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UNIVERSITÉ DE FRIBOURG UNIVERSITÄT FREIBURG

Activity Report 2019-20



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Welcome from the President

Fit for the Future. In the last two years, the Department of Biology continued its path of consolidation, removing the last administrative remains of the former "units". We now have a uniform hierarchy, established minimally structured working groups that deal with diverse organizational tasks, and streamlined administration that gives us more flexibility to tackle future challenges. The separation of the Botanical Garden into an independent Institute will support its growth and further underscores its importance for the University as a whole. The successful recruitments of excellent scientists on junior and senior levels provide additional evidence of the successful development and attractiveness of our Department. Taken together, our Department is fit for the future and we will continue to increase the quality of our research and teaching. In the coming years one important focus will be the further strengthening of our teaching endeavours. The establishment of the joint Fribourg Graduate School of Life Science and Medicine, supported financially by the University, allows us to optimally support the next generation of young scientists. The establishment of two new Master programs in Environmental Biology and Molecular Life and Health Sciences aims to equip our students with the best knowledge to cope with two critical areas of current challenges: climate change and ageing Western societies. All of this is only possible due to the remarkable involvement and dedication of all members of our Department. Without them this positive development would not have been possible. Thank you!

> President of the Department of Biology Prof. Jörn Dengjel

Research Support

Our research groups benefit from the support of our technical and administrative teams. They ensure the good working of our Department to allow researchers to focus on what they do best.







Thomas Gruet







Olga Sudan







Canaan Abebe

Adeline Guélat

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



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BICORE

The Bioimage Core Facility (BICORE) of the Departments of Biology and Medicine was established in 2013 to accommodate the increasing demand in light microscopy and image processing at the Faculty of Science and Medicine. The facility is managed by Felix Meyenhofer (Bioimage Analyst and Microscopist) and Boris Egger (Facility Coordinator and Microscopist). Currently, about 100 active researchers from the Departments of Medicine and Biology, the Adolphe Merkle Institute, the Department of Physics, the Department of Chemistry and SICHH use the services provided by the facility.

BICORE gives training on various high-end microscopes and can be consulted for experimental design, image acquisition and image processing. The facility also organizes master and doctoral courses in light microscopy and image processing for life sciences.

unifr.ch/bioimage

ec



Bugfri

The Bioinformatics Core Facility (established in 2013) is a joint platform between the Department of Biology and the section of Medicine. It is managed by Dr Laurent Falquet. The expertise of the platform is primarily the analysis of Next Generation Sequencing data, with emphasis on genome assembly and comparative genomics, as well as DNA methylation. We also perform other analyses, such as RNAseq, ChIPseq, metagenomics, and any large scale data analysis upon request. For more details see page 24.

Please contact us at bugfri@unifr.ch

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY

Metabolomics and Proteomics Platform Mission of the Platform

The Metabolomics and Proteomics Platform (MAPP) is a service of the Department of Biology of the University of Fribourg. The mission of the platform is to provide expertise, instrumentation, and manpower to enable state-of-the-art implementation of metabolomic and proteomic analyses. To this end, the MAPP offers support in the planning and execution of experiments, including custom-tailored method development, sample preparation, data acquisition and analysis, and researcher training. Since its official start in January 2017, the MAPP has provided its services to many research groups of the Department of Biology as well as to some external customers. Notably, our activities have already contributed to several publications.

Metabolomics and Analytics Unit

The Metabolomics and Analytics Unit provides both analytical services (molecule identification and quantification by the platform staff) and teaching in analytics to researchers that prepare their samples under the supervision of the platform staff. Our mission is to assist the scientific community in implementing currently existing protocols as well as designing specific analytical methods related to their own research. Our unit is currently equipped with two HPLC systems coupled to a diode-array detector, a fluorescence detector and a fraction collector module, and two GC systems coupled to a flame-ionization detector and a single quadruple mass spectrometer. Following the successful R'Equip grant in 2018, we setup a novel GC-MSgTOF in 2019 that enlarges our analytical capabilities, in particular for low abundance compounds. The Metabolomics and Analytics Unit is currently assisting ongoing research projects developed by nine research groups of the Department of Biology of the University of Fribourg as well as projects currently conducted at the University of Geneva, Bern and Lausanne, at the Leibniz Institute for Zoo and Wildlife research in Berlin, and at a private Swiss company. Research projects notably include the identification and quantification of compounds of interest such as fatty acids, neurotransmitters, bacterial volatiles, hormones or psychotropic alkaloids, from animal samples (mice, Drosophila, bats), plant samples (Arabidopsis, maize, Australian endemic species and legal Cannabis) and from soil samples.

Proteomics Unit

The Proteomics Unit offers mass spectrometric (MS) analyses of protein samples as well as support for the expression and purification of proteins. Due to a successful R'Equip grant application, the Proteomics Unit is since April 2018 in the fortunate situation to have two high-end nanoLC-ESI-MS/MS instruments, the newly purchased Q Exactive HF-X and a Q Exactive Plus (in use since 2016), at disposition for their MS analyses.

In the last two years, 14 of the 27 research groups of the Department, as well as seven external research groups, have utilized the services of the Proteomics Unit. For these customers, we have mainly provided the following services: (i) identification of interaction partners in immunoprecipitations either by determining the protein identity within gel bands or by on-bead digestion followed by label-free quantitative mass spectrometry; (ii) identification of phosphorylation sites after *in vitro* kinase assays or at a proteome-wide level by deep phosphoproteome analyses; (iii) quantitative (either label-free or upon SILAC, dimethyl, or TMT labelling) determination of changes in protein composition within cell or tissue extracts. Notably, together with the Dengjel laboratory, we have established and started to implement a powerful TurboID-based proximity-labelling approach that enables the rapid identification of dynamic protein-protein interaction in yeast. Besides these MS-analyses, we have also offered our support for the expression and purification of recombinant proteins as well as for yeast-two hybrid interaction assays to several research groups.

Selected publications

Fasel N, McMillian K, Jakop U, Mène-Saffrané L, Engel K, Genoud M, Muller K, Christe P. Modification of sperm fatty acid composition during epididymal maturation in bats. Reproduction doi:10.1530/REP-18-0463 (2018)

Pellaud S, Bory A, Chabert V, Romanens J, Chaisse-Leal L, Doan AV, Frey L, Gust A, Fromm KM, Mène-Saffrané L. Wrinkled1 and Diacylglycerol Acyltransferase1 regulate tocochromanol metabolism in Arabidopsis. New Phytologist. doi: 10.1111/nph.14856 (2018)

Selected publications

Duman M, Vaquié A, Nocera G, Heller M, Stumpe M, Siva Sankar D, Dengjel J, Meijer D, Yamaguchi T, Matthias P, Zeis T, Schaeren-Wiemers N, Hayoz A, Ruff S, Jacob C. (2020) EEF1A1 deacetylation enables transcriptional activation of remyelination. Nat Commun. 11(1):3420

Dawoody Nejad L, Stumpe M, Rauch M, Hemphill A, Schneiter R, Bütikofer P, and Serricchio M. (2020) Mitochondrial sphingosine-1-phosphate lyase is essential for phosphatidylethanolamine synthesis and survival of Trypanosoma brucei. Scientific Reports 10(1):8268

Team: Dr Laurent Mène-Saffrané (Head of Metabolomics and Analytics Unit), Dr Dieter Kressler (Head of Proteomics Unit), Dr Michael Stumpe (Platform Manager)



Selected publications

Felber F, Guerra V, Bétrisey S, Kozlowski G (2020). Trésor botanique. Comment sauvegarder nos plantes menacées. Editions Haupt, Bern. pp. 112 (ISBN : 978-3-258-08212-7).

Felber F, Guerra V, Bétrisey S, Kozlowski G (2020). Botanischer Schatz. Wie man bedrohte Pflanzen vor dem Aussterben rettet. Haupt Verlag, Bern. pp. 112 (ISBN: 978-3-258-08213-4).

Team

Director & scientific manager: Prof. Gregor Kozlowski • Technical manager: Alain Müller • Communication and event manager: Annick Monod • Scientific collaborators: Sébastien Bétrisey, Yann Fragnière • Gardeners: Benoît Clément, Marianne Herren, Hélène Huguet-Sahli, Christine Jakob, Manuela Moduli, Josef Schöpfer, Jacques Sciboz, Hans Tschachtli • Trainees: Mathilde Schouwey, Frédéric Chassot.

We only protect well what we know well

Plants are the backbone of life on our planet. But to protect them well, we still need to know them. One of the missions of the Botanical Garden of the University is to pass on knowledge and awareness of the importance of plants to the general public. The Garden, a magnificent public park, is open free of charge every day, and welcomes nearly 200,000 visitors a year. A true open-air museum, it presents a living collection of 5,000 plant species, classified in sectors and thematic greenhouses. The Garden also offers a rich program of public events, from workshops to exhibitions, conferences or courses. Why are some plants threatened? What can we do to preserve them? From 10th of September 2020 to 31st of October 2021, the Botanical Garden presents a major outdoor exhibition: "Plant Treasure. How to save our endangered species" (bilingual: French / German). Using seven key words observe, monitor, legislate, evaluate, study, conserve and predict - the exhibition tackles these questions in a comprehensive way, while providing elements of an answer to the great challenge of conserving this precious endangered heritage. The event is organized in partnership with the Lausanne Botanical Museum and Garden and the University of Bern. To learn more about the Botanical Garden, please visit: www3.unifr.ch/jardin-botanique

jardin botanique

Trésor végétal Comment sauvegarder nos plantes menacées **Botanischer Schatz** Vie man bedrohte Pflanzen vor dem Aussterben retter avec les photographies de / mit Forographie von Mario Del Curto

The outdoor exhibition "Plant treasure" will be open from September 10th, 2020, until October 31st, 2021, in the Botanic Garden of Fribourg as well as in the Lausanne Botanical Museum and Garden.

DEPARTMENT OF BIOLOGY In figures - 2019/2020



215 Collaborators

30 Nationalities



187 Researchers

29 Research groups

258 Publications



69 PhD students

88 Master students

237 Bachelor students



3.1 M CHF

7.7 M CHF External funding



RESEARCH



Prof. Urs Albrecht

Analysis of circadian clocks and sleep in mammals

Circadian clock and sleep Does lifestyle affect sleep and health?

The earth's rotation around its axis causes periodic exposure of half of its surface to sunlight. This daily recurring event has been internalized in most organisms in the form of cellular circadian clock mechanisms. These cellular clocks are synchronized with each other in various ways to establish circadian networks that build the circadian program in tissues and organs, coordinating physiology and behavior in the entire organism. and shift-work conditions, affects normal brain function and can lead to metabolic problems, sleep disturbance, and accelerated neurological decline. We aim to decipher the ways through which the circadian system can coordinate normal brain function and how waste clearance in the brain could be modulated by the circadian clock. Disturbances in these processes will lead to sleep problems and age-related cognitive decline, which are on the rise in modern society.

In the mammalian brain, the suprachiasmatic nuclei (SCN) receive light information via the retina and synchronize their own neuronal clocks to the light signal.

Subsequently, the SCN transmits this

information to the network of clocks in tissues and organs, thereby synchronizing body physiology and behavior. Disruption of cellular clocks and/or destruction of the synchronization between the clocks, as experienced for instance in jet-lag

" Chronic and age-related diseases are rooted in the misregulation of the circadian clock "

> A variety of molecular, biochemical, genomic, proteomic and metabolomic methods are applied towards the understanding of clock-sleep-metabolism relationships.

ships between the circadian clock and these neurological disorders.

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We are using

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order to study

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mice in



The image shows NIH 3T3 fibroblasts in which the DNA ist stained blue (DAPI), the PER2 protein is green, and phosphorylated PER2 and serine 394 (pSer394 PER2) is stained in red. Note that pSer394 PER2 (red signal) can not be detected in the nucleus.

Group Members



Stéphanie Aebischer



Andrea Brenna





Tomoko Amano



Antoinette Hayoz

Iwona Olejniczak





Tomaz Martini



Jürgen Ripperger

Ashot Sargsyan

Katrin Wendrich

Selected publications

Amano, T., Ripperger, J. A. & Albrecht, U. Changing the light schedule in late pregnancy alters birth timing in mice. Theriogenology 154, 212–222 (2020).

Brenna, A. et al. Cyclin-dependent kinase 5 (CDK5) regulates the circadian clock. eLife 8, e50925 (2019).

Cederroth, C. R. et al. Medicine in the Fourth Dimension. Cell Metabolism 30, 238–250 (2019).

Martini, T., Ripperger, J. A. & Albrecht, U. Measuring Food Anticipation in Mice. Clocks & Sleep 1, 65–74 (2019).





Ecology in the Anthropocene Alien species: the good, the bad and the ugly

Humans change the planet faster than ever before in history. These changes create challenges for science and society, but also opportunities to create better futures. Our research contributes to understanding the mechanisms and consequences of these changes, developing strategies how we can prevent harmful impacts and how we can use this knowledge to enhance ecosystem services we receive from nature. We collaborate with researchers all over the world and advise organizations such as the International Union for Conservation of Nature (IUCN), the Intergovernmental Science-Policy Plat-

form on Biodiversity and Ecosystem Services (IPBES), and the European Commission (EC).

Which are the worst invasive alien species?

The number of alien species is increasing exponentially worldwide and there are many more species than can be managed. There are more than 14000 alien species in Europe, but not all of them cause problems to the environment or human well-being. The seemingly simple and straightforward question "which are the worst invaders?" is difficult to answer because the impacts of alien species can be manifold and comparisons need to work for species as different as for example snails, insects, mammals and plants. We developed methods that allow classifying alien species according to the magnitude of their environmental and socio-economic impacts (S/EICAT), which are now adopted as international standards by the IUCN.

Are all alien species bad?

" Alien species are a major

threat to biodiversity and

human well-being "

Not all alien species are harmful, some can even be beneficial for native species or humans. Current research incorporates beneficial impacts into S/EICAT for more comprehensive understanding of how alien species change local ecosystems and human well-be-

ing.

Improving

biological control In collaboration with the Swiss Federal Research station Agroscope we are improving biocontrol of import-

ant insect pests such as pollen beetles (*Brassicogethes* spp.) and spotted wing fruitfly (*Drosophila suzukii*).

Can we improve wine quality with biodiversity?

In the European project PromESSinG (www.promessing.eu) we investigate how we can use biodiversity-friendly agricultural management techniques to improve grape quality.

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Mario Coiro, Anna Probert, Lisanna Schmidt, Giovanni Vimercati, Anne-Laure Fragnière, Deborah Kaiser, Lara Reinbacher, Silvia Rossinelli, Magdalena Steiner, Lara Volery

> directed by **Sven Bacher**

Group Members







Mario Coiro



Deborah Kaiser









Anna Probert

Lara Reinbacher









Lisanna Schmidt

Magdalena Steiner





Lara Volery

Selected publications

Bacher, S. et al. The Environmental Impact Classification for Alien Taxa First edition. Gland, Switzerland and Cambridge, IUCN EICAT Categories and Criteria. UK: IUCN. X + Xpp. IUCN (2020).

Essl, F. et al. A Conceptual Framework for Range-Expanding Species that Track Human-Induced Environmental Change. BioScience 69, 908-919 (2019).

Bacher, S. et al. Socio-economic impact classification of alien taxa (SEICAT). Methods Ecol Evol 9, 159-168 (2018).



Prof. Louis-Félix Bersier

Microbial systems and the structure and organisation of natural communities

Community ecology Community structure and functioning

Natural communities are composed of numerous species that interact between themselves and with their physical environment. Communities deliver essential "ecosystem services" like food provisioning, carbon sequestration, or nutrients recycling. Understanding how communities are organised and how they function is thus a primary task for ecologists. However, the inherent complexity and variability of most natural communities makes this undertaking conceptually and methodologically challenging. Microbial systems inhabiting

the pitcher-shaped leaves of Sarracenia purpurea are perfectly suited to tackle many fundamental questions in community ecology. This system is simple enough to be captured in mathematical models and to be amenable to replicated experiments, but complex enough to reflect larger-scale systems. In collaboration with Dr.

Rohr, Prof Arditi, and Prof Gabriel, we revisit classical population models with the aim of obtaining a deeper mechanistic understanding of their underlying assumptions. This work generates predictions that can be tested with our microbial system. For example, Samantha Coinus and co-workers explored experimentally how parameter estimation can be biased and their results shed new light on this basic question. Aside from theoretically-driven experiments, we are also interested in the structure of these communities in natural conditions. We use next-generation sequencing and metabarcoding (determination of species based on DNA) to analyse the species present in 160 Sarracenia leaves and their surrounding in five sites in Switzerland. Rachel Korn is responsible for this project and she designed the experiment with a careful choice of primers and the use of mock communities to assess genotyping reliability. This work benefits from collaboration with Dr. Gerhard Thallinger (Graz Uni-

"The benefits of biodiversity for ecosystem productivity are impacted by increasing temperature"

> tional meeting for researchers using Sarracenia as a model organism, with the aim of sharing methodologies and research interests. This one-week symposium took place at the University of Fribourg in Summer 2019 and saw the creation of SPIN, the Sarracenia purpurea International Network.

erhard Thallinger (Graz University) for the molecular part, and Dr. Jim Grace (USGS) for the analyses. The first results reveal intriguing differences in the spatial structure between the first trophic level (bacteria) and their consumers (protozoans), as well as between Sarracenia communities and those found in the surrounding bogs. Dr. Sarah Gray obtained funding from the SNSF to organise the first interna-



The Sarracenia pitcher-plants attract insects that drown inside the rain-water filled leaves. This characteristic is appealing not only for ecologists studying the microbial communities that decompose the drowned prey, but also for spiders like this Dolomedes. (CC BY-SA 4.0).

Group Members





Samantha Coinus

Sarah Gray Rachel Korn



Nilgun Sailer

er

Selected publications

Brose, U. et al. Predator traits determine food-web architecture across ecosystems. Nat Ecol Evol 3, 919–927 (2019).

Parain, E. C., Gray, S. M. & Bersier, L.-F. The effects of temperature and dispersal on species diversity in natural microbial metacommunities. Sci Rep 9, 18286 (2019).

Parain, E. C., Rohr, R. P., Gray, S. M. & Bersier, L.-F. Increased Temperature Disrupts the Biodiversity–Ecosystem Functioning Relationship. The American Naturalist 193, 227–239 (2019).



Dr Simon Blanchoud

Whole-body regeneration in Botrylloides leachii

Marine biology and regeneration Exploring the extraordinary world of colonial tunicates

Tunicates are marine invertebrates that belong to the Tunicata subphylum. Together with the more basal Cephalochordata (i.e. the lancelets) and the Vertebrata (i.e. us), they compose the Chordata phylum. Tunicates are estimated to have separated from the vertebrates 500 million years ago, which thus makes them our closest invertebrate relatives! This unique taxonomic position renders the study of these animals particularly relevant to investigate the evolution of chordates

and the emergence of the vertebrates. In addition to this broader perspective, tunicates display a variety of physiological and morphological traits that are truly fascinating.

There are currently over 3'000 different species of tunicates identified. The majority of these organisms are benthic (i.e. ses-

sile) filter-feeders, while the others are pelagic (i.e. floating). Tunicates have a tissue complexity reminiscent of vertebrates, and a morphology organized around a barrel-shaped body with two siphons to filter water. Tunicates are named after the structuring semi-rigid layer of cellulose-based extracellular matrix that encompasses their body.

"Every facet of these animals is mesmerizing"

The diversity of adult forms ranges from from the 15 cm-long Korean delicacy *Halocynthia* to the developmental model organism *Ciona*, from the solitary carnivorous abyssal *Dicopia* to the colonial invasive subtidal *Botrylloides* and from the 1 mm-long dioecious *Oikopleura* that builds extra-corporeal houses for funneling its food to the bioluminescent *Pyrosoma* that assembles into up to 18 m-long tube-shaped pelagic colonies.

> In our lab, we are particularly interested in the powerful regenerative capacity of *Botrylloides*. Extraordinarily, these animals can regenerate a fully functional adult from a minute fragment of its vascular system in just 10 days. In this species, one tissue has thus the stem-like capacity to recreate all other tissues of an animal! In addition to this dramatic process, we are investigating other fascinating

facets of these animals, including asexual reproduction, locomotion, taxonomy and genomics. Our group works at the interface between engineering and biology, innovating solutions to dissect the unusual scientific questions brought to us by these tunicates. As an initial and necessary step for our research, we have already been able to bring the oceans to Fribourg by developing the first in-land breeding system for colonial tunicates. Join us in our exploration of the biology of these marine invertebrates, there is amazing science coming up!



Side-view of a colony of Botrylloides.

Group Members





Alessandro Bilella

Ana Hernandez Lopez

Lluis Matas







Silvia Moreno Forero Marta Wawrzyniak

Selected publications

Blanchoud, S., Rinkevich, B. & Wilson, M. J. Whole-Body Regeneration in the Colonial Tunicate Botrylloides leachii. in Marine Organisms as Model Systems in Biology and Medicine (eds. Kloc, M. & Kubiak, J. Z.) 337–355 (Springer International Publishing, 2018).

Blanchoud, S., Rutherford, K., Zondag, L., Gemmell, N. J. & Wilson, M. J. De novo draft assembly of the Botrylloides leachii genome provides further insight into tunicate evolution. Sci Rep 8, 5518 (2018).

Blanchoud, S., Zondag, L., Lamare, M. D. & Wilson, M. J. Hematological Analysis of the Ascidian Botrylloides leachii (Savigny, 1816) During Whole-Body Regeneration. The Biological Bulletin 232, 143–157 (2017).

RESEARCH



Prof. Jörn Dengjel

Cellular signaling events regulating autophagy

Staying healthy by recycling How does a cell decide what to degrade when and where?

Autophagy comprises several evolutionary conserved cellular degradation pathways that commonly act cytoprotective and lead to degradation of biomolecules. We study the regulation and function of autophagy by analyzing proteins, which carry out the underlying molecular reactions. As many autophagy processes are characterized as being regulated on

a posttranslational level, we rely on quantitative mass spectrometry-based proteomics approaches to characterize mechanisms driving autophagy and regulating protein turnover.

Our focus is the analysis of macroautophagy (hereafter referred to as auto-

phagy) which summarizes specific and non-specific lysosomal degradation pathways. Non-specific autophagy is a constitutive process, whereas specific autophagy leading to the degradation of defined subsets of organelles and/or proteins is regarded as stress-induced. Dysregulation of autophagy has been linked to many human diseases, most notably to neurodegeneration, cancer, and metabolic syndromes, as well as to ageing. We aim to characterize new proteins being crucial for functional autophagy, or being specifically degraded by autophagy, presumably to ensure cell survival under stress conditions. In parallel, we study proteins known to be involved in autophagy regulation, specifically kinases and phosphatases, to better understand their function and to be able to better assess their potential to be used

in therapeutic approaches targeting human

diseases. A special focus is the crosstalk between the cellular microenvironment, i.e.

extracellular matrix and soluble proteins,

and autophagy regulators. Here, we use skin as a model system to study the role of auto-

phagy in wound healing employing primary

skin fibroblasts and keratinocytes in 3D cell

"Keep calm and recycle !"

culture systems.

We combine mass spectrometry method development with mass spectrometry-based screens, biochemical analyses of single proteins, and characterizations of phosphorylation and ubiquitination events to identify new players being relevant in autophagy function. Our aim is to generate new insights into a fundamental biological process that is crucial for human health.



Phosphorylation-based signaling pathways regulating autophagy in yeast

Group Members





Esther Martinez

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Kaeser-Pebernard





Carole Roubaty

Devanarayanan Siva Sankar

Bich Vu

Michal Stumpe







Christine Vionnet

Jianwen Zhou



Alexandre Leytens

Selected publications

Berberich, B. at al. Proteomic Profiling of Fibroblasts Isolated from Chronic Wounds Identifies Disease-Relevant Signaling Pathways. Journal of Investigative Dermatology 140.2280-2290.e4.

Hatakeyama, R. et al. Spatially Distinct Pools of TORC1 Balance Protein Homeostasis. Molecular Cell 73, 325-338. e8 (2019).

Hu, Z. et al. Multilayered Control of Protein Turnover by TORC1 and Atg1. Cell Reports 28, 3486-3496.e6 (2019).

RESEARCH



Prof. Claudio De Virgilio

Nutrient signaling and control of quiescence in yeast

Nutrients and cell proliferation **Baker's yeast with an EGO** complex

All living cells can exit the normal cell cycle and enter into a resting state termed quiescence or GO. Interestingly, most eukaryotic cells, whether they exist as single cells or as part of a multi-cellular organism, spend most of their life time in such a quiescent state. The regulatory mechanisms controlling entry into or exit from quiescence, however, are still largely elusive. Because the disruption of these mechanisms is thought to be associated with cellular transformation (in multi-cellular organisms) or dramatically reduced life span (in

unicellular organisms), it is likely that research in this area will not only enhance our basic understanding of diseases such as cancer, but also be instrumental for the development of

"A little eukaryote makes big contributions to science"

phatases (GTPases).

The latter assemble into heterodimeric complexes consisting of Gtr1 and Gtr2 in yeast, or RagA or RagB and RagC or RagD in mammalian cells. These heterodimers are integral to larger complexes coined

EGO (exit from

rapamycin-in-

diagnostic and therapeutic tools to treat these diseases.

To address the basic aspects of quiescence experimentally, we have chosen the unicellular eukaryote baker's yeast as a model system. Our current data indicate that a conserved protein complex, coined target of rapamycin complex 1 (TORC1), plays a central role in yeast in coordinating both entry into and exit from GO in response to nutrient levels.

This fits well with the reported role of TORC1 in coupling nutrient, energy, and hormonal signals with cell growth, division duced growth arrest) complex (EGOC) in yeast or Rag-Ragulator complex in mammalian cells, which are predominantly tethered to vacuolar or lysosomal membranes, respectively. In this context, our current research is focused on deciphering the amino-acid sensitive events upstream of the Rag GTPases in yeast, which likely involve both vacuolar and cytoplasmic amino acid sensors. Due to the evolutionary conservation of the EGOC and its regulators, our studies in yeast are expected to contribute to the understanding of the molecular mechanisms leading to diseases that are associated with hyperactive mammalian TORC1 including cancer, type 2 diabetes, and neurodegeneration.

and metabolism in higher eukaryotic cells. Notably, amino acids

are important and primeval cues that stimulate TORC1 to pro-

mote anabolic processes (such as ribosome biogenesis and pro-

tein translation initiation) and inhibit catabolic processes (such

as macroautophagy) via the conserved Rag guanosine triphos-



Amino acids stimulate the target of rapamycin complex 1 (TORC1) to promote anabolic processes and inhibit catabolic processes via the conserved EGO complex. The surface view of the pentameric EGOC highlights the Ego1, Ego2, and Ego3 subunits, which provide a scaffold for the heterodimeric Gtr1-Gtr2 Rag GTPase module.

Group Members







Ladislav Dokládal

Riko Hatakeyama Malika Jaguenoud







Raffaele Nicastro

Guillermo Osuna

M.-Pierre Péli-Gulli













Susanne Stumpe

Selected publications

Hatakeyama, R. & De Virgilio, C. TORC1 specifically inhibits microautophagy through ESCRT-0. Curr Genet 65, 1243-1249 (2019).

Hatakeyama, R. et al. Spatially Distinct Pools of TORC1 Balance Protein Homeostasis. Molecular Cell 73, 325-338. e8 (2019).

Hu, Z. et al. Multilayered Control of Protein Turnover by TORC1 and Atg1. Cell Reports 28, 3486-3496.e6 (2019).

Kvainickas, A. et al. Retromer and TBC1D5 maintain late endosomal RAB7 domains to enable amino acid-induced mTORC1 signaling. Journal of Cell Biology 218, 3019-3038 (2019).

Zhang, T. et al. Structural insights into the EGO-TCmediated membrane tethering of the TORC1-regulatory Rag GTPases. Sci. Adv. 5, eaax8164 (2019).



Dr Boris Egger

Neural stem cell states in the brain of *Drosophila melanogaster*

Neural development The ins and outs of neural stem cells

Neural stem cells go through phases of proliferation and differentiation. During early development, pools of neural stem cells are expanded through symmetric proliferative divisions. Later neural stem cells transition to differentiative division modes to self-renew and to generate more specialized cell types, such as neurons and glial cells. Stem cell state transitions are tightly regulated by a combination of cell intrinsic and environmental factors. Failures in the regulatory mechanisms can lead to tumorous overgrowth or small brain phenotypes, also called miFor this we are using advanced live cell imaging and genetic methods to monitor and manipulate cell cycle progression in cultured fly brains. We also aim to understand how environmental factors interact with cell intrinsic regulators to control stem cell states. The availability of oxygen can have an instructive role to regulate stem cell behavior in central nervous system. We are using a biosensor to investigate an intriguing correlation between hypoxia and various neural stem cell types in the *Drosophila* brain.

crocephaly.

The progression through the cell cycle has an important role in the transition from one stem cell state to another. Often, stem cells are temporally arrested in a par"Stem cell state transitions are tightly regulated by a combination of cell intrinsic and environmental factors"

The genetic mechanisms that we are studying in the fly brain are evolutionary conserved in mammalian species.

ticular cell cycle phase while cellular changes are executed for the transformation to a new state. We are investigating the question of how cell cycle regulators interact with cell fate factors to control neural stem cell state transitions. Therefore, our findings will most likely provide us with insights into our own brain development under normal and disease conditions.



Image by Karolina Miszczak and Dotun Adeleye Adeyinka shows a single developing brain hemisphere. Neural stem cells are labelled by immunofluorescence (blue) and cell cycle phases are marked by a fluorescent biosensor (green and red).

Group Member



Dotun Adeleye Adeyinka

Selected publications

Baccino-Calace, M., Prieto, D., Cantera, R. & Egger, B. Compartment and cell-type specific hypoxia responses in the developing *Drosophila* brain. Biology Open 9, bio053629 (2020).

Guillermin, O., Perruchoud, B., Sprecher, S. G. & Egger, B. Characterization of tailless functions during *Drosophila* optic lobe formation. Developmental Biology 405, 202–213 (2015).

Misra, T. et al. A genetically encoded biosensor for visualising hypoxia responses in vivo. Biology Open 6, 296–304 (2017).

Miszczak, K. & Egger, B. Live Cell Imaging of Neural Stem Cells in the *Drosophila* Larval Brain. in Brain Development (ed. Sprecher, S. G.) vol. 2047 153–160 (2020).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Dr Laurent Falquet

Microbial Genomics & Metagenomics

Toxin-antitoxin systems A TASer to identify the good, the bad and the shiny

Bacterial toxin-antitoxin systems (TAS) are involved in several key intracellular biological functions by activation of the toxin mainly as a response to stresses (e.g. antibiotics) or to maintain plasmids via post-segregational killing (PSK) or to protect against attacks from phages. TAS are organized in two or more consecutive genes located on a chromosome or a plasmid and working jointly (the antitoxin neutralizing the toxin in normal situation).

Recently, we announced the TASmania database (Akarsu et al., 2019) a collection based on more than 41'000 bacterial ge-

nomes from ENSEMBL-Bacteria database and annotated for the presence of known and new TAS, together with their associated HMMs.

However, TASmania restricts the results to the genomes in ENSEMBL-Bacteria and cannot highlight the TAS present in any new coming genome.

To extend the capabilities of TASmania, we developed a sister pipeline called TASer to identify TAS in any bacterial genome using the HMMs identified by the TASmania database and an associated web user Interface generated with R Shiny. The user can upload its own small genome (<15Mbp) in FASTA format, a limit suitable for bacteria or phages. The validated genome file is then processed by a Python script on a High-Performance Computing cluster.

"We highlight the TAS in bacterial genomes"

The processing starts by the gene prediction allowing the user to select the appropriate genetic code. Both the protein predicted as well as the intergenic regions are

searched against the collection of 682 TASmania HMMs for toxins and antitoxins. The hits for TA identification are filtered reporting only significant E-values (chosen by the user) and formatted in a table similar to the TASmania output. As TASer creates a personal session ID, the main and accessory result tables can be downloaded during 10 days on our server.

TASer is a powerful, easy and efficient tool to identify quickly TAS in any new bacterial genome by using a High-Performance Computing cluster and a shiny server hosted at University of Bern.

Group Members

COST AND A CONTRACTOR





José Antonio Agüero

Co-supervised PhD







Tess Bonato

Vivien Pichon

Valentin Scherz

Selected publications

Agüero, J. A., Akarsu, H., Aguilar-Bultet, L., Oevermann, A. & Falquet, L. Large-Scale Comparison of Toxin and Antitoxins in Listeria monocytogenes. Toxins 12, 29 (2020).

Akarsu, H., Aguilar-Bultet, L. & Falquet, L. deltaRpkm: an R package for a rapid detection of differential gene presence between related bacterial genomes. BMC Bioinformatics 20, 621 (2019).

Akarsu, H. et al. TASmania: A bacterial Toxin-Antitoxin Systems database. PLoS Comput Biol 15, e1006946 (2019). Josi, C. et al. Large-Scale Analysis of the Mycoplasma bovis Genome Identified Non-essential, Adhesion- and Virulence-Related Genes. Front. Microbiol. 10, 2085 (2019).

Jores, J. et al. Removal of a Subset of Non-essential Genes Fully Attenuates a Highly Virulent Mycoplasma Strain. Front. Microbiol. 10, 664 (2019).

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TASer tool: https://bugfri.unibe.ch/taser | TASmania database: https://bugfri.unibe.ch/tasmania

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RESEARCH



Prof. Thomas Flatt

The genetics and genomics of adaptation in *Drosophila*

Genomics of adaptation Using fruit flies to find the genes that underlie adaptation

A fundamental aim of evolutionary biology is to understand the genetic basis of how organisms adapt to their environment. Our laboratory seeks to identify the genes and molecular polymorphisms that underpin adaptations by applying genomics and genetics to natural and laboratory populations

of the vinegar fly, Drosophila melanogaster, a powerful model organism with a rich history of fundamental discoveries in genetics, evolution and development over the last 100 years.

To do so, we employ populations of flies that differ

genetically and phenotypically in fitness-related traits (socalled life history traits), for example in terms of their growth, size, fecundity and lifespan; such traits are the direct targets of natural selection and hence of major importance for our understanding of adaptation. By investigating the genomes and transcriptomes of such flies with next-generation sequencing and by using population genetics we can identify candidate genes and alleles that are likely shaped by selection and examine their properties and effects. To do so, we use the versatile genetic tool box available in Drosophila (e.g., mu-

"Finding the genes that underlie adaptation is a central problem in evolutionary biology" tants, transgenes, deletions, balancers, CRISPR/Cas9, recombinant populations) in order to test how promising candidate genes and alleles affect fitness-related traits and tradeoffs between them. In our recent work we are using these approaches to dis-

cover how a large chromosomal inversion (a "supergene") affects multiple fitness traits, including body size, lifespan and stress resistance, along environmental gradients; how genetic variation in the insulin/insulin-like growth factor signaling (IIS) pathway contributes to adaptive variation in size and stress resistance; and how immunity genes in the Toll signaling pathway underlie the evolution of longevity.



To examine genetic changes in natural populations we regularly collect fruit flies in the wild, in collaboration with the European Drosophila Population Genomics Consortium (DrosEU).

Group Members





Patrick Favre



Marta Bellone





Katja Hoedjes

Envel Kerdaffrec Margot Paris



Marisa Rodrigues

Selected publications

Flatt, T. Life-History Evolution and the Genetics of Fitness Components in Drosophila melanogaster. Genetics 214, 3-48 (2020).

Hoedjes, K., et al. 2019. Distinct Genomic Signals of Lifespan and Life History Evolution in Response to Postponed Reproduction and Larval Diet in Drosophila. Evolution Letters 3:598-609 (2019).

Kapun, M., et al. Genomic analysis of European Drosophila melanogaster populations reveals longitudinal structure, continent-wide selection, and unknown DNA viruses. Molecular Biology and Evolution 37:2661-2678 (2020).

Ramaekers, A., et al.. Altering the temporal regulation of one transcription factor drives evolutionary trade-offs between head sensory organs. Developmental Cell 50:780-792 (2019).



Dr Markus Geisler

Biochemical analysis of hormone transport in plants

Hormone transport and ABC transporters When hormones turn crazy

The motto of my lab is "Exploring the future without forgetting the past." Under this framework our group has a long-lasting interest and expertise in analyzing transmembrane transport processes in plants on a biochemical level. While we were over the years able to assign transporters of different sub-classes to distinct plant hormones, our main focus still lies on the fascinating cell-to-cell movement of the plant signaling compound, auxin. This event, called polar auxin transport, represents a unique, plant-specific mechanism that virtually controls all aspects of plant growth and performance and represents a hotspot in plant biology.

The bending of plant roots toward the gravity field, called gravitropism, is one of the best-understood examples of auxin-controlled growth and in the last two years we have been analyzing auxin flows and transporter expression in plants that

are growing without gravitropism (see photo).

Further, we have been performing a structure-function analysis of the ABC-type auxin transporter, ABCB1, in the model plant Arabidopsis. Using a mutational approach, we were able to identify a short D/E-P motif that is essential for auxin transport and that seems to define Auxin-transporting ABCBs, so-called ATAs (Hao **et al.** 2020). With the help of this motif we know now that 11 of the 22 full-size AB-CBs of Arabidopsis are most likely auxin transporters but are now also able to predict ATAs in other plant genomes. Moreover, we have been continuing to explore the functional relevance of the interaction between the auxin exporter, ABCB1, and the FKBP42, TWISTED DWARF1. It appears that TWISTED DWARF1 functions as a co-chaperon for so-called Heat-Shock Proteins (HSPs) that stabilize ABCB-type auxin transporters at the plasma membrane. This complex module of ABC transporter regulation seems to be conserved between auxin-transporting ABCBs (ATAs) in plants and mammalian ABC transporters, such as the cystic fibrosis transmembrane conductance regulator (CFTR), whose malfunction causes cystic fibrosis (di Donato and Geisler 2019). Another relevant function of TWISTED DWARF1 is connected with its

"Exploring the future without forgetting the past"

tern et al. 2019).

ability to affect cytoskeleton dynamics by regulating the bundling of actin filaments. Currently, we are studying how TWISTED DWARF1 interferes with actin and membrane dynamics by using pollen tubes and tobacco cells as a model system. Moreover, we are investigat-

ing the clinically relevant phenomenon of multidrug resistance by dissecting a dual substrate specificity in the ABC transporter, ABCG36/PEN3/PDR8, that is involved in plant development and disease resistance. We could show that ABCG36 is a specific exporter of the auxin precursor, IBA (Aryal *et al.* 2019), and sub-

strates that stimulate bacterial-induced callose deposition (Ma-



GeislerLab goes to space: since years we are interested in understanding how plants sense and adapt to altered gravity. Beside genetic and pharmacological tools, another elegant way to do so is to grow plants under zero gravity conditions on earth (by using so-called random positioning machines) or by space flights; the latter we are aiming for the future.

Group Members





Martin Di Donato



Laurence Charrier

Pengchao Hao



Selected publications

Aryal, B. et al. ABCG36/PEN3/PDR8 Is an Exporter of the Auxin Precursor, Indole-3-Butyric Acid, and Involved in Auxin-Controlled Development. Front. Plant Sci. 10, 899 (2019).

Donato, M. & Geisler, M. HSP 90 and co-chaperones: a multitaskers' view on plant hormone biology. FEBS Lett 593, 1415–1430 (2019).

Hao, P. et al. A conserved D/E-P motif in the nucleotide binding domain of plant ABCB/PGP-type ABC transporters defines their auxin transport capacity. http://biorxiv.org/lookup/doi/10.1101/2020.05.08.084087 (2020).

Matern, A. et al. A substrate of the ABC transporter PEN3 stimulates bacterial flagellin (flg22)-induced callose deposition in Arabidopsis thaliana. J. Biol. Chem. 294, 6857-6870 (2019).



Prof. Dominique Glauser

Analysis of nociception and avoidance behaviours in *Caenorhabditis elegans*

Nociception and plasticity How to shut off pain signal

Like most animals, we are able to detect damaging or potentially damaging stimuli, through a process called nociception. Nociception underlies important protective behaviours to avoid injuries and favour healing. However, in pathological situations pain may also become persistent with no actual benefit. Chronic pain affects more than a billion people worldwide.

Because available drugs are either only moderately effective or have detrimental side effects, there is an essential need for improved pain management solu-

"There is an essential need for improved pain management"

screens, we identify conserved genes required for thermal nociception and avoidance behaviours. E.g. we have discovered mutants with impaired sensitivity to noxious heat, as well as mutants unable to habituate to repeated noxious stimuli, or habituating faster. These mutants are essential entry points to discover and characterize novel molecular pathways controlling nociception

and plasticity mechanisms in the nociceptive pathway.

Furthermore, we use a combination of cutting-edge in vivo imaging techniques, proteomic, transcriptomic, optogenetics and computer-as-

tions. Progress in the field is hindered in human and mammalian models by ethical concerns, by the size and the complexity of the nervous system, as well as by the difficulty to bridge the gaps in our understanding at the molecular, neuronal, and physiological/behavioural levels.

To circumvent these limitations, our lab uses the simple model organism *Caenorhabditis elegans* and has developed a series of fruitful approaches to investigate the mechanisms controlling nociception. Using forward and reverse genetic sisted analysis of behaviour to better understand the implicated mechanisms at the molecular, cellular and circuit levels. As a whole, our integrative research both provides a fundamental knowledge on the mechanisms underlying pain sensation and aversive behaviours and brings insight on new potential drug targets for future pain treatment translational development.



Uncovering the functioning logic of the nociceptive circuit in *C. elegans*. With this optogenetics setup, we can remotely control the activation of different neurons in a population of free-moving animals, while simultaneously recording their behaviour.

Group Members



Stéphanie Aebischer

Georgina Gomez Saldivar





Laurence Bulliard



Filipe Alberto Gonçalves Marques

es Domenica Ippolito









Lisa Schil





Martina Rudgalvyte Saurabh Thapliyal

Selected publications

Lia, A.-S. & Glauser, D. A. A system for the high-throughput analysis of acute thermal avoidance and adaptation in C. elegans. J Biol Methods 7, 129 (2020).

Marques, F. et al. Identification of avoidance genes through neural pathway-specific forward optogenetics. PLoS Genet 15, e1008509 (2019).

Saro, G. et al. Specific Ion Channels Control Sensory Gain, Sensitivity, and Kinetics in a Tonic Thermonociceptor. Cell Reports 30, 397-408.e4 (2020).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY

RESEARCH



Dr Ora Hazak

Receptor-Peptide Mediated Pathways guiding Xylem development

Plant Signaling Mechanisms How do plants adapt to the water deficit?

Plant roots are amazing branching structures that explore the soil searching for water and minerals. Because water is vital for every single biological process, plant roots developed a fascinating mechanism of growing towards water (hydrotropism), they efficiently uptake the water by tiny root hairs and transport it through the system of lignified perforated capillaries called xylem. In the end, the water leaves the plant by evaporation through the stomata which creates a negative pressure in the whole xylem system and water continues to

move from the roots to the shoot. Remarkably, even a little change in the structure or the amount of the xylem capillaries, the thickness of the waterproof polymers layer, the capatitivity of the stamat

sensitivity of the stomata to open or to close under the stressful conditions will significantly impact the plant ability to survive under water stress conditions. Today, when our planet faces the global climate change and higher temperatures, and drought are going to affect more and more the agriculture, we have to build a basis for the crops of the future that will better resist the global warming.

Therefore, our lab is keen to uncover the mechanisms that shape the water conducting capillaries and to understand better the plant adaptation mechanisms to water stress. More specifically, we focus on small signaling peptide molecules that are secreted in roots within the xylem tissues and control cell divisions and building the lignin (a waterproof polymer) layer. We already could map two peptides (CLE9 and CLE22) and we continue our research to study the sensing machinery including receptors and co-receptors as well as cell-specific transcriptional responses induced by these peptide hormones.

Another focus in our lab is to identify stress-specific signaling peptides that are released upon stress (drought, high salinity) and act in adaptation. Here we use a powerful genetic approach

" Uncovering the secrets of plant water management "

to screen the collection of *Arabidopsis* mutants in peptide genes in stress conditions. It appears, that number of peptides act during

the stress and we now study whether different peptides induce specific cellular responses or they act on the same transcriptional target to allow the adaptation. Importantly, here we use not only the model plant Arabidopsis, but also a crop plant Tomato as a model plant in the lab. Based on our phylogenetic analysis, many peptide genes in Arabidopsis have the homologs in Tomato genome. Using genome editing tools like CRISPR-Cas9, we induce loss of function of the candidate genes in Tomato in hope to create a plant with better ability to resist the drought and high salinity. In both projects, we use state-of-the-art confocal microscopy.



Optical cross section in the young Arabidopsis root. Calcofluor white staining was used for visualisation of the cell walls (grey) and Basic Fuchsin (green) for the lignin staining of the mature xylem vessels.

Group Members







Samy Carbonnel

Salves Cornelis

<u>Ur</u>sina Ratgheb

Selected publications

Breda A.S., Hazak O., Schultz P., Anne P., Graeff M., Simon R. & Hardtke C.S. A cellular insulator against CLE45 peptide signaling. Current biology 2019.

Hazak O., Mamon E., Lavy M., Sternberg H., Behera S., Schmitz-Thom I., Bloch D., Dementiev O., Gutman I., Danziger T., Schwarz N., Abuzeineh A., Mockaitis K., Estelle M., Hirsch J., Kudla J., Yalovsky S. A novel Ca2+-binding protein that can rapidly transduce auxin responses during root growth. PLoS Biology 2019.

Hardtke C.S. 2017 Perception of root-active CLE peptides requires CORYNE function in the phloem vasculature. EMBO Rep. 2017 Jun 12. pii: e201643535.

Breda A.S., Hazak O., Hardtke C.S. 2017 Phosphosite charge rather than shootward localization determines OCTOPUS activity in root protophloem. Protocols of National Academy of Science U S A. 2017 Jul 11;114(28): E5721-E5730.

Hazak O, and C. Hardtke. 2016 "CLAVATA1-type receptors in plant development" Journal of Experimental Botany 2016 Aug;67(16):4827-33.

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Dr Gwenaël Jacob

Tracking the causes of population decline

Ecology of Capercaillie and Hazel grouse Revealing the unobservable: the secret life of Grouse

The spatial distribution and census size of populations are relevant criteria to assess the conservation status of species at local and regional scales. This task is challenging for secretive species, because of the elusive nature of individuals and the time and human resources necessary to find and exploit reliable sources of DNA. Once technical and methodological difficulties are overcome, non-invasive genetic monitoring

provide a valuable tool to track individuals. study the dynamics of genetic diversity and the role of ecological corridors between populations. We use non-invasive samples collected along transects to monitor

"From observations to theoretical and applied research questions"

In particular, we are interested on the consequence of habitat fragmentation on the local dynamics of these species. Our results will provide valuable insight for the management of species in human-altered habitats, as was done with the Eurasian otter (Lutra lutra, Pigneur et al 2018).

Since 2018, Hazel grouse Project has been established which

aims at exploring the ecology of Hazel grouse in the Swiss Prealps by combining field studies, geographic information systems (GIS) and molecular analyses. The project provides Master and Bachelor students with their first research

populations of two Galliformes species, Western capercaillie (Tetrao urogallus) and Hazel grouse (Tetrastes bonasia), study their breeding behaviour and assess the rate of dispersal between neighbouring forest patches.

Our 6-year monitoring program was key to reveal ecological and evolutionary processes shaping the genetic structure of populations (Cayuela et al 2019). Ongoing research projects aim at studying the interaction between mate choice strategies and immigration and their consequences on the level of inbreeding in populations (Jacob, Prévot & Baudry 2016).

experience. Students have the opportunity to select their topic of interest, design and set up their own study, coordinate field and lab work with co-workers and transmit acquired knowledge and expertise to other students.

Research topics ranged from assessing extrinsic factors affecting winter occurrence in Hazel grouse to the design and assessment of standardized linear transect methods for summer monitoring, and are relevant both at the scale of the Swiss Prealps and for the monitoring of other Galliformes species worldwide.



Group Members



Francesco Foletti

Selected publications

Cayuela, H. et al. Kin-dependent dispersal influences relatedness and genetic structuring in a lek system. Oecologia 191, 97–112 (2019).

Jacob, G., Prévot, A.-C. & Baudry, E. Feral Pigeons (Columba livia) Prefer Genetically Similar Mates despite Inbreeding Depression. PLoS ONE 11, e0162451 (2016).

Pigneur, L-M. et al. Apport de la génétique pour l'étude de la dynamique des populations de Loutre d'Europe Lutra lutra (Linnaeus, 1758) en France. Naturae 2018:63-71 (2018).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY




RESEARCH



Prof. Anna Jazwinska

Exploring heart, fin and retina regeneration in zebrafish

Organ regeneration Zebrafish regrow their injured hearts and amputated fins

Our group studies the cellular and molecular mechanisms through which zebrafish can grow back parts of their injured organs. This includes fins after an amputation, retina, and even hearts after an injury similar to a myocardial infarction. This natural restorative ability relies on the plasticity of mature cells in the wounded organs. Activated cells proliferate and reproduce fully functional tissues. We aim to better understand this process. In the last year, we identified that Cilliary Neurotrophic Factor, CNTF, stimulates pro-regenerative processes in the zebrafish heart. This finding revealed a new molecular effector of cardiac preconditioning, which renders the heart more resilient to injury. To conduct this study, we established a new method for delivery of dissolved proteins into pericardial cavity. In another project, we tested whether regenerative capacities can be exhausted by a series of myocardial infarctions. Our results demonstrated that the cardiac regeneration is maintained even after six subsequent cy-

We use the zebrafish as a model organism because of many experimental advantages, such as effi-

"Fishing for secrets of organ regeneration"

cles of injury/regeneration, despite enhanced fibrosis. We also made discoveries about fin regeneration. First, we demonstrated that initiation of fin restoration involves a transient ex-

cient reproduction, maintenance and a well-annotated genome. For functional studies, we apply diverse genetic approaches, namely CRISPR/Cas9 mutagenesis, CreERT-loxP cell-lineage tracing, fluorescent gene reporters and inducible gene overexpression. We describe the biological processes by means of microscopic photography of live animals, histological staining of fixed tissues, multi-color fluorescence imaging and in situ-hybridization for visualization of gene transcription.

pression of serotonin. Following this finding, we also discovered a specific population of solitary paraneurons in the epidermis of the zebrafish fin that co-express serotonin, calretinin and synaptic vesicle glycoprotein. We used an interdisciplinary approach to demonstrate that hydrodynamic forces regulate the distribution of these paraneurons throughout the fin surface. After amputation, these cells were able to regenerate together with all other tissues. Our findings provide a new perspective for regenerative therapies, aiming in stimulation of organ regeneration in mammalian models and humans.



Group Members





Hendrick Oudhoff





Désirée König



Verena Zimmermann

Selected publications

Bise, T., de Preux Charles, A.-S. & Jaźwińska, A. Ciliary neurotrophic factor stimulates cardioprotection and the proliferative activity in the adult zebrafish heart. npj Regenerative Medicine 4, 1–14 (2019).

González-Rosa, J. M., Burns, C. E. & Burns, C. G. Zebrafish heart regeneration: 15 years of discoveries: González-rosa et al. Regeneration 4, 105–123 (2017).

Jaźwińska, A. & Blanchoud, S. Towards deciphering variations of heart regeneration in fish. Current Opinion in Physiology 14, 21–26 (2020).

König, D. et al. Distribution and Restoration of Serotonin-Immunoreactive Paraneuronal Cells During Caudal Fin Regeneration in Zebrafish. Front. Mol. Neurosci. 12, 227 (2019).

Pfefferli, C. & Jaźwińska, A. Lymphatic vessels help mend broken hearts. eLife 8, e52200 (2019).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Prof. Gregor Kozlowski

Conservation biology of relict, endemic and endangered plants

Conservation biology and biogeography Understanding and preventing extinctions

"The Earth is facing

an unprecedented

biodiversity loss"

cycles.

The accelerated loss of biological diversity will be without doubt one of the most severe human-made global problems of the 21st century. Recent reports talk even about the biological annihilation via ongoing sixth mass extinction. Understanding why species are becoming rare and extinct is one of the main challenges of conservation biology.

Our research group explores various aspects of biology, evo-

lution and biogeography of threatened, endemic and relict plant species. Through our studies, we aim to provide the basic knowledge in order to efficiently protect species at the brink of extinction. The trademark of our group is an inten-

sive field-work, both locally (e.g., Switzerland, Alps) and globally (e.g., Mediterranean, Arctic, Transcaucasia, Eastern Asia, North- and Central America).

Globally, our main model organisms are threatened woody species, with special focus on relict trees. Relict trees are remnants of past populations that have become fragmented by climate-driven changes and habitat loss. These remnants were left behind during past range shifts and can persist today only in enclaves with favorable environmental conditions in areas with inhospitable regional climates. The major model organisms of our research are the relict tree genera *Zelkova* (Ulmaceae) and *Pterocarya* (Juglandaceae), possessing today pronounced disjuctions between the Western and Eastern Eurasia. Our group coordinates the activities of an international and interdisciplinary relict tree Project *Zelkova* (network of more than 30 researchers from ca. 15 countries).

At the local scale, the main subject of our investigations are threatened and/or endemic alpine-arctic and boreal plants (e.g.,

Nuphar pumila, Papaver occidentale, Pinus cembra). The Alps, along with the neighboring mountain ranges, played an important role in forming the biogeographical patterns in Europe and acted as a refugium for many taxa throughout several ice age

Our group is directly linked with the Botanical Garden of the University of Fribourg (G. Kozlowski is the director of the garden), as well as intensively collaborating with the Natural History Museum Fribourg (NHMF) and with the Office of Forest and Nature (SFN/WNA) of the State of Fribourg. Internationally, our group is tightly associated with the Shanghai Chenshan Botanic Garden in China (Plant Systematics and Evolutionary Biology Group at the Shanghai Chenshan Plant Science Research Center of the Chinese Academy of Sciences).



Alpine poppy (Papaver occidentale) is an endemic plant of Western Prealps in Switzerland and France. All populations of this glacial relict are threatened by an accelerated global warming.

Group Members



Sébastien Bétrisey





Laurence Fazan





Salvatore Pasta

Benoît Clément



Yann Fragnière

François Rion





Yi-Gang Song

Selected publications

Bétrisey, S. et al. Glacial relicts in the Alps: the decline and conservation strategy for Nuphar pumila (Nymphaeaceae). Alp Botany 130, 89-99 (2020).

Naciri, Y. et al. Species delimitation in the East Asian species of the relict tree genus Zelkova (Ulmaceae): A complex history of diversification and admixture among species. Molecular Phylogenetics and Evolution 134, 172-185 (2019).

Song, Y. et al. Global biogeographic synthesis and priority conservation regions of the relict tree family Juglandaceae. J Biogeogr 47, 643-657 (2020).

RESEARCH



Dr Dieter Kressler

Analysis of eukaryotic ribosome biogenesis in Saccharomyces cerevisiae

Molecular midwives Escorting ribosomal proteins from birth to assembly

Ribosomes are the molecular machines that carry out the synthesis of all cellular proteins from mRNA templates. Eukaryotic 80S ribosomes are composed of two unequal subunits, a small 40S and a large 60S subunit, which contain a total of four different mature ribosomal RNAs (rRNAs) and ~80 ribosomal proteins (r-proteins). At first glance, the assembly of these rRNAs with the r-proteins may look like a rather trivial task – however, research carried out over the last 50 years, main-

ly with the yeast Saccharomyces cerevisiae, revealed that the biogenesis of eukaryotic ribosomes is a tremendously complex process. The act of building a

ribosome begins in the nucleolus, where the ribosomal DNA is transcribed into a long precursor rRNA (35S pre-rRNA in yeast), and involves the ordered assembly of the r-proteins with the pre-rRNA, which is concomitantly processed into the mature rRNA species. These assembly and processing events are not only tightly coordinated, but they occur within pre-ribosomal particles that travel, as maturation progresses, from the nucleus to the cytoplasm, where they are ultimately converted into translation-competent ribosomal subunits. Given

its gargantuan complexity, it is not surprising that this spatially and temporally controlled assembly process strictly depends on a multitude (>300) of mostly essential biogenesis factors. Despite the enormous recent progress, fuelled by ground-breaking advances in cryo-electron microscopy enabling the near-atomic visualization of pre-ribosomal particles, in understanding how this gigantic molecular jigsaw puzzle is pieced together, the precise role of many biogenesis factors and the molecular mechanisms

"Ribosomal protein homeostasis is of unanticipated complexity" driving ribosome assembly remain in many instances to be determined. Recent work from my laboratory has considerably contributed to the discovery and conceptual ap-

preciation of dedicated chaperones of r-proteins – these selectively protect, in many cases by already capturing their client in a co-translational manner, and promote the assembly of individual r-proteins. To pursue this avenue of research, our ongoing studies are aimed at the identification and functional characterization of novel dedicated chaperones. We expect that our research will help to better understand the aetiology of ribosomopathies, diseases frequently caused by alterations of r-proteins.



The path of r-proteins from their cytoplasmic synthesis to nuclear incorporation into pre-ribosomes. Simplified model highlighting the multifaceted roles of dedicated chaperones in promoting the fail-safe delivery of r-proteins. Nascent r-proteins can be captured by their dedicated chaperone in a co-translational manner. Importins enable the nuclear import of r-proteins either by binding directly to them or by interacting with their dedicated chaperone. Dedicated chaperones may also facilitate the transfer of the r-protein from the importin to the assembly site. To prevent a collapse of cellular proteostasis due to r-protein aggregation, excess r-proteins are targeted for proteasomal degradation by the E3 ubiquitin ligase Tom1.

Group Members





Alfonso



Sébastien Favre

Beniamin Pillet Méndez-Godoy

Selected publications

Martín Villanueva, S., Fernández Pevida, A., Fernández, J., Kressler, D. & de la Cruz, J. Ubiquitin release from eL 40 is required for cytoplasmic maturation and function of 60S ribosomal subunits in Saccharomyces cerevisiae. FEBS J 287, 345-360 (2020).

Martín-Villanueva. S., Fernández-Pevida, Kressler & de la Cruz. The Ubiquitin Moiety of Ubi1 Is Required for Productive Expression of Ribosomal Protein eL40 in Saccharomyces cerevisiae. Cells 8, 850 (2019).

Mitterer, V. et al. Conformational proofreading of distant 40S ribosomal subunit maturation events by a long-range communication mechanism. Nat Commun 10, 2754 (2019).

Pillet, B., Mitterer, V., Kressler, D. & Pertschy, B. Hold on to your friends: Dedicated chaperones of ribosomal proteins: Dedicated chaperones mediate the safe transfer of ribosomal proteins to their site of pre-ribosome incorporation. BioEssays 39, e201600153 (2017).

Rössler, I. et al. Tsr4 and Nap1, two novel members of the ribosomal protein chaperOME. Nucleic Acids Research 47, 6984-7002 (2019).



Dr Adria Leboeuf

Biochemical and evolutionary analysis of a social fluid exchange

Evolution of social behavior The power of a kiss: manipulation through social fluids

After just a few minutes of watching ants who have discovered something tasty in your kitchen, you may quickly observe a behavior that looks like two individuals kissing. Upon closer inspection, you might even see droplets of fluid pass from one insect to another. This behavior is called trophallaxis.

Trophallaxis is a nutritive fluid-exchange behavior and means of communication observed in ants, bees, wasps, termites, some nonsocial insects, and even in some birds and mammals. Amongst ants, some species engage in this behavior

and others do not. The most robust predictor of trophallactic behavior across ant phylogeny is whether the species' diet includes liquid food: either honeydew collected from aphids and similar plant pests or liquid collected directly from plants

" How do you make collective long-term decisions?" and to explore the evolutionary economics of collective invest-

Our research harnesses this fluid exchange to study the evolution of behavior, indirect genetic effects, evolutionary economics, manipulation and control. We use proteomics to explore these fluids passed between individuals and guantitative behavioral and developmental tracking to see how components of these fluids impact receivers. We look over the ant phylogeny at how this fluid has evolved and how its component proteins in a given species reflect the roles that trophallaxis plays in that species. Using big-data, fluorescence microscopy and computer vision, we mon-

> itor each individual in the colony, from a tiny larva to the queen, and observe how trophallactic fluid flows over the social network. We also use these tools to assess the function of transmitted molecules

through specialised structures called extrafloral nectaries. The fluid passed between ants during trophallaxis is rich with information beyond simply the food it contains. There are many components of trophallactic fluid produced by the ants, proteins, miRNA, nestmate recognition cues and growth hormones that enable complex communication and consensus building in ant colonies. Some of these growth-regulating components are under strong positive selection and influence larval development.

ment in care.

What began as food-for-protection mutualism between ants, plants and honeydew-producing insects has evolved into an important social behavior instrumental in ants' ecological dominance. The derived version of this behavior, seen in Formicine ants for example, creates a social circulatory system that enables within-colony cooperation and long-term collective decision making.



Ants sharing food and information through mouth-to-mouth exchange.

Group Members







Sanja Hakala

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Marie-Pierre Meurville





Amritansh Vats

Selected publications

LeBoeuf, A.C. Trophallaxis. Current Biology, 27 (24), 2017 10.1016/J.CUB.2017.10.047.

LeBoeuf, A.C., Waridel, P., Brent, C.S., Gonçalves, A.N., Menin, L., Ortiz, D., Koto, A., Soares Z.G., Riba-Grognuz, O., Privman, E., Miska, E.A., Benton, R. and Keller, L.* Oral transfer of chemical cues, growth proteins and hormones in social insects. eLife, 2016; 10.7554/eLife.20375 [OA].

LeBoeuf, A.C., Cohanim, A.B., Brent, C.S., Stoffel, C., Waridel, P., Privman, E., Keller, L. and Benton, R. Molecular evolution of juvenile hormone esterase-like proteins in a socially exchanged fluid. Scientific Reports 2018 10.1038/ s41598-018-36048-1 [OA].



Prof. Félix Mauch

Molecular basis of pathogen virulence

Plant immunity Molecular warfare in plants under microbial attack

The immune system of plants consists of a number of plasma membrane localized immune receptors that can recognize conserved pathogen derived molecules and as a response activate a multitude of immune reactions. The efficacy of the plant immune system forced pathogens to evolve counter strategies in form of effector molecules that are delivered as virulence factors into host cells. Their aim is to sabotage plant

immunity and create an environment suitable for pathogen invasion. In response host plants evolved a second class of cytoplasmic receptor proteins, known as disease resistance proteins, that can recognize the presence of virulence factors and trigger a strong immunity response. This results in an ongoing arms race in which pathogens continually

develop new virulence factors and host plants evolve new disease resistance proteins.

Our main focus in recent years was to better understand how pathogens exactly manage to undermine plant disease. We concentrate our efforts on virulence factors of the oomycete plant pathogen *Phytophthora*. Interestingly, we found virulence factors that interfere with secretion of antimicrobial resistance. The question we address is: What do virulence factors actually do in the plant cell at the molecular level? Proteins or cell-to-cell transport via plasmodesmata (see references). Two other virulence factors target plasma membrane micro domains (see figure) indicating an as of yet unrecognized role of these special mem-

"The hidden life of pathogen virulence factors" brane domains in plant immunity. Knowledge about the molecular targets of virulence factors can contribute to new strategies of plant protection. By applying a decoy strategy it may be possible to disarm individual virulence factors.

A second focus of the Mauch lab is antimicrobial proteins. We wonder whether antimicrobial

proteins from non-plant sources can be used as tools for plant protection. To this end these proteins are expressed in plants and their effect on disease resistance is tested. As an example: A lectin protein from the fungus *Coprinus* enhanced plant fresh weight and mediated broad range protection against nematodes, fungi and bacteria and may have potential for agricultural applications.



Confocal microscopy picture showing the localization of a GFP-tagged virulence factor (green) of *Phytophthora brassicae* to plasma membrane micro domains of a leaf cell. Chloroplasts are in yellow.

20 µm

Group Members





Fanny Louviot







Aboubakr Moradi

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Mohamed El-Shetehy

Katia Zbinden

Selected publications

Gamir, J. et al. The sterol-binding activity of PATHOGENESIS-RELATED PROTEIN 1 reveals the mode of action of an antimicrobial protein. Plant J 89, 502–509 (2017).

Tomczynska, I., Stumpe, M., Doan, T. G. & Mauch, F. A Phytophthora effector protein promotes symplastic cell to cell trafficking by physical interaction with plasmodesmata localised callose synthases. New Phytol 227, 1467–1478 (2020).

Tomczynska, I., Stumpe, M. & Mauch, F. A conserved RxLR effector interacts with host RABA-type GTPases to inhibit vesicle-mediated secretion of antimicrobial proteins. Plant J 95, 187–203 (2018).



Dr Laurent Mène-Saffrané

Plant nutrigenomics bioinformatics & analytics

Plant nutrigenomics and bioinformatics The biosynthesis of vitamin E and plant genomes

1) Vitamin E diversity in seed plants

Tocochromanols (tocopherols and tocotrienols) are organic compounds exhibiting vitamin E activity that is essential for animal reproduction. Meta-analysis studies have previously shown that several human populations, including some in developed countries, do not consume enough vitamin E and are chronically deficient. Tocochromanols are primarily produced by plants and among the different isomers produced by these organisms, α -tocopherol is by far the compound exhibiting the highest biological activity in animals. In collaboration with 20 botanical gardens located on the five continents, we

analyzed the seed tocochromanol composition of 1,001 different plant species. Our first results indicate that many unused edible seeds might be interesting alternatives to deliver high-quality vitamin E compounds to humans.

"Eating correctly is becoming more and more challenging"

and to search and localize mutations of interest. At its launching in June 2020, The Arabidopsis Mutant Exchange database encompassed more than 500,000 high-quality genetic variants. (534) with Phoenix Bioinformatics (https://www.phoenixbioinformatics. org), the organism in charge of maintaining the reference genome of this very popular plant model organism. Based on these data, the decision was made in July 2020 to produce a new version of the Arabidopsis reference genome (expected for 2021).

3) Correction of the Arabidopsis thaliana reference genome The analysis of genetic variants in numerous Arabidopsis genomes

> (see previous project) led to a significant finding globally affecting the Arabidopsis research community: we identified approximately 3,500 sequence errors (SNPs, insertions and deletions) in the current version of the Arabidopsis reference

2) The Arabidopsis Mutant Exchange database

We developed The Arabidopsis Mutant Exchange (TAME; www. arabidopsis.bio), the first public database of high-quality genetic variants (SNPs and Indel) induced by random mutagenesis of the plant genetic model Arabidopsis thaliana. This database is opened to the scientific community both to share their unused mutations identified by Next-Generation Sequencing, genome (TAIR10) that is used worldwide. These sequence errors notably change the amino acid sequences of 352 proteins (as of July 2020). These data have been shared with Phoenix Bioinformatics (https://www.phoenixbioinformatics.org), the organism in charge of maintaining the reference genome of this very popular plant model organism. Based on these data, the decision was made in July 2020 to produce a new version of the Arabidopsis reference genome (expected for 2021).

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Selected publications

Anand A, Chinchilla D, Tan C, Mène-Saffrané L, L'Haridon F, Weisskopf L. Contribution of hydrogen cyanide to the antagonistic activity of Pseudomonas strains against Phytophthora infestans. (2020). Microorganisms 28;8(8):E1144.

Sela A, Piskurewicz U, Megies C, Mène-Saffrané L, Finazzi G, Lopez-Molina L. Embryonic photosynthesis affects postgermination plant growth. (2020). Plant Physiology 182:2166-2181. doi: 10.1104/pp.20.00043.

Chinchilla D, Bruisson S, Meyer S, Zühlke D, Hirschfeld C, Joller C, L'Haridon F, Mène-Saffrané L, Riedel K, Weisskopf L. A sulfur-containing volatile emitted by potato-associated bacteria confers protection against late blight through direct anti-oomycete activity. (2019). Science Reports 30;9(1):18778. doi: 10.1038/s41598-019-55218-3.

Currie SE, Mène-Saffrané L, Fasel NJ. Valuable carcasses: postmortem preservation of fatty acid composition in heart tissue. (2019). Conservation Physiology 20;7(1):coz005.

Fasel NJ, McMillian K, Jakop U, Mène-Saffrané L, Engel KM, Genoud M, Müller K, Christe P. Modification of sperm fatty acid composition during epididymal maturation in bats. (2019). Reproduction 157(1):77-85.



Prof. Heinz Müller-Schärer

Ecology and evolution of plant antagonist interactions

Weeding with insects A beetle aginst allergies

Hardly any other plant is as allergenic as Ambrosia. But now there is a glimmer of hope – thanks to the accidentally introduced beetle Ophraella communa into Europe. Native to North America, it may have landed as a stowaway at the Milano Malpensa airport around 2013. From there it began to spread out in Northern Italy and Southern Switzerland.

Such intruders – a by-product of globalisation – are usually unwelcome; after all they often represent a threat to domestic fauna and flora. However, in this case it's different: the main

food source of both larvae and adults is common ragweed, Ambrosia artemisiifolia. Its highly allergenic pollen makes it one of the main triggers for hay fever and itchy eyes; it can also

lead to illnesses such as eczema or allergic asthma. In a recent interdisciplinary and international research programme, we could show that prior to the accidental arrival of the leaf beetle in 2013, some 13.5 million people suffered from ragweed-induced allergies in Europe, causing economic costs of approximately Euro 7.4 billion annually. This humble bug has the potential help to relieve more than 2 million sufferers of allergies in Europe while also saving more than Euro 1 billion in health costs annually, mainly by reducing ragweed pollen up to more than 80 percent. In view of improving predictions for future long-term benefits and risks of this potential biological control program, we recently initiated a novel experimental evolutionary approach to assess the beetle's potential to select for resistant/tolerant ragweed populations, as well as the beetle's potential for evolutionary adaptation to novel biotic (host plants) and abiotic (colder temperature for the yet unsuitable habitats in Central Europe, and considering climate change) conditions, using next generation sequencing and bioassay approaches. This is the first attempt to rigorously and simultaneously assessing the evolvability of a biological control

"The economic impact of invasive alien plants is so far highly underestimated" agent and its target weed.

Biological introductions provide excellent opportunities to study fundamental processes in ecology and evolution, such as adap-

tive responses to novel local biotic and abiotic conditions. Adaptation can occur rapidly after introductions likely from selection on the genetic variation available in introduced populations. This holds true for both pest species and introductions of potential biological control agents from the area of origin of the pest invader.



The ragweed leaf beetle Ophraella communa feeding on the invasive common ragweed Ambrosia artemisiifolia. All three larval stages and the adults feed on the plant, with up to four generations in Southern Switzerland and Northern Italy.

Group Members













Nilgün Saile

Antoine Pou







Selected publications

Augustinus, B. et al. Predicting impact of a biocontrol agent: integrating distribution modelling with climate-dependent vital rates. Ecological Applications, 30(1) (2020).

Müller Schärer, H. et al. How to better predict long-term benefits and risks in weed biocontrol: an evolutionary perspective. Current Opinion in Insect Science 38, 84-91 (2020).

Muller-Scharer, H. & Schaffner, U. Editorial overview: Biological control of plant invaders: a continued stimulus and yet untapped potential to link and advance applied and basic research. Current Opinion in Insect Science 38, v-viii (2020).

Sarah, B., Laurent, F. & Heinz, M.-S. Genome assembly of the ragweed leaf beetle: a step forward to better predict rapid evolution of a weed biocontrol agent to environmental novelties. Genome Biology and Evolution evaa102 (2020).

Schaffner, U. et al. Biological weed control to relieve millions from Ambrosia allergies in Europe. Nat Commun 11, 1745 (2020).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Dr Alessandro Puoti

Genetic networks regulating gamete sex determination in *Caenorhabditis elegans*

RNA and developmental biology How do germ cells choose their destiny?

Reproduction through gametes ensures genetic variability and is used in almost all eukaryotes. While spermatids and oocytes originate separately from male and female organisms, the hermaphroditic nematode *Caenorhabditis elegans* produces spermatids during larval development and oocytes as an adult. Consequently, gametes of both sexes originate from the same pool of precursor cells. A central question in our laboratory is how this decision is made at the molecular level.

Several lines of evidence indicate that the switch from spermatogenesis to oogenesis in *C. elegans* hermaphrodites is controlled through post-transcriptional mechanisms, comprising the stabilization or decay of specif-

"Big decisions in a small worm"

esis in their otherwise female body, but continue producing spermatids throughout their life. Intriguingly, *C. elegans mog* genes code for proteins that are homologous to pre-mRNA splicing factors in vertebrates and yeast. Consequently, some aspects of sex determination in worms could depend on the splicing of specific target mRNAs. Central questions include the identification of such target mRNAs, and their respective molecular roles. In this context, we study mRNAs that are deregulated in *mog* mutants and

the usage of splicing signals for alternative splicing.

Very convenient to maintain and with a reproductive cycle of only 3 days, *C. elegans* offers powerful genetic and molecular tools, the availability of numerous mutants, and if needed, the possibility to

ic mRNAs, the processing of pre-mRNAs, and of course the regulation of translational processes. Our laboratory focuses on the role of genes that have been identified through mutant screens for hermaphrodites that show abnormal gamete sex determination. For example, the *mog* genes are needed for the switch from spermatogenesis to oogenesis in the transition from the L4 larva to the young adult hermaphrodite.

As such, *mog* loss-of-function mutants never switch to oogen-

create mutants by genome editing. This tiny worm is therefore the ideal model to study fundamental questions about genetic pathways and their role in regulating sex determination of germ cells. Over the last years, we have identified several potential targets of *mog* genes and their molecular role in germline sex determination. The discovery of alternatively-spliced pre-mRNAs controlling the sexual fate of gametes in *C. elegans* opens an interesting parallel with the sex determination cascade in the fruit fly *Drosophila melanogaster*.

Group Members



Kim Charrotton



Christine Déforel

Maria Tarca



Zanetti, S., Meola, M., Bochud, A. & Puoti, A. Role of the C. elegans U2 snRNP protein MOG-2 in sex determination, meiosis, and splice site selection. Developmental Biology 354, 232–241 (2011).

Zanetti, S. & Puoti, A. Sex Determination in the Caenorhabditis elegans Germline. in Germ Cell Development in C. elegans (ed. Schedl, T.) vol. 757 41–69 (2013).

Zanetti, S. et al. The sperm-oocyte switch in the C. elegans hermaphrodite is controlled through steady-state levels of the fem-3 mRNA. RNA 18, 1385–1394 (2012).



Worms coming to life: Hatching of three C. elegans eggs over a 2-hour period (from left to right). The elongated 3-folded embryo moves inside the eggshell until it breaks and releases the L1 larva. (400 x magnification; differential interference contrast; scale bar, 50 µm)



Prof. Didier Reinhardt

How plants control their fungal and bacterial symbionts

How Cells invade Cells **Cellular programs required** for symbiosis of plants with microbes

with photosynthetic bacteria that evolved into chloroplasts. Subsequently, most plants have evolved the capacity to engage in symbiosis with various fungal and bacterial partners The second component, VAPYRIN (VPY), was studied at the levthat improve their nutrition and stress tolerance. A central question is how the plant selects the appropriate symbionts, and how it controls the establishment and maintenance of a beneficial interaction. These questions are central, because based on the colocalization with diagnostic marker genes (Ba-

the microbial symbionts are accommodated within the cells of the host, and get access to its resources, hence it is essential that the plant avoids to become exploited.

We have studied two central proteins required for the establishment of the arbuscular mycorrhizal (AM) symbiosis with

soil fungi. The first is a LysM receptor-like kinase in Petunia hybrida (PhLYK10) that is required for the recognition of AM fungal signals, the second is the VAPYRIN protein that is reguired for intracellular accommodation of bacterial and fungal symbionts in root cells. PhLYK10 was characterized based on its knockout phenotype, its binding characteristics to its ligands (symbiotic signals known as myc factors), and its ability to complement symbiosis in heterologous plant hosts (Girar-

"Symbioses are precisely controlled by an old genetic program in the plant host"

The success of plants began with the intracellular symbiosis din et al., 2019). Taken together, these experiments showed that LYK10 is a bona-fide receptor for recognition of AM fungal symbiosis signals.

> el of its cell biology. VPY localizes to small subcellular particles, known as VPY-bodies, which we characterized as endosomal compartments with post-Golgi/recycling endosome characteristics,

paume et al., 2019). VPY has earlier been found to be essential for symbiosis in petunia as well as in Medicago truncatula, hence, it is likely to represent a well conserved component in symbiosis. While plants that cannot engage in symbiosis have in general lost VPY, an orthologue (VPY-Like, VPYL)

was identified in the non-symbiotic moss Physcomitrella patens. This surprising finding suggests that VPY and/or VPYL must have non-symbiotic functions, at least in the moss. Indeed, knocking out VPYL, which is expressed at high levels in rhizoids (see Fig. 1), resulted in defects in branching patterns and cell division control (Rathgeb et al., 2020). Taken together, these findings shed light on the origin of the cellular and molecular pathways involved in the evolution of intracellular symbioses.



Image shows protonemal cell files of the moss Physcomitrella patens with a bud that represents the first stage of the shooty gametophores. A blue cell at the base of the bud is a rhizoid initial that shows the activity of the VPYL promoter driving the GUS reporter. (From Rathgeb et al. 2020)

Group Members





Nazli Dursun









Takoua Gritli

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Yukari Kuga







Martine Schorderet

Selected publications

Bapaume, L. et al. VAPYRIN Marks an Endosomal Trafficking Compartment Involved in Arbuscular Mycorrhizal Symbiosis. Front. Plant Sci. 10, 666 (2019).

Dursun, N. M., Nouri, E. & Reinhardt, D. The symbiosis of Medicago truncatula with arbuscular mycorrhizal fungi. in The Model Legume Medicago truncatula (ed. de Bruijn, F.) 471-484 (2020).

Girardin, A. et al. LCO Receptors Involved in Arbuscular Mycorrhiza Are Functional for Rhizobia Perception in Legumes. Current Biology 29, 4249-4259.e5 (2019).

Liu, G. et al. Strigolactones Play an Important Role in Shaping Exodermal Morphology via a KAI2-Dependent Pathway. iScience 17, 144-154 (2019).



Dr Rudolf Rohr

Theoretical ecology and evolution

Eco-Evolutionary dynamic How can co-evolution enhance biodiversity and ecosystem functioning?

Understanding biodiversity maintenance and how it relates to the ecosystem functioning is a key question in ecology. During the last years, we have been developing new theoretical approaches to understand coexistence in species-rich communities - the structural approach of coexistence - and to the relationship between biodiversity and ecosystem-functioning (BEF). These concepts have paved the way to a new integrative view of biodiversity and ecosystem-functioning. However, evolution has shown that it can act at short time scale. For

example, empirical data shows that changes in pollinator comaffect munity plant evolution

question is not only whether evolution can enhance biodiversity, but can we disentangle the scenarios leading to an enhancement from the ones leading to a degradation.

In a recent contribution, we study how eco-evolution impact population properties such as growth rates and biomass production. Contrary to the common belief that evolution climbs the fitness landscape and maximises growth rate or biomass production r-selection or K-selection paradigm – we argue that this is a particular case of evolutive selection. Such particular cases arise when

"Evolution can also act against the good of biodiversity."

after only eleven generations (Gervasi & Schiestl 2017). This pleads that one cannot fully understand biodiversity maintenance and ecosystem functioning without incorporating evolutionary aspects.

Our group aims at understanding how eco-evolutionary dynamics impacts biodiversity and ecosystem-functioning. For example, we study to what extent evolution could enhance biodiversity maintenance by relaxing coexistence constraints such as niche differentiation. It is important to realise that species coevolution can also lead to more constraint systems, which ultimately leads to evolutionary driven extinction; the so-called evolution murder or suicide. Therefore, the key

tally incompatible with emergence of polymorphism and ultimately of biodiversity through branching points. Although, we study ecology and evolution from a theoretical perspective, our research is also key in empirical applications such as conservation, argoecology, and invasion ecology. For example, evolution toward larger intrinsic growth rates has direct implications for conservation and invasion biology, positive for the conservation of rare species, but detrimental when considering invasive species. Similarly, evolution toward larger biomass has direct implications for a sustainable agroecology or for the long-term maintenance of harvested species.

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Group Members





Edgard Djahoui

Vasco Lepori

Selected publications

Godoy, O., Bartomeus, I., Rohr, R. P. & Saavedra, S. Towards the Integration of Niche and Network Theories. Trends in Ecology & Evolution 33, 287–300 (2018).

Parain, E. C., Rohr, R. P., Gray, S. M. & Bersier, L.-F. Increased Temperature Disrupts the Biodiversity– Ecosystem Functioning Relationship. The American Naturalist 193, 227–239 (2019).

Rohr, R. P. & Loeuille, N. Effects of evolution on niche displacement and emergent population properties, a discussion on optimality. http://biorxiv.org/lookup/doi/10.1101/2020.05.04.075994 (2020).

Saavedra, S. et al. A structural approach for understanding multispecies coexistence. Ecol Monogr 87, 470–486 (2017).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Prof. Roger Schneiter

Biogenesis of lipid droplets from specialized subdomains of the endoplasmic reticulum

Energy Homeostasis Giving birth to lipid droplets

Lipid droplets (LDs) constitute a widely conserved fat storage compartment that fulfill crucial roles in physiology and metabolism. Growing evidence implicates LDs in many cellular processes, including the endoplasmic reticulum (ER) stress response, protein degradation, membrane trafficking, and even the assembly of infectious viruses. Defects in LD function in hepatocytes, macrophages and adipocytes lead to pathological conditions, including hepatic steatosis, cardiovascular diseases and obesity. LDs are composed of a core of

neutral lipids, mainly triacylglycerols (TAG) and steryl esters, surrounded by a monolayer of phospholipids. The LD surface harbors many lipid metabolic enzymes including lipases and acyltransferases, and structural proteins, such as peril-

ipins (Pet10 in yeast). The biogenesis of LDs takes place in the ER membrane, where the enzymes that catalyze neutral lipid formation are located. Yeast expresses two TAG-synthesizing enzymes, Lro1 and Dga1, both convert diacylglycerol (DAG) to TAG and thereby promote LD formation in the ER. The resulting neutral lipids then accumulate within the ER bilayer, where they coalesce into lens-like structures, which grow in size, and eventually emerge as LDs. Whether these neutral lipid lenses

form randomly within the ER membrane, or at specific sites, however, remained to be defined.

In our recent study, we show that the biogenesis of LDs occurs at discrete ER subdomains defined by two membrane proteins, Fld1 and Nem1. Fld1 (seipin in human) localizes to ER-LD contact sites and fulfills a key function in LD biogenesis. Nem1, on the other hand, is part of a protein phosphatase complex that activates Pah1, a key enzyme for the production of DAG. Remarkably, Fld1

"Spatial and temporal ordering of complex events or Dga1, as well as ad-ditional factors that transforms chaos into life"

and Nem1 colocalize together at ER subdomains to recruit the TAG-synthases, Lro1 ditional factors that promote LD biogenesis. This highly localized formation of TAG is important, because in cells lacking either

Fld1 or Nem1, TAG synthesis occurs ectopically throughout the ER. Such ectopically formed LDs do not contain the complete set of LD proteins and hence are impaired in function. Based on these findings, we propose a model for a stepwise initiation of LD biogenesis and a spatially and temporally ordered recruitment of proteins and lipids to ensure a regulated biogenesis of functional LDs (Figure).



Model of LD biogenesis from specialized ER subdomains. Subdomains of the endoplasmic reticulum (ER) are first established by the colocalization of seipin (Fld1) and Nem1, an activator of diacylglycerol (DAG) production. These Fld1/ Nem1-sites then recruit additional factors such as Yft2 and Pex30 and they become enriched in DAG. Sites containing Fld1/Nem1/Yft2/Pex30 and DAG then recruit the neutral lipid synthesizing enzymes Lro1 and Dga1. These enzymes convert DAG into triacylglycerol (TAG) thereby promoting a highly localized biogenesis of lipid droplets (LDs). Newly formed LDs become stabilized by Pet10, a perilipin homolog and LD scaffolding factor, and recruit Erg6 and other bona fide LD proteins.

Group Members





Vineet Choudhary

Stéphanie Cottier







Aslihan Ekim

Ola El Atab

Elissa El Feghaly

Selected publications

Choudhary, V., El Atab, O., Mizzon, G., Prinz, W. A. & Schneiter, R. Seipin and Nem1 establish discrete ER subdomains to initiate yeast lipid droplet biogenesis. Journal of Cell Biology 219, e201910177 (2020).

Cottier, S., Darwiche, R., Meyenhofer, F., Debelyy, M. O. & Schneiter, R. The yeast cell wall protein Pry3 inhibits mating through highly conserved residues within the CAP domain. Biology Open 9, bio053470 (2020).

Dawoody Nejad, L. et al. Mitochondrial sphingosine-1phosphate lyase is essential for phosphatidylethanolamine synthesis and survival of Trypanosoma brucei. Sci Rep 10, 8268 (2020). RESEARCH



Prof. Daniele Silvestro

Computational methods and software to study evolutionary processes

Computational Evolutionary (Paleo)Biology Past, present and future of biodiversity

We share planet Earth with millions of species and this staggering biodiversity is facing unprecedented challenges in a rapidly changing Anthropocene world. Yet, living species represent a small fraction of all species that have ever existed throughout the long history of life on Earth, during which organisms have faced major climate change events and mass extinctions. We study the fossil record and molecular data, the most direct evidence of past biodiversity, to understand how organisms have evolved and adapted to changing environ-

ments and how present biodiversity patterns came to be.

We couple empirical data with mathematical modeling and artificial intelligence methods to test hypothesis

about the factors driving species richness and biodiversity loss through time and in space. These factors include climate change, competition for resources, contingencies. We seek to apply these models to quantify anthropogenic impacts on recent biodiversity loss and to predict future dynamics. Using these methods, we have recently shown that our ancestors, early hominins in East Africa, already had a detrimental effect on biodiversity long before the origin of Homo sapiens.

"We seek to understand the dynamics of past and ongoing extinctions"

Early anthropogenic impact on biodiversity likely drove several large carnivore species to extinction. We think this was driven by a process named kleptoparasitism, which is the practice of stealing newly killed prey from other predators, for example when a lion steals a kill made by a cheetah. Anthropogenic impact by early hominins could have led to the demise of large carnivores (such as saber-toothed cats) in East Africa, showing that the impact of our lineage on nature has been far greater and longer-lasting than previously thought.

> In collaboration with sociologists and archeologists, we also apply similar diversification models to study the evolution of another type of diversity: the diversity

of human cultures, which – like biological species – originate and go extinct over time. Through these analyses we discovered that the diversity of human cultures and technologies experience rapid diversification, competition and even mass extinctions, thus following similar dynamics to biological systems.



A Dinofelis saber-toothed cat eating (illustration by Mauricio Antón). Dinofelis has been considered a predator that human ancestors feared. But our research suggests that it was human ancestors that may have caused the eventual extinction of the species along with other major predators.

Group Members





Tobias Andermann

Rebecca Brown Cooper Torsten Hauffe





Bernard Koch

Quiyue Zhang

Selected publications

Faurby S, Silvestro D, Werdelin L, Antonelli A. Brain expansion in early hominins predicts carnivore extinctions in East Africa; 2019, Ecology Letters.

Pimiento C, Leprieur F, Silvestro D, Lefcheck J, Albouy C, Rasher D B, Davis M, Svenning J-C, Griffin J N. Functional diversity and the fate of marine megafauna in the Anthropocene; 2020 Science Advances.

Silvestro D, Castiglione, S; Mondanaro A, Serio C, Melchionna M, Piras P, Di Febbraro M, Carotenuto F, Rook L, Raia P. A 450 million years long latitudinal gradient in age-dependent extinction; 2019 Ecology Letters.

Gjesfjeld E, SILVESTRO D, Chang J, Koch B, Foster J G, Alfaro M E. A quanti- tative workflow for modeling diversification in material culture; 2020 PLOS ONE.



Prof. Simon Sprecher

Cellular, molecular and functional neurogenetics

Genetics and neurodegeneration Understanding the brain: Deciphering its normal functions towards neurodegenerative diseases

One of largest mysteries remains how our brain actually works and what goes wrong in an aging brain or neurodegenerative diseases. While science makes continuous progress in understanding the complexity of the brain, much remains unknown. In particular with more than hundred billion neurons and a trillions of synaptic connections the human brain will remain unresolvable for decades despite rapid technical advances.

Since the molecular and genetics nature of all nervous systems are shared among all animals the only way of understanding how the brain works is studying animal

" Looking at small brains allows us to understand how the brain works "

models with less complicated brains. In our laboratory we use diverse, impacting genetic model systems to understand the brain.

Resolving the brain at single-cell resolution

The nervous system is without any doubt the most complex organ. How is such a complicated organ with thousands of highly interconnected cell types formed? How do cells know what how they fit into this complex puzzle? We study the genetic and molecular mechanisms that control the fate of neurons. Using single-cell transcriptomics in combination with powerful molecular genetic techniques we decipher the processes that allow neurons to diversify and how neural networks are able to function in the way they do.

Forgetting: humanizing flies to understand Alzheimers disease

While some memories are kept for years other memories are rapidly forgotten. However forgetting is not a passive, random process but underlies tightly controlled molecular machinery. Neurodegenerative

diseases such as Alzheimers disease cause problems with the formation of memories or enhance the forgetting process. Studying the memory center of the fruit fly allows us to unveil these mechanisms. We therefore used CRISPR/Cas9 to convert the flies Alzheimer Precursor Protein gene to the hereditary mutations of human Alzheimer Precursor Proteins, allowing us to study the molecular and genetic processes of this disease.







Group Members







Brunet Lucia De An







5

Abhishek Mishra

neglia Marta Sprecher

Selected publications

Brunet Avalos, C., Maier, G. L., Bruggmann, R. & Sprecher, S. G. Single cell transcriptome atlas of the Drosophila larval brain. eLife 8, e50354 (2019).

Fritsch, C. et al. Multilevel regulation of the glass locus during Drosophila eye development. PLoS Genet 15, e1008269 (2019).

Humberg, T.-H. et al. Dedicated photoreceptor pathways in Drosophila larvae mediate navigation by processing either spatial or temporal cues. Nat Commun 9, 1260 (2018).

Qin, B. et al. Muscarinic acetylcholine receptor signaling generates OFF selectivity in a simple visual circuit. Nat Commun 10, 4093 (2019).

Widmer, Y. F. et al. Multiple neurons encode CrebB dependent appetitive long-term memory in the mushroom body circuit. eLife 7, e39196 (2018).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Prof. Stefano Vanni

Molecular biophysics of cellular membranes

Membrane biophysics How do cells look like, atom by atom ?

In our group, we use computer simulations to understand the inner workings of cells down to molecule-by-molecule and atom-by-atom detail. Traditionally, biologists have been studying how cells work and behave in living organisms - in vivo - and in their lab tubes - in vitro - but many features are too complex and too small to

understand in this way.

To overcome this limitation and understand complex biological problems with atomistic-level resolution, we develop new computational approaches to study biological systems in silico, and we combine these investigations with biochemical and biophysical approaches. Our main methodology is called molecular dynamics (MD) simulations. "We investigate living matter by studying the jiggling and wiggling of atoms"

use Feynman words, we investigate living matter by studying the "the jiggling and wiggling of atoms".

Currently, the main focus of the lab is to understand how specific lipids and membrane properties influence intracellular traffick-

ing processes and fat storage in eukaryotic cells. In fact, cellular membranes are continually remodelled to achieve communication between intracellular compartments and to selectively exchange materials between them.

The energetics of these remodelling processes are governed by the interplay between specialized proteins and membrane properties, but in most cases, we still lack a detailed molecular

Using this approach, we can describe molecular systems in the range of 1-100 nanometers with atom-level accuracy. To

explanation of how these processes are controlled. Our goal is to understand these processes, and specifically how lipid sensors, transporters, and lipid remodelling enzymes maintain lipid homeostasis in the cell.



Molecular representation of the Berardinelli-Seip Congenital Lipodystrophy 2 protein complex embedded in a lipid bilayer.

Group Members





Laura Berstis

Pablo Campomanes Emanuele Petretto



Ardham



Janak Prabhu

Sriraksha Srinivasan







Selected publications

Campomanes, P., Zoni, V. & Vanni, S. Local accumulation of diacylglycerol alters membrane properties nonlinearly due to its transbilayer activity. Commun Chem 2, 72 (2019).

Jiménez-Rojo, N. et al. Conserved function of ether lipids and sphingolipids in the early secretory pathway (2019).

Zoni, V. et al. Lipid droplet biogenesis is driven by liquidliquid phase separation (2019).

RESEARCH





Evolution and Conservation Tracking species through space and time

Nature is change. On short time-scales, species and populations change in their numbers and distributions, while on larger time-scales they evolve, diverge and sometimes die out. We develop and use modern computational and statistical methods to quantify, characterize, and ultimately understand these changes across all time-scales. Using such methods, we recently shed light on the ongoing hybridization between poplar species in Europe, or showed that olive trees were initially domesticated in the eastern part of the Mediterranean, from where they were brought to the west and crossed with local wild olives (oleasters) to form the famous varieties now grown in Spain and Italy.

Increasingly, we also focus on characterizing population size

One way by which we do so is by characterizing evolutionary

histories from DNA samples. The basic idea is simple: genetic data is informative about genealogical relationships. We all have two parents, eights grandparents and more than a thousand ancestors 10 generations

ago. The more recent ancestors two individuals share, the more genetically similar they are. Siblings, for instance, share half of their DNA, cousins about one eights.

Our goal is to link patterns of relationships to evolutionary histories. Two randomly drawn samples from a large population, for instance, should not be closely related, but they might easily turn out to be cousins if sampled from a small population. But if done right, relationships tell us much more: they are informative about population size changes, migration between and mixing of past populations.

"Nature is inherently dynamic, at all levels"

changes on ecological time-scales. Our work is motivated by the need for cost-effective tools for conservation management in remote regions

such as the Chinko Nature Reserve in the Central African Republic, to which we contribute with ongoing biodiversity monitoring. Using long-term population data from this region, we could for instance show that an illegal influx of transhumant pastoralists led to a crash in the local populations of apex predators such as lions, leopards or wild dogs. However, we could also show that these species rebounded after the management increased its effort to keep pastoralists and their cattle out of the park.



A picture of a leopard (Panthera pardus) taken by one of our camera traps in the Chinko Nature Reserve in the Central African Republic.

Group Members





Madleina Caduff



Thierry Aebischer



Sadoune Ait-Kaci





Zuzana Hofmanova









Liam Singer



Selected publications

Aebischer, T. et al. Apex predators decline after an influx of pastoralists in former Central African Republic hunting zones. Biological Conservation 241, 108326 (2020).

Bresadola, L. et al. Admixture mapping in interspecific Populus hybrids identifies classes of genomic architectures for phytochemical, morphological and growth traits. New Phytol 223, 2076–2089 (2019).

Burger et al. Low prevalence of lactase persistence in bronze age Europe indicates ongoing strong selection over the last 3,000 years. Curr.Biol. 30(21), 4307-4315 (2020).

UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY

RESEARCH



Prof. Laure Weisskopf

Microbial volatiles as mediators of plant health

Plant Microbiome The Power of the Small

Like the human skin, plant roots and leaves are densely colonized by diverse communities of bacteria and other microbes. We now know that these plant-colonizing bacteria are involved in protecting their host against environmental stress, as well as against diseases caused by phytopathogenic organisms. Our main interest lies in understanding the mechanisms underlying such microbiome-mediated protection against plant pathogens. We focus specifically on the property of

plant-associated bacteria to emit volatile organic compounds with a wide range of biological activities on the plant and the

disease-causing agents threatening plant health.

These "bacterial smells" – some of which we would not chose as our preferred perfume... – have been shown to stimulate plant immunity, to promote root growth, as well as to inhibit the development of various plant pathogens. In particular, our group has shown that these bacterial metabolites can protect plant health against a range of devastating diseases including potato late blight, which caused the Great Famine in Ireland in the middle of the 19th century. We therefore consider these volatiles and the bacteria emitting them as promising source of natural weapons that could be used to fight such diseases in an environmentally friendly way. Using state-of-the-art methods in analytical chemistry, phytopathology and molecular biology, we are deciphering the chemical nature and biological functions of volatile organic compounds emitted by a wide range of plant-associated bacteria.

"Don't trust your nose!"

We mainly work on Pseudomonas, Bacillus and Actinobacteria strains, which have been previously

isolated from plants of agronomical relevance such as grapevine or potato. Our work follows basic research lines to understand the modes of action of bacterial volatiles on the plant pathogens and to identify the genetic determinants underlying the emission of plant-protecting volatiles by bacteria. In addition, we also pursue more applied projects, in which we investigate the potential of microbiome isolates and of their emitted volatiles to protect crops against important diseases like potato late blight or grapevine downy mildew. Our research aims at discovering new strains and active molecules to be used as alternative to synthetic fungicides, thereby contributing to preserve environmental and human health.



This picture illustrates the power of bacterial volatiles, using a simple split Petri dish system allowing only air-borne signals to be exchanged between the two interacting organisms: the pathogen Phytophthora infestans (grown in the upper side of the Petri dish) is restricted in its growth when exposed to the volatiles of Pseudomonas bacteria isolated from the plant microbiome (lower side of the Petri dish, right picture).

Group Members





Sébastien Bruisson

Abou Mansour

Eliane





Delphine Chinchilla

Mout de Vrieze Floriane L'Haridon





Abhishek Anand



Vivien Pichon

Alexander Wenger

Monica Zufferey

Selected publications

Bruisson, S. et al. Endophytes and Epiphytes From the Grapevine Leaf Microbiome as Potential Biocontrol Agents Against Phytopathogens. Front. Microbiol. 10, 2726 (2019).

Chinchilla, D. et al. A sulfur-containing volatile emitted by potato-associated bacteria confers protection against late blight through direct anti-oomycete activity. Sci Rep 9, 18778 (2019).

De Vrieze, M. et al. Linking Comparative Genomics of Nine Potato-Associated Pseudomonas Isolates With Their Differing Biocontrol Potential Against Late Blight. Front. Microbiol. 11, 857 (2020).

Joller, C. et al. S-methyl Methanethiosulfonate: Promising Late Blight Inhibitor or Broad Range Toxin? Pathogens 9, 496 (2020).



Dr Chantal Wicky

Chromatin function in C. elegans development

Chromatin function Defining the appropriate gene repertoire for a perfect genome music

Chromatin is defined as a complex of DNA and proteins and it is in this form that our genome is packed in the nucleus of a cell. Proteins associated with the genome are responsible for packaging the DNA in the nucleus, organizing the nuclear architecture and regulating the transcription of genes in response to various cellular and extracellular signals.

Several studies revealed the importance of chromatin in nor-

mal processes such as the development of an organism from the zygote to the adulthood. However, aberrant chromatin structures are also associated with diseases such as cancer. To investigate the function of chromatin during development, our lab is using the model organism

Caenorhabditis elegans. Most of the chromatin factors are conserved in this one-millimeter long worm, which allows us to study the function of chromatin at the molecular level in a living organism with the potential to learn how chromatin works in human.

Using genetic tools, our research uncovered chromatin factors that are key regulators of the postembryonic development of the worm. Without the activity of these factors, cells in the body that give rise to adult structures, such as the egg lying organ, do not divide and differentiate. As a consequence, worms do not grow to adulthood and do not reproduce. When we inspected the genes that are deregulated in the absence of these chromatin factors, we found that the wrong repertoire of genes was expressed. It was the set of genes that is required for the production of gametes (oocytes and sperm).

The results that we obtained, allowed us to learn which gene

"The potential to learn how chromatin works in human"

repertoire is needed for post-embryonic development and which one is required for the production of gametes and how these two are regulated by chromatin. Altogether we propose that the chromatin factors are necessary to

correctly interpret the score written by the genome so that the music of development is perfect.

Our lab is also involved in various outreach activities under the name of "Lab2rue". Financed by "Les Académies Suisses des Sciences", we developed workshops to teach genetics at schools with lab experiments. Along the same line we are also trying to introduce in schools, experiments using the model organism *C. elegans* under the name of "Apprendre avec elegans" with the aim to explain fundamental biological processes, such as reproduction using a living organism.



C. elegans germline nuclei where homologous chromosomes are undergoing pairing. DNA appears in blue, the chromatin protein LSL-1 in red. Homologous chromosomes are held together by synaptonemal complex proteins (HTP-3 in green). (Image by David Rodriguez Crespo).

Group Members



Shweta Rajopadhye

Selected publications

Erdelyi, P., Wang, X., Suleski, M. & Wicky, C. A Network of Chromatin Factors Is Regulating the Transition to Postembryonic Development in Caenorhabditis elegans. G3 7, 343-353 (2017).

Saudenova, M. & Wicky, C. The Chromatin Remodeler LET-418/Mi2 is Required Cell Non-Autonomously for the Post-Embryonic Development of Caenorhabditis elegans. JDB 7, 1 (2018).

The year 2020 was marked by distance learning.

The teaching was mainly held at a distance in 2020, but some courses with limited numbers of students, such as practical works, could be held in person, to the delight of our students and professors.



Camille Thiébaud Bachelor in Biology Switzerland

J'ai décidé d'étudier la biologie pour différentes raisons. D'abord, durant mes études au gymnase, mon enseignant m'a énormément inspiré. De plus, je suis persuadée que la biologie puisse être une solution au problème écologique. À mon avis, les plantes sont notre avenir. Nous devons les connaitre et les étudier afin de sauver notre société. Ensuite, j'ai décidé d'étudier cette branche à l'université de Fribourg, car elle offre de la proximité dans tous les sens du terme.

Mes études dans ce département m'ont offert beaucoup d'opportunités: une connaissance étendue dans plusieurs domaines de la biologie, un stage en laboratoire de la durée d'un semestre, un rôle actif au sein du comité des élèves et des contacts privilégiés avec certain.e.s enseignant.e.s. Ce qui est du futur n'est pas encore défini. Ce cursus ouvre plusieurs portes: la voie de la recherche, du travail en industrie mais également la voie de l'enseignement dans le secondaire II. Cela reste très ouvert.



Rares Cristea Master in Bioinformatics & Computational Biology Romania

I'm in love with the natural world, and am passionate about preserving ecosystems, as well as studying what make them tick. Although I have an ecologist soul, I chose a Masters in Bioinformatics and Computational Biology in order to have a more comprehensive view of bio-statistical analysis, DNA data management, and even of image processing. These are skills that are, in my opinion, essential for more fine-scale approaches in the emerging studies of today. To my knowledge, the University of Fribourg is one of the only ones that give such a broad overview of bioinformaticians skills. Plus, the size of the Biology department makes it very easy to interact with fellow students, and with our friendly professors, who are always keen on helping when one asks ! This networking ease has brought not only good internship opportunities, but also friends, and a sense of belonging to the academic community, without which I wouldn't be so motivated today.



Dotun Adeleye Adeyinka PhD in Biology Nigeria

I chose to study biology because I wanted to explore "living things". During my Master's degree in Microbiology, I stumbled on an article on "Neural stem cell states", a completely different research field. This captivated me and I became curious. I decided to learn more about the subject in the context of neuro and developmental biology and Dr. Boris Egger gave me this opportunity.

This Doctoral journey has availed me the opportunity to learn, develop and integrate into a multi-disciplinary research system that allows students to function "independently" with maximum guidance and support. My communicative and presentation skills, competence level in analytical techniques and research methodological skills have greatly improved. I am lucky to be trained and mentored by two great researchers, Dr Boris Egger and Prof. Simon Sprecher.

For the future, I would like to still be in academia and also be involved in science communication.



The Department of Biology is continually adapting its academic offerings to meet current needs.

New Masters launched in 2021

As of Fall 2021, the Department of Biology will replace its Master in Biology by two new Master's programmes: the MSc in Molecular Life and Health Sciences (5 options), and the MSc in Environmental Biology (4 options). The very successful joint BeFri MSc in Bioinformatics and Computational Biology completes our offer to students who wish to deepen their knowledge and enthusiasm.

With this initiative, the Department aims to strengthen and provide more visibility to its core research areas. Both programs are a continuation of master specializations established in 2017, which were very well received by the students and led to a twofold increase in student numbers in 2018. The two new programs will address current challenges in molecular life and environmental sciences and will teach state-of-the-art approaches. The master program Molecular Life and Health Sciences will focus on basic molecular mechanisms and cell biological processes related to human health. The program Environmental Biology will center on plant health and applied and evolutionary ecology, both aimed at tackling the world's environmental challenges.



We are also a training Department

Each year, we hire two new apprentices as "CFC" laboratory technicians in biology. Under the guidance of Julien Comelli, chief laboratory technician, their main tasks are to prepare the practical work and the related exams for the Faculty of Sciences and Medicine second year students (medical, biology, biochemistry, chemistry and biomedical students). It allows them to learn in details the main aspects of laboratory clinical chemistry such as glucose, blood or cholesterol to just name a few.

Fribourg Graduate School of Life Sciences

The Fribourg Graduate School of Life Sciences (FGLS) offers a coordinated doctoral training program for PhD students in the Life Sciences. The program offers a wide variety of courses to the PhD students, ensures regular thesis committee meetings, supports the PhD students in scientific and personal matters and offers mentoring and counseling. The FGLS students also self-organize a number of activities for the doctoral students, including a retreat and different workshops, etc. FGLS still evolves and will become FGLM, a collaboration between the Departments of Biology and Medicine, in 2021.



UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY

News & Events

Prizes & Grants





SINERGIA projects awarded in the Department

Sinergia is a program of the Swiss National Science Fund that supports ambitious collaborative projects between two to four groups in Switzerland and abroad, on breakthrough research. Obtaining Sinergia funding is remarkable because the competition is high, and interdisciplinary collaborations are often challenging to set up. 2 successful DepBioL **professors, Jörn Dengjel and Stefano Vanni** have been selected among the tough competition and will be granted funding for their research.

Vigener Prize for best PhD Thesis

The Vigener Prize, instituted in 1908 after a donation from Joseph Vigener. honours doctoral work standing out by their excellence. We are very proud to announce that one of our students. Vivian Link. has won the Vigener Prize for the best PhD thesis in theoretical sciences. Dr Vivian Link, under the direction of **Prof. Daniel Wegmann**, wrote her PhD thesis on "Statistical inference of genetic diversity: computational tools for low-depth and ancient sequencing data". During her PhD, Vivian was interested in gaining information from noisy data, and most of her projects dealt with ancient, prehistoric DNA. She explains that "the DNA fragments extracted from ancient bones are very damaged, and it is difficult to reconstruct the original DNA sequence". Therefore, Vivian developed a program that corrects for errors that degradation introduced in the ancient DNA, called "ATLAS" (Analysis Tools for Lowdepth and Ancient Sequences).

(*) TAS mania

Research

TASmania, A new bacterial Toxin-Antitoxin Systems database

In the framework of a successful Sinergia collaboration funded by the SNSF on studying toxins and antitoxins in bacteria, the group of Dr Laurent Falquet published an important article describing TASmania, a new database. Their results validated six out of eleven studied putative new TAS (Toxin-Antitoxin Systems) of Mycobacterium tuberculosis tested in vivo at Prof. Genevaux lab in Toulouse. Mycobacterium tuberculosis is the causative agent of tuberculosis. Understanding TAS is a crucial issue in the fight against antibiotic resistance.



A beetle against allergies

Hardly any other plant is as allergenic as Ambrosia. But now there is a glimmer of hope – thanks to an accidentally introduced beetle, *Ophraella communa*. A study, in which the DepBioL was a participant, has shown that a natural enemy of the weed can relieve more than two million European allergy sufferers of their symptoms. The scope of the study also included a calculation of the consequences of the increasing spread of *Ambrosia* for health costs – with and without the effect of the beetle. This part of the study was initiated and directed by **Prof.** *Heinz Müller-Schärer*. He says: "we were able to show that the economic effects of Ambrosia had until now been vastly underestimated." According to Müller-Schärer, the invasive plant causes immense costs to the whole European economy, namely 7.4 billion euros annually, but thanks to Ophraella, this is going to change: "Our calculations show that the costs may well go down by 1.1 billion euros per year." The faster the beetle spreads, the greater the effect."

Reducing pesticide use with nanoparticles

One of the biggest challenges facing agriculture today is the extensive use of fertilizers and pesticides. There is an urgent need for sustainable protection of crop plants. With this in mind, NCCR Bio-Inspired Materials (AMI) and Department of Biology in Fribourg aimed to create an environmentally safe nano-agrochemical for the targeted delivery of silicic acid and to stimulate plant defense. They synthesized silica nanoparticles with similar properties to those found in plants. To test their efficiency, they applied the nanoparticles on Arabidopsis thaliana (thale cress), a widely used plant model, infected with the bacterial pest Pseudomonas syringae, another model organism.

DEPARTMENT SEMINARS

SPECIAL EVENTS

2019

17.01	REPP-SO Winter Meeting
05.04	BEFRI Research Colloquium
09-10.05	BEFRI Research Retreat
22.06	FGLS Retreat
05.09	Chronobiology Meeting
09-10.09	The Temporal Dynamics of Evolution
11.09	Metabolomics Platform Inauguration
12.09	Swiss Society for Phytopathology Meeting
13.09	LS2 Autophagy Workshop
13.09	Getting Started - Welcome for new students
25.10	BEFRI Genomics Day
20& 27.11	InfoDays
00.11	Recheler 9 Meeter Evening

28.11 Bachelor & Master Evening

2019

- 26.02 The Evolution of Developmental Regulation in Spiders and Flies: Diversification of Body Plans and Body Parts, A.P. Mc Gregor, Oxford Brookes University
- 12.03 The Retromer complex, much more than just endosomal recycling, F. Steinberg, University of Freiburg , Germany
- 16.04 Unravelling non-native species ecology to inform people and policy, Prof. Helen Roy, Center for Ecology and Hydrology, NERC
- 07.05 Mapping the human mitochondrial proteome in multiple dimensions, B. Warschied, University of Fribourg, Germany
- 14.05 Host-controlled intracellular entry and passage of symbiotic bacteria, T. Ott, TU Munich
- 21.05 Deciphering the volatile vocabulary in plant-microbe interactions the smell of fungi, J-P. Schnitzler, Helmoltz Zentrum Munich
- 28.05 Mitochondrial mutational spectrum differs between fast and slow dividing cells providing a functional marker of longevity, K. Popadin, University of Lausanne
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