainly) versus resources allocated to production of other cellular proteins. The alarmone ppGpp plays a key role in resource-allocation-regulation by binding to RNA polymerase, thereby decreasing the transcription of ribosomal genes. In this project, we focus on how E. coli reallocates resources for protein synthesis during phosphate (P) starvation. In P-starved E. coli cells, ppGpp levels rise abruptly and transcription of ribosomal genes is terminated. We find that E. coli even degrades part of its existing ribosomal RNA, presumable to release nucleotides that can be recycled for transcription of other genes during P starvation. Supporting this, a mutant that excessively degrades ribosomal RNA shows increased protein production over wildtype during P starvation. Furthermore, we show that expression of a long-lived mRNA in P-starved cells is sufficient to increase total protein production, suggesting that mRNA is limiting for protein synthesis. The enzymes SpoT and RelA can produce ppGpp. RelA is activated by the presence of uncharged tRNA in the ribosomes, which was not expected during P starvation. Hence, SpoT was assumed to be responsible for ppGpp synthesis. Here, we show that ppGpp is produced by RelA under P starvation. Our latest results suggest that $tRNA^{gly}$ becomes uncharged in P-starved cells, and could activate ppGpp-production by RelA, thereby initiating the resource re-allocation. The mechanism underlying for $tRNA^{gly}$ decharging is our current focus.

29. Romain Lefèvre - Ecology and Evolution

Equivocal: in-vivo and ex-vivo evidence for the production of two fundamental frequencies in horses' vocalizations

Biphonation is a rare phenomenon in mammals, which consists in producing two fundamental frequencies that are not harmonically related. Interestingly, this phenomenon has been observed in the whinnies of horses, a highly social species that use different acoustic cues to organize its social structure and behave accordingly. Previous research has shown that, while the lowest of these two frequencies ("F0") provides information about the emotional arousal (i.e., intensity) of the horse, the highest fundamental frequencies ("G0") encodes its emotional valence (i.e., positive vs. negative). In this project, we explored the structures involved in the production of these two frequencies at the level of horse vocal apparatus through a unique combination of in vivo and ex vivo studies; 1) First, we relied on endoscopic videos to allow an *in vivo* visualization of the functioning of the larynx and surrounding structures during vocal production. 2) Second, we recorded and analyzed vocalizations from horses suffering from laryngeal hemiplegia, which results from atrophy of the intrinsic laryngeal muscles. 3) Third, we performed excised larynx experiments to simulate sound production *ex vivo* by forcing air through a dissected larynx. 4) Finally, we performed CT scans on excised larynges to help us correlate the sounds produced from ex-vivo experiments to the anatomical structures involved in vocal production. This study provides a unique insight into the laryngeal structures involved in horse vocal production and documents the means through which these animals can transmit multiple and independent pieces of information simultaneously.

30. Shuai Tong - Freshwater Biology

Climate-smart rice

The ongoing climate changes have already resulted in more frequent and severe flood and drought events, and the world's rice producing countries have not been left unaffected. Climate-smart rice is aiming at identifying functional root and shoot traits that enhance the resilience of rice cultivars with special focus on tolerance to flooding, drought and salinity stress. Here we report on a root trait that can be considered a 'Jack of all trades', i.e. this trait is likely enhancing root performance during soil flooding, during drought and in salinized soils. The barrier to radial O2 loss (ROL) is part of the root exodermis in rice and until recently, this trait was only considered essential for root growth in flooded soils where molecular O2 is absent. However, our research has shown that the ROL barrier also restricts loss of water from roots to the surrounding bone-dry soils. Moreover, since the ROL barrier is also an apoplastic barrier, we propose to further explore its reputed role in Na and Cl exclusion at the root level. We are convinced that tolerance to abiotic stress in rice can be increased via constitutive formation of the barrier to ROL, and therefore we suggest to include these traits in the breeding strategies aimed at improving flooding, drought and salinity tolerance of rice.

31. Shuanshuan Xu - Microbiology

Anti-defense genes of archaea viruses

There are around 10^{31} virus on the earth which is tenfold more than the prokaryotic organisms. Among them, the archaea virus are separated in diverse hypersaline and hyperthermophilic environments, where archaeal cells dominate. Under the pressure from the huge amount virus, archaea have evolved multiple against systems to prevent the viruses' infection, like CRISPR (clustered regularly interspaced short palindromic repeats)-Cas (CRISPR-associated proteins) and TA (toxin and antitoxin) systems. But the viruses also evolved some defense mechanisms to escape CRISPR-Cas immunity, like the Acrs. In our studies, gp15 of the SIFV2 was proved to be an Acr for Type IA CRISPR-Cas system. More unexpectedly, gp44y of Rey15A can bind to the toxin like the anti-toxin protein of the host. Our findings suggest that archaea viruses have evolved a variety of mechanisms to resist various defenses from archaea.

32. Suzanne Schmidt - Ecology and Evolution

Do high CO2 levels help protect Termitomyces against antagonists?

Termites of the subfamily Macrotermitinae are extremely successful due to their symbiotic lifestyle with their Termitomyces fungal crop. The termites provide their fungus with nutrition in the form of plant material, protection as well as optimal growing conditions. In return, the fungal symbiont aids in digestion and provides nutrition to its host. Protecting these fungal gardens is essential for maintaining this symbiotic relationship. The termites built large and complex mound structures which are built to enhance nest ventilation and maintain nest interior microclimates favourable for the growth of Termitomyces. When colonies mature, the fungal and termite metabolism increases, resulting in up to 6.4 % CO2 concentrations within mounds. The termites themselves can tolerate high CO2 conditions, however it might negatively affect the growth of Termitomyces which would limit the termite's food supply and consequently the colonies growth. Using eight Termitomyces strains as well eight pathogenic fungal strains we compared the growth rate under ambient and high (5%) CO2 conditions. Our results revealed that in contrast to other fungi, Termitomyces is generally not affected by high CO2. This suggests that the high levels of CO2 we see inside the nest is not an unfortunate trade-off between ventilation and humidity but instead could be an adaptive trait evolved through million years of coevolution between termites and Termitomyces. As CO2 is a stressor to most fungal species, maintaining the nest at high CO2 levels could not only provide optimal growth conditions, but also assist in defending the symbiosis against pathogens.

33. Veronica Marie Sinotte - Ecology and Evolution

Shaping the Tripartite Symbiosis: Termite Microbiome Composition and Function Directed by Horizontal Acquisition of Fungal Symbiont

Horizontal acquisition of coevolved symbionts presents a unique opportunity to investigate the adaptive functions. Fungus-growing termites engage in a 30 MYA obligate mutualism with a horizontally acquired fungal cultivar and gut microbes that collectively enable symbiotic digestion of plant material. The tripartite symbiosis exhibits considerable phylogenetic congruence and co-adaptation, yet it remains unclear precisely how horizontal transmission of the fungus shapes microbiome structure, function, and evolution. Here we examine the change in microbiome composition and metabolism before and after fungus acquisition the fungus-growing termite Macrotermes natalensis. Using 16S rRNA amplicon sequencing, we identify microbes that increase in abundance with fungus acquisition, some of which are vertically transmitted with the termite host, and transient microbes present only before that event. Further, we estimate putative differences in carbohydrate active-active enzymes with gut metagenomics and gut enzymatic activity using AZCL-polysaccharide assays. Our findings point to distinct gut microbiome composition and lack of enzymes for degradation of complex fungal carbohydrates prior to fungus comb acquisition. Thus, the horizontally acquired mutualist likely drives dynamic shifts in bacterial contributions over the ontogeny of the symbiosis. Ultimately, fungus acquisition shapes persistent and coevolved microbiome structure and function, and the contrast in horizontal and vertical transmission of the gut microbes potentiates further co-adaptation, cooperation, and conflict within the symbiosis.

34. Weijia Feng - Ecology and Evolution

Extrachromosomal circular DNA in cancer genomes and their impact on tumor evolution

For many years, researchers have observed smaller lengths of DNA alongside the chromosomes that are organized in circular forms, which have been referred to as extrachromosomal circular DNA (eccDNA). eccDNA is a much-overlooked contributor to genetic variation and only in cancer have eccDNA been found to drive tumorigenesis when an oncogene is trapped on the eccDNA. But its medical impact is largely unknown. My research will further reveal the role of eccDNA in tumorigenesis and evolution.

35. Xue Liang - Ecology and Evolution

An atlas of extrachromosomal circular DNA (eccDNA) in mice

Extrachromosomal circular DNA(eccDNA) refers to a type of circular DNA located outside conventional chromosomes.There is currently increasing concern about the connection between eccDNA and cancer since many studies have shown that eccDNAs promote oncogenesis and drive poor outcomes across many cancer types[1-4]. However, their effects on normal tissues have not been profiled extensively, especially in studies of multiple tissues throughout the life cycle. In this study, we generate the first comprehensive healthy mouse eccDNA atlas across ten tissues and four age groups to provide a new resource for understanding tissue-specific characteristics, as well as age-related dynamic changes of eccDNA. We hypothesized that 1) eccDNAs exit in various healthy tissues throughout the whole life cycle of mice, and 2) they contribute to aging through the expression of full-length or truncated genes.

36. Xuyang Li - Functional Genomics

Functional Study of the viral transcriptional regulator SIRV2_gp21

Since the first living organisms, viruses and cells are likely to co-existed, their interaction remains to be elucidated. Also, the study of Archaea viruses is still at an early stage, the knowledge of their biology and basic molecular processes, including infection, virus-host interactions, transcription regulation, is limited.

Here we are using the *Sulfolobus islandicus* rod-shaped virus 2 (SIRV2), a virus of the *Rudiviridae* family, to study the interactions with its host *Sulfolobus islandicus LAL14*/1. Our project focuses on the conserved SIRV2 gene *gp21*, which has homologs in the genomes of crenarchaea and their viruses. It contains a ribbon-helix-helix domain, suggesting it acts as a transcriptional regulator. Our results show this small protein may interfere with the cell cycle by inhibiting the cell division machinery. The aim of this project is: 1) identify the gp21 binding sites (target genes) to test if it acts as a repressor or activator. 2) investigate the role of SIRV2_gp21in the regulation of cell division.

37. Yeasmeen Ali - Cell Biology and Physiology

TGFbeta-ativated kinase 1 (TAK1) and TAK1-binding Protein 2 (TAB2) function at the primary cilium to control cardiomyogenesis and heart development

The development of the heart is a tightly regulated process that requires the spatiotemporal regulation of multiple cellular signaling pathways. These include TGFbeta/BMP signaling that via the primary cilium (specialized sensory organelle) control developmental processes in vertebrates. Consequently, aberrant regulation of this pathway or ciliary dysfunction is associated with congenital heart disease (CHD), which comprises the most common congenital anomaly in newborns. We previously identified mutation of TAB2 as a novel cause of CHD and patients with TAK1 mutations affecting TAB2 display cardiac developmental defects affecting the outflow tract, the valves and the ventricular septum. Despite these findings, little is known on the mechanisms by which TAB2 and TAK1 coordinate cellular events during heart development. Here we show that TAB2 and TAK1 localize to primary cilia, and that TAK1, which modulates signaling through NF-kappaB and MAPK, is activated by TGFbeta/BMP signaling at this site. Further, recruitment and activation of TAB2/TAK1 were increased at the primary cilium during in vitro cardiomyogenesis. Finally, to investigate the role of TAB2 and TAK1 in heart development in vivo, we used zebrafish as a vertebrate model. Fish subjected to knockout of tab2 or tak1 displayed increased cardiac chamber size in conjunction with increased heartbeat. Taken together, these results suggest a functional role of TAB2 and TAK1 at the primary cilium in cardiogenesis and current experiments, including deciphering of TAK1 phosphorylations in mouse and zebrafish embryos, are underway to decode spatiotemporal signaling networks at primary cilia in the context of heart development and CHD.

38. Zilong Li - Computational and RNA Biology

PCAone: one PCA method to rule them all!

Principal Component Analysis (PCA) is a widely used unsupervised linear dimensionality reduction technique used to both analyse and visualize modern high throughput genomics data sets. Notable examples include analysing population structure using millions of genetic markers, single cell RNA sequencing data of millions of cells and microbiome composition for millions of bacteria. As the size of these data sets are increasing exponentially, there is a need for tools that can perform PCA efficiently and accurately on an affordable commodity hardware.

Here we present PCAone, a new ultra-fast and accurate PCA method with both in-core and out-of-core implementation. We show that PCAone is faster and more accurate than existing start-of-the-art methods such as FlashPCA2, FastPCA, TeraPCA and ProPCA. PCAone is quite accurate even when the top eigenvalues are low where other fast PCA methods fail. We also show that the algorithm is many magnitudes faster than other low memory methods, which allows us to analysis any single cell RNA-seq experiment in seconds and even the largest genetic data sets can be run in a few hours such as the UK biobank data with millions SNPs and individuals. Moreover, PCAone is designed to be extensible to accept multiple different file formats. In conclusion, PCAone allows us to do PCA analyses without making trade-off between accuracy, speed and system memory, which is the only one we need.

39. Guangshuo Li - Ecology and Evolution

Isolation, characterization and genomes of novel yeasts from the intestinal tract of termites

Bioconversion of hemicelluloses into simpler sugars leads to production of a significant amount of pentose sugars, such as D-xylose. However, efficient utilization of pentoses by conventional yeast production strains remains challenging, especially due to inhibition by hexose co-fermentation. Recently, research found that wild yeast isolated from termites gut have a potential utilization to ferment cellulose and hemicellulose. Now 18 species belong to 10 genera of Ascomycetous and Basidiomycetous yeasts were isolated from three fungus-farming termites. Those yeasts can provide new industrially relevant characteristics to bypass these inhibitions and efficiently utilize pentose sugars. To explore this strategy, we isolated gut-residing yeasts from the termite *Macrotermes bellicosus* collected in Comoé National Park, Côte d´Ivoire. The yeasts were classified through their Internal Transcribed Spacer (ITS) and Large subunit ribosomal (LSU) gene sequence, and genomes of three new strains and species were sequenced and annotated. We identified a novel yeast species, which we name *Barnettozyma botsteinii* sp. nov. 1118^T and two new strains of *Kurtzmaniella quercitrusa*: var. nov. 1112 and var. nov. 1120. The two *K. quercitrusa* strains grow 15% faster on synthetic glucose medium than *Saccharomyces cerevisiae* $CEN.PK^T$ in acidic conditions (pH = 3.2) and both strains grow on D-xylose as the sole carbon source at a rate of 0.35 h^{-1}. At neutral pH, the yeast form *of K. quercitrusa* var. nov. 1120, but not var. nov. 1112, switched to filamentous growth in a carbon source-dependent manner, revealing phenotypic diversity among strains within species. Our findings increase the understanding of microbial diversity within fungus-farming termite guts, and the utilisation of plant-derived sugars by *K. quercitrusa* implies potential for a mutualistic relationship between this yeast and host termites.

40. Felix Teufel - Computational and RNA Biology

SignalP 6.0 achieves signal peptide prediction across all types using protein language models

Signal peptides (SPs) are short N-terminal amino acid sequences that control protein secretion and translocation in all living organisms. As experimental characterization of SPs is costly, prediction algorithms are applied to predict them directly from protein sequence data. However, existing methods are still unable to detect all types of SPs known to exist in nature.

We introduce SignalP 6.01, the first model capable of detecting all five SP types in all domains of life. In addition to detecting a SP, the model accurately identifies the positions of different regions within SPs, enabling research into the defining biochemical properties that underlie the function and evolution of SPs in vivo.

Results show that SignalP 6.0 has improved prediction performance across all types and reveal great differences in the protein translocation strategies employed by different organisms. Additionally, by leveraging protein language models to model the full natural diversity of proteins, it is the first predictor that is applicable to metagenomic data of unknown taxonomic origin.

41. Fenne Dijkema - Biomolecular Sciences

The enzyme that plankton uses to scare off fish

The copepod Gaussia princeps has a fascinating strategy for escaping predators in the twilight zone of the ocean. When it feels a disturbance in the water, it secretes a liquid that makes a flash of light, allowing it to swim away safely while the predator is distracted. The compounds in the liquid that are responsible for the flash are the enzyme Gaussia luciferase and its substrate coelenterazine. Gaussia luciferase catalyzes the reaction of coelenterazine with oxygen, a reaction that frees up a lot of chemical energy in the form of light. A light-producing enzyme (a luciferase) like this is extremely useful as a reporter to visualize biomolecular processes in model systems. Compared to luciferases from other organisms, Gaussia luciferase is very small and produces very bright light, which means that its light is easy to measure and it interferes little with the system in which it is used. Although this luciferase has been known for decades and is very widely used as a reporter, surprisingly little is known about its structure and the biochemistry of the reaction that it catalyzes.

We wished to fill this gap, so to study the properties of Gaussia luciferase, we produced it in E. coli cells and purified it in the lab. We have studied its reaction with coelenterazine, its light emission and its three-dimensional structure. This work is still in progress, but most of what we have discovered so far about this enzyme is highly peculiar and both its structure and catalytic properties are completely unique, perhaps due to its peculiar function in scaring off fish.

42. Marc Horlacher - Computational and RNA Biology

Sequence-to-Signal Learning for CLIP-Seq Data

RNA-binding proteins (RBPs) are a family of over 2,000 proteins that bind to coding and non-coding RNAs, usually through recognition of short sequence features commonly known as motifs. They are involved in virtually every aspect of eukaryotic post-transcriptional regulation, including modification, stabilization, localization and translation of RNAs. Experimental protocols such as Cross-Linking Immunoprecipitation followed by Sequencing (CLIP-Seq) and its derivatives allow for accurate transcriptome-wide profiling of binding sites. Given an RBP of interest, these methods can generate a per-nucleotide signal along the transcriptome whose magnitude correlates with the RBP's likelihood of binding. Analysis of experimentally identified RNA binding-sites can give insight into an RBP's functional role as well as the mechanism(s) by which it identifies and binds to its RNA targets. Here, we present RBPNet which can learn a direct mapping of RNA sequence to CLIP-Seq signal. Further, we demonstrate that RBPNet reaches near replicate-level performance for a number of RBPs, thus capturing the full bandwidth of information generated by CLIP-Seq experiments. By additionally modeling the control signal via an auxiliary task, RBPNet allows one to extract the unobserved, bias-free protein-specific signal. Finally, through model interrogation, RBPNet identifies highly predictive sub-sequences corresponding to known canonical RBP binding motifs. As RBPNet directly models the raw CLIP-Seq signal rather than binary labels, we believe that it represents a significant advancement compared to current state-of-the-art classification-based approaches.