



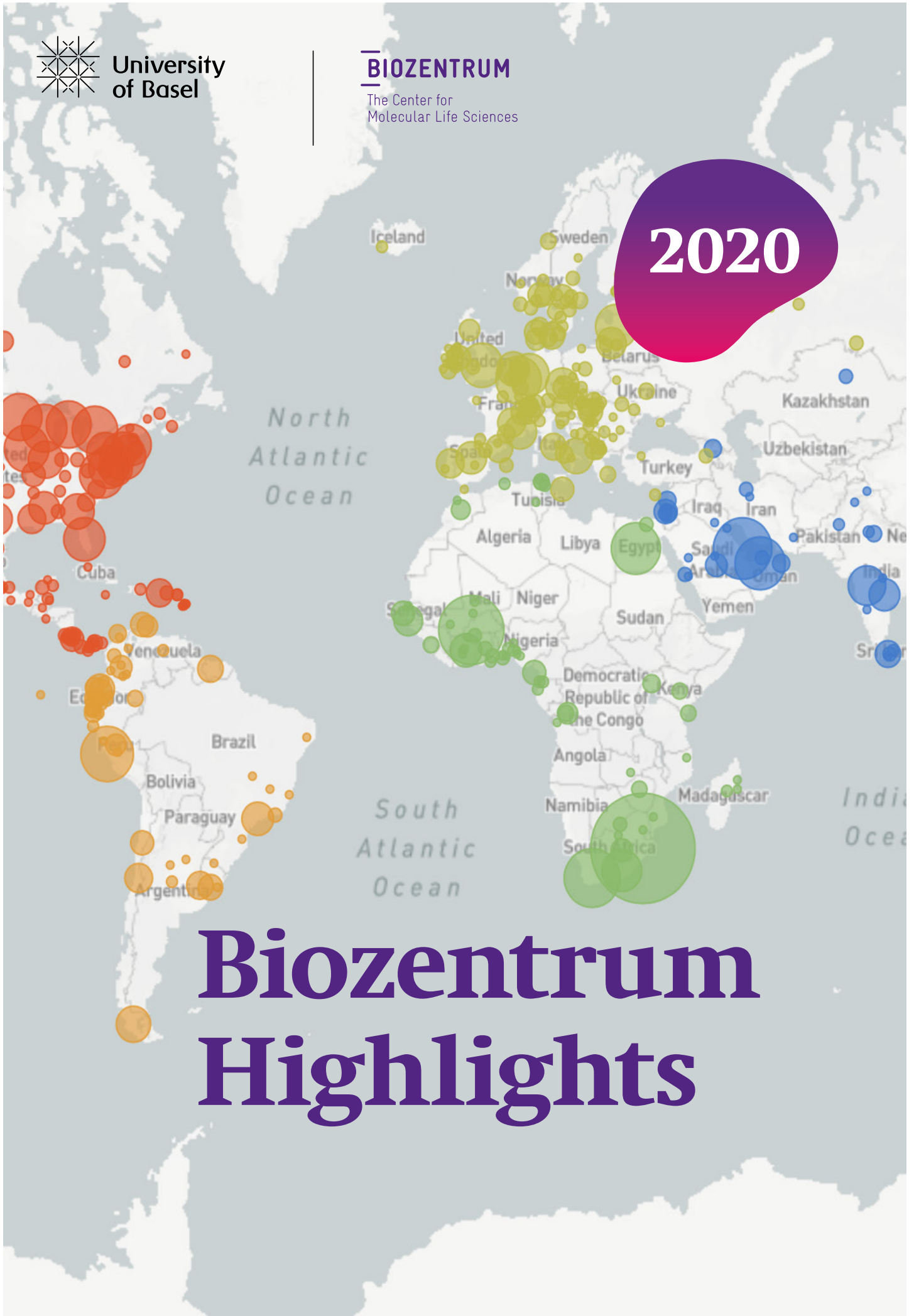
University
of Basel

BIOZENTRUM

The Center for
Molecular Life Sciences

2020

Biozentrum Highlights





Prof. Alex Schier,
Director of the Biozentrum,
University of Basel.

Dear readers

At the end of December I accompanied 102-year old Susan Mango Sr. to the Messehalle in Basel, where she was vaccinated against SARS-CoV-2. Susan was born during the 1918 flu pandemic. Her grandfather died but she survived.

Seeing Susan receive the SARS-CoV-2 vaccine was a jubilant end to a roller coaster year and a reminder how we as scientists can make the world a better place. In 1918 no one knew of the DNA double helix, restriction enzymes or B cells; no one could imagine injecting mRNA as a vaccine. But now, 102 years later, science is putting our lives back on track.

It was our predecessors in Basel – Friedrich Miescher, Werner Arber, Georges Koehler and many others – who helped lay the scientific foundations on which the SARS-CoV-2 vaccine was built. With little awareness of their long-term impact, these scientists were driven by the desire to solve intellectual puzzles and find out how the world works.

Our predecessors' discoveries remind us that our own curiosity-driven research can improve the world, even as we struggle with difficult experiments and uninterpretable results, or are frustrated by inequalities, uncertainty, hype and bureaucracy. While some of our research, such as *Nextstrain*, a web tool to track the spread of pathogens in real-time (see page 12), has immediate practical impact, most of us Biocentrics will not diagnose, track, prevent or cure diseases today or tomorrow. But as we solve fundamental puzzles with creativity, passion, curiosity, ambition and rigor, we build the foundation for a better world.

102 years from now someone might read this issue of Biozentrum Highlights and recognize the seeds of discoveries that would one day contribute to the betterment of humanity. In the meantime, with a new era dawning, let us intensify our efforts to do great science. To paraphrase T. Roosevelt (Sorbonne 1910): *Let us spend ourselves in a worthy cause and know the triumph of high achievement, and if we fail, at least fail while daring greatly, so that our place shall never be with those cold and timid souls who know neither victory nor defeat.*

A handwritten signature in black ink, appearing to be 'A. Schier'.

Prof. Dr. Alex Schier
Director of the Biozentrum, University of Basel

2020 at a glance.



Prof. Michael N. Hall has been awarded the Sjöberg Prize 2020 of the Royal Swedish Academy of Sciences and the BBVA Foundation Frontiers of Knowledge Award.

The Biozentrum is part of two BRCCH Multi-Investigator Projects

The research groups of Prof. Médéric Diard and Prof. Dirk Bumann are participating in two of four Multi-Investigator Projects which have been launched for the first time by the Botnar Research Centre for Child Health (BRCCH). Both projects are funded with a total of 8 million Swiss francs for the next four years. The researchers led by Médéric Diard are contributing to the project "Precision Microbiota Engineering for Child Health", Dirk Bumann's team is part of the project "Living Microbial Diagnostics to Enable Individualized Child Health Interventions". The BRCCH in Basel was co-founded by the University of Basel and the ETH Zurich in 2018. The Centre is funded by a contribution of 100 million Swiss francs from the Fondation Botnar.



Kiss and run: How cells sort and recycle their components

Recycling, the reuse of material, saves energy and resources. In the cells, tiny organelles, so-called endosomes, separate the delivered cellular material into reusable material and waste. However, how exactly the endosomes sort the material remains an enigma. The team led by Prof. Anne Spang has now discovered that a cellular machine, called "FERARI", is a key player in this process. By coordinating both the fusion of the endosome with the recycling vesicle (kiss) as well as the pinching off of the recycling vesicle after it has been loaded with the cargo (run), FERARI distributes the recyclable molecules, mainly transport proteins and receptors, and reintroduces them into the cellular cycle. In this way, valuable cell components do not have to be constantly produced anew, which not only saves energy but also time.

Solinger et al., *Nature Cell Biology*



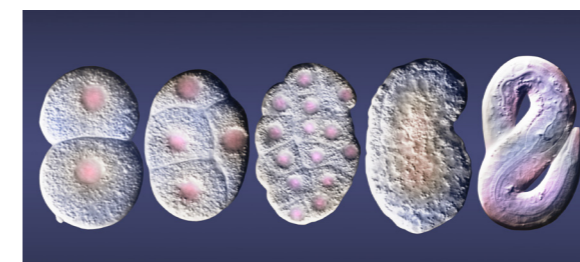
Awards for Biozentrum junior researchers

In the past year, the achievements of many young scientists at the Biozentrum have been recognized in the form of fellowships and research grants. Creating an ideal environment for research as well as supporting young scientists in all aspects is a long-standing priority at the Biozentrum. This year three postdocs received a Marie Skłodowska-Curie Individual Fellowship and three PhD students have been supported by the Boehringer Ingelheim Fond. Four scientists have each received an EMBO Post-doctoral Fellowship or a SNSF SPARK Grant and also the Prize of the Faculty of Science went this year to a PhD student of the Biozentrum for her outstanding thesis. All awards are listed at the end of the brochure.

Nanocontainers introduced into the nucleus of living cells

A challenge in the field of nanomedicine is to develop a reliable method of introducing active substances specifically into the cell nucleus. An interdisciplinary team from the University of Basel, including Prof. Rod Lim's group, has succeeded in creating a direct path for artificial nanocontainers to enter into the nucleus of living cells. To this end, they produced biocompatible vesicles that can pass through the pores in the nuclear membrane. In this way, it might be possible to transport drugs directly into the cell's control center.

Zelmer et al., *PNAS*



GPS for chromosomes: Reorganization of the genome during development

The spatial arrangement of genetic material within the cell nucleus plays an important role in the development of an organism. In collaboration with scientists from Harvard University, Prof. Susan Mango's team has developed a method to trace the chromosomes in individual cells. Using this method, they have now been able to demonstrate that chromosomes reorganize during embryonic development. This reorganization accompanies cell maturation and represents a milestone in the development of a complex organism. The correct chromosomal architecture is crucial to prevent developmental disorders.

Sawh et al., *Molecular Cell*

NATIONAL ACADEMY OF SCIENCES



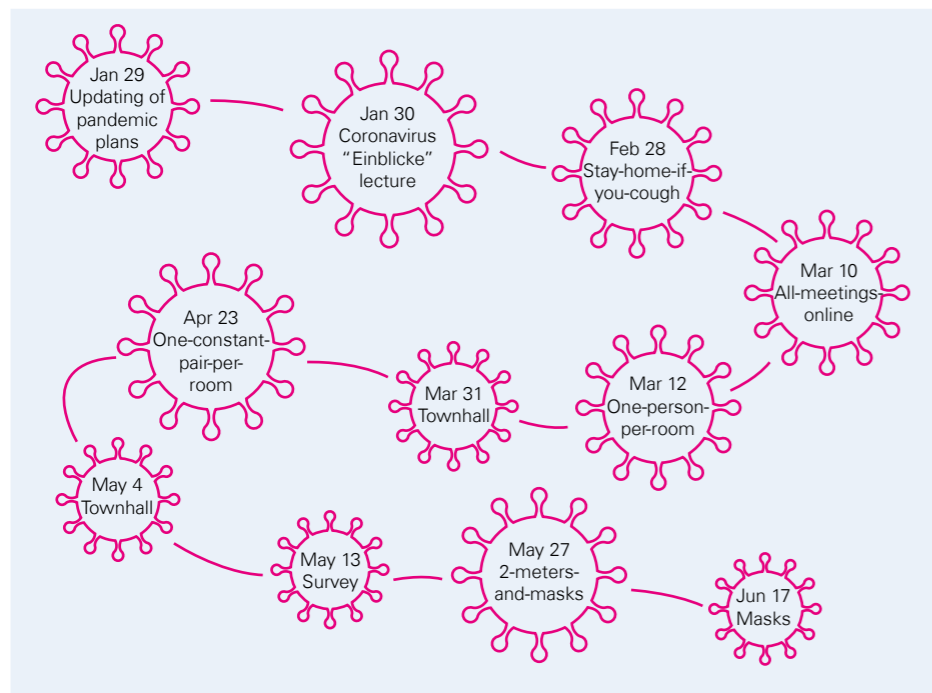
Prof. Alex Schier has been elected as a new member of both the United States National Academy of Sciences (NAS) and the Academia Europaea. He received these high distinctions for his outstanding and pioneering scientific achievements. For his work leading to multiple advancements in the zebrafish field, he received the George Streisinger Award of the International Zebrafish Society.

Peter Scheiffele participates in EU-funded project CANDY

The CANDY research project investigates the biological links between neurodevelopmental disorders and co-occurring somatic illnesses and how treatment of affected patients can be improved. Sixteen partners of six EU-countries, including Prof. Peter Scheiffele's team are closely collaborating in this international research consortium, coordinated by Radboud University in the Netherlands. As part of the "Horizon 2020" programme, the European Commission is funding the five-year CANDY project with a total of six million euro. Scheiffele's project specifically focuses on alterations in lipid transport and homeostasis as a mechanism that widely impacts neuronal function.

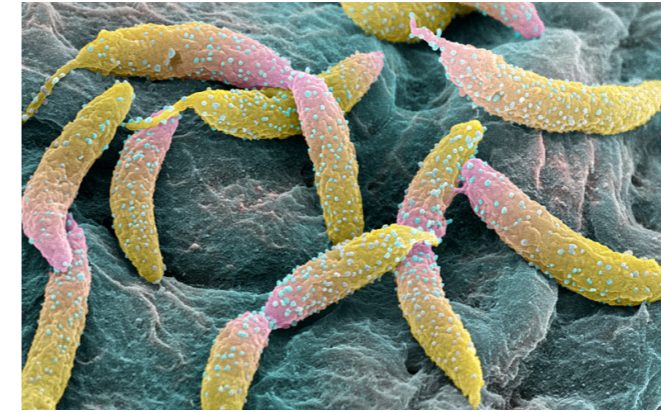


Prof. Silvia Arber has joined the ranks of the United States National Academy of Sciences (NAS) as a new member. The neurobiologist has also been awarded the Lelio Orci Award 2019 for her work on neuronal circuits controlling motor behavior.



Contending with the SARS-CoV-2 pandemic

Each member of the Biozentrum was affected by the SARS-CoV-2 pandemic. Teaching and meetings moved online, research and training slowed down, and social interactions were limited. But thanks to long-standing pandemic preparation plans, in-house expertise (see page 12), appreciation for the common good, broad consultation, and excellent relations with the university leadership, the Biozentrum stayed open for research while keeping everyone safe. All essential functions, including the research infrastructure, could be maintained by a dedicated staff. The Biozentrum community made major efforts to continue research and teaching and found creative ways to connect with and support each other. Importantly, the University and the Biozentrum have provided flexible solutions to meet the needs of students and junior researchers, alleviating some of the stress associated with the pandemic. Towards the end of 2020, the launch of successful vaccines lifted the spirit of Biocentrics as a triumph of science and as a glimmer of hope for the new year.



Inner "clockwork" sets the time for cell division in bacteria

The ability of pathogens to multiply in the host is crucial for the spread of infections. The speed of bacterial division greatly depends on the environmental conditions. But how do bacteria know when it is time to enter the next round of cell division? An interdisciplinary team headed by Prof. Urs Jenal has now identified a central switch for reproduction in the model bacterium *Caulobacter crescentus*: the signaling molecule *c-di-GMP*. In their study, they report that this molecule initiates a "clockwork" mechanism that determines when individual bacteria reproduce. The researchers assume that this mechanism enables bacteria to precisely coordinate growth and development.

Kaczmarczyk et al., *Nature Communications*

Sabotage attack: How a bacterial protein tricks our innate immune response

Upon sensing an infectious agent our immune system triggers inflammation in order to clear the infection. Prof. Christoph Dehio's team has discovered a new pathway explaining how bacterial pathogens can sabotage this innate immune response. They have demonstrated that a bacterial effector protein activates STAT3 signaling in the host cell and triggers an anti-inflammatory program in favor of establishing chronic infection. Beyond the paradigm of pathogen-induced STAT3 activation and anti-inflammatory response, the effector protein may also inspire new treatment options for chronic infection and inflammatory diseases.

Sorg et al., *Cell, Host & Microbe*

Special "Einblicke Biozentrum" on novel coronavirus outbreak

At the beginning of this year, the Biozentrum continued the successful public lecture series "Biozentrum Einblicke". The talks given by Prof. Anne Spang on aging processes and Prof. Peter Scheiffele on the development of neuronal networks attracted a broad audience and led to lively discussions during the following reception. As part of the "Einblicke" series, the Biozentrum organised a special public event on the outbreak of the novel coronavirus at the end of January. In short lectures, three experts from the University of Basel shed light on the background of the outbreak and recent developments. Prof. Richard Neher, biophysicist at the Biozentrum, presented his platform "Nextstrain" for real-time virus tracing and reported on the origin and the global spread of the SARS-CoV-2 virus. With the measures to reduce the spread of the coronavirus, all upcoming "Einblicke" lectures have been postponed until further notice.



The American Society for Cell Biology ASCB selected Prof. Anne Spang to be a Fellow.

ARTIDIS announced successful clinical trial

The company ARTIDIS, a spin off from the Biozentrum and the Swiss Nanoscience Institute of the University of Basel, announced that its nanotechnology platform is able to detect breast cancer with a high sensitivity. This has been shown in the "NANO" study, which was designed to demonstrate the clinical utility of a novel nanomechanical biomarker for breast cancer diagnosis. The Basel-based health-tech company has developed the first nanomechanical biomarker for cancer diagnosis and treatment optimization.



Biozentrum PhD Fellowships

Twice a year, the Biozentrum encourages talented, ambitious and highly motivated young scientists from all over the world to apply for its prestigious and sought-after fellowships. The "Biozentrum PhD Fellowships" are awarded on a competitive basis to a maximum of ten candidates per open call. Recipients are offered a unique rotation-based selection of a research group of choice and a number of other incentives that foster the scientific excellence and the career prospects of these PhD candidates. Since its inception in 2006, 56 PhD students from 26 countries – about half of them women – have completed their doctorate. There are currently 42 fellows conducting research at the Biozentrum.

100th Birthday of Biozentrum founding member-Eduard Kellenberger

The Biozentrum commemorates the 100th anniversary of the birth of Prof. Eduard Kellenberger. The physicist has not only gone down in the history and textbooks as a pioneer of electron microscopy but also as an early representative and advocate of the scientific discipline "molecular biology". He also played his part in the history of the Biozentrum at an early stage: He was one of the five most important promoters from the scientific community, the University of Basel and private industry, championing the establishment of the interdisciplinary molecular biology research institute in Basel. Already in developing the concept for the Biozentrum, it was a matter of great importance to Kellenberger to bring together diverse disciplines such as genetics, biochemistry and biophysics under one roof. His lifelong driving desire and motivation was to create knowledge to serve the common good.



Fiona Doetsch, Professor of Molecular Stem Cell Biology, has been elected as a new member of the prestigious European Molecular Biology Organization.

Protective shield: How pathogens withstand acidic environments in the body

Prof. Camilo Perez's team has elucidated an important mechanism by which Gram-positive bacteria, including the dangerous nosocomial pathogen MRSA, protect themselves from acidic conditions in our body and thus ensure their survival. By moving hydrogen ions across the cell membrane, a so-called flippase transporter flips an "anchor" molecule for lipoteichoic acid production from the inside of the bacterial membrane to the outside. Lipoteichoic acids are important biopolymers that provide stability to the cell wall of Gram-positive bacteria, facilitate colonization of the host and contribute to repelling antibiotics. The researchers have also been able to show that bacteria lacking the flippase display severe growth defects upon acidic stress. The flippase is essential for the survival of *Staphylococcus aureus* in the human body and could be considered a new pharmacological target for the treatment of dangerous MRSA infections.

Zhang et al., *Nature Structural & Molecular Biology*



Newly appointed Assistant Professor Maria Hondele receives ERC Starting Grant

In June this year, Maria Hondele was appointed as a new Assistant Professor of Biochemistry with Tenure Track. Her research focuses on the fate of RNA molecules in the cell and the role of membraneless organelles in this process. In recognition of her outstanding scientific achievements, Hondele has already been awarded several prizes and fellowships, including a long-term postdoctoral fellowship from the European Molecular Biology Organization (EMBO) and the Human Frontier Science Program (HFSP), the PhD Prize of the Munich University Society and last year an ETH Career Seed Grant. Recently, the biochemist has been awarded one of the highly coveted Starting Grants by the European Research Council (ERC). In her project, Hondele wants to investigate how certain membraneless organelles assemble and function, how they selectively accumulate macromolecules and thus, for example, control the fate of messenger RNAs.

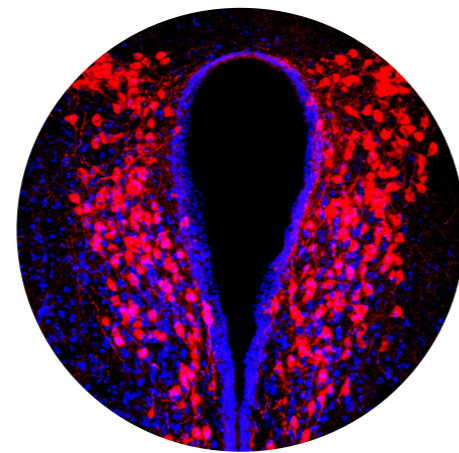


Biozentrum Research Summer for Bachelor students

The coronavirus pandemic also affected the Biozentrum "Research Summer 2020". Nevertheless, four Bachelor students from Switzerland and abroad participated in this year's program. For Victoire Tribout from the EPFL Lausanne it was an exciting experience: "This internship is really a great opportunity to discover at an earlier stage in your career what lab work is all about and you can participate without much experience." With the "Research Summer" internship, the Biozentrum offers undergraduate students from various disciplines in the natural sciences the opportunity to immerse themselves for several weeks in cutting-edge research projects, learning new lab techniques, how to document and present research results and training scientific thinking.

Bacterial cancer treatment on the path to enter clinical phase

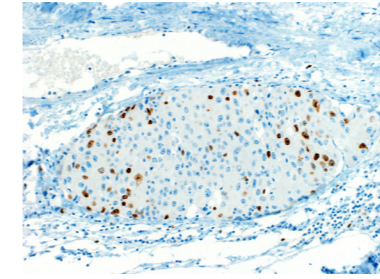
The Basel-based biotech company and Biozentrum spin-off T3 Pharmaceuticals AG is breaking new ground in the treatment of cancer by using live bacteria. The closing of the third financing round allows the company to start clinical testing of their bacterial cancer therapy. The funds of more than 25 million Swiss francs will be used primarily to support the progress of the lead candidate through early clinical studies. The clinical trial in patients with solid tumors is planned to start early next year.



Autism: How gene alteration modifies social behavior

Autism occurs in about one percent of the population and is characterized by alterations in communication, repetitive behavior and social difficulties. Hundreds of different genes are involved in the development of autism, including the gene encoding the synaptic adhesion molecule neuroligin-3. Prof. Peter Scheiffele's team has demonstrated for the first time that an autism associated mutation in the neuroligin-3 gene disrupts the oxytocin signaling pathway in the neurons of the brain's reward system in mice and, as a consequence, reduces social interactions between mice. The researchers also report on a treatment approach that could normalize social behavior in autism. They have already achieved promising results in an animal model.

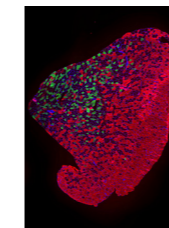
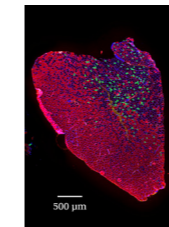
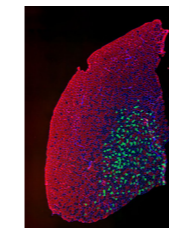
Hörnberg et al., *Nature*



New way for breast cancer cells to escape self-destruction

In the body, the so-called programmed cell death prevents cells with irreparable damage from surviving and turning into cancer cells. In their current study, the researchers led by Prof. Mihaela Zavolan demonstrate that two variants of the protein Argonaute 1 which differ in length have an influence on whether the cell's suicide program is initiated or not. Unlike the previously-known shorter variant, the long Argonaute 1 protein, which is more abundant in breast cancer cells, deprives the cells of an important apoptosis signal and thus promotes proliferation of tumor cells. Eliminating the long form could be a novel approach to reactivating apoptosis in cancer cells and limiting tumor growth.

Gosh et al., *EMBO Journal*



Muscle Aging: Stronger for longer

With life expectancy increasing, age-related diseases are also on the rise, including sarcopenia, the loss of muscle mass due to aging. The causes of sarcopenia are diverse, ranging from altered muscle metabolism to changes in the nerves supplying muscles. Researchers led by Prof. Markus Rüegg have now discovered that mTORC1 also contributes to sarcopenia and its suppression with the well-known drug rapamycin slows age-related muscle wasting. To help the scientific community further investigate how gene expression in skeletal muscle changes during aging or in response to rapamycin treatment, they developed the user-friendly web application "SarcoAtlas".

Ham et al., *Nature Communications*

Appointment of two professors

Anissa Kempf has been appointed to be an Assistant Professor of Neurobiology and Knut Drescher an Associate Professor of Microbiology and Biophysics. Both will take up their new positions next year and start with their groups in the new Biozentrum building.



Sleep behavior has long been a subject of research, yet the most important question "Why do we sleep at all?" still remains unanswered. In her research, Anissa Kempf wants to get to the bottom of this biological phenomenon. Her aim is to uncover how neurons in the brain control sleep-wake cycles and the specific role played by mitochondrial metabolism in the cell.



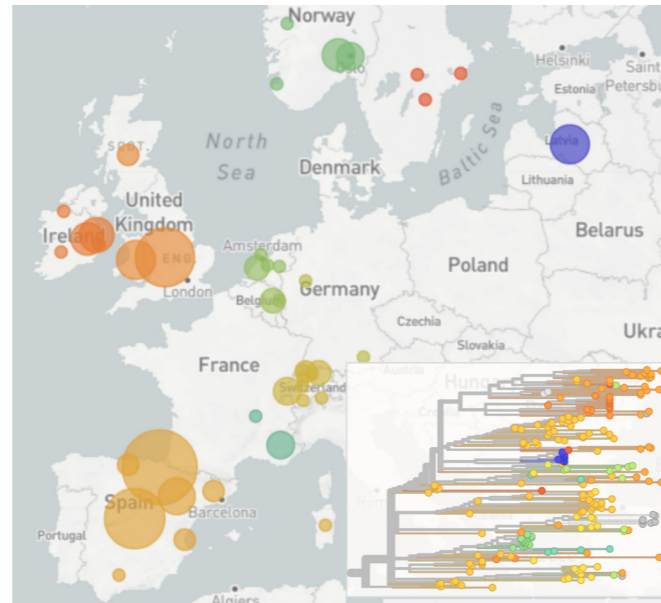
Knut Drescher combines biological processes with physical principles to deal with bacterial communities. His interest lies in how bacteria interact with each other to form resistant biofilms. These play an important role in many infections. Drescher's work could reveal new ways of preventing or dissolving biofilms.

Tracing the spread of novel SARS-CoV-2

This year, the world has witnessed how a local virus outbreak evolved into a global pandemic. Using phylogenetics, the team led by Prof. Richard Neher, who is a member of the expert group "Data & Modelling" of the Swiss National COVID-19 Task Force, tracks the global spread of the novel coronavirus. Some years ago, Neher and his colleague Trevor Bedford from the Fred Hutchinson Cancer Research Center in Seattle developed the open source web application "Nextstrain.org" to follow the spread of pathogens such as the Ebola or flu viruses in real-time. During the coronavirus pandemic the platform has been literally overrun, the website has been accessed a million times. For launching this tool, the Nextstrain.org team has been awarded the 2020 Webby Special Achievement Award. Richard Neher and his postdoc Emma Hodcroft have also become highly sought-after experts by the media on questions about the coronavirus pandemic.

In a recent study, Neher's team together with researchers at the ETH Zurich in Basel and the SeqCOVID-Spain consortium has identified a novel SARS-CoV-2 variant, named 20A.EU1, that has spread widely across Europe in summer 2020. While there is no evidence of this variant being more dangerous, its spread may give insights into the efficacy of travel policies adopted by European countries during the summer.

Hodcroft et al., preprint on *MedRxiv*



Prof. Flavio Donato has been awarded an Eccellenza Grant by the Swiss National Science Foundation.



Prof. Camilo Perez has been selected to be an "EMBO Young Investigator" by the European Molecular Biology Organization EMBO. The structural biologist is one of 30 junior researchers to receive the distinction this year.

How bacteria reinforce their protective shield against stress

In order to survive unfavorable conditions, bacteria must be able to continuously replace damaged outer membrane proteins and adapt their arsenal of proteins to the specific needs. This is the job of the bacterial chaperone Skp. Based on its atomic structure, the researchers led by Prof. Sebastian Hiller have now uncovered how it modulates its activity. Under stress conditions, many individual inactive Skp proteins are quickly recruited from a pool in the periplasmic space. They become active when three proteins assemble into a stable structure around the protein to be transported. Using *Salmonella* as a model, their collaboration partner Dirk Bumann has also demonstrated that Skp is important for the virulence and survival of pathogens in hostile host environments.

Mas et al., *Science Advances*



Médéric Diard receives ERC Consolidator Grant

Prof. Médéric Diard has been honored with an ERC Consolidator Grant, a highly competitive award from the European Research Council (ERC) for excellent scientists. In his project "ECOSTRAT", funded with about 2 million euro for five years, he will study the evolution and colonization strategies of multidrug-resistant gut bacteria in order to identify novel antibiotic-free treatment approaches.

The Biozentrum on the move

The long-awaited move to the state-of-the-art research building represents a milestone for the Biozentrum. "Here we will write the next chapter of our almost 50-year success story," says the Director Prof. Alex Schier, who is looking forward to the move into the new Biozentrum building in 2021. "Thanks to the excellent infrastructure, we will remain competitive in the global academic arena and be able to bring the world's best scientists to Basel."



Facts & Figures.

Members of staff

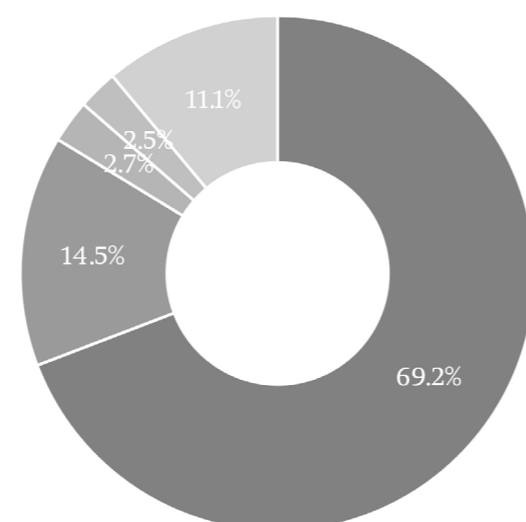
Total members of staff: 482
Scientists from over 60 countries



- Professors
- Postdoctoral researchers
- PhD students
- Scientific staff
- Master students
- Lab staff/ Technicians
- Administration

Annual financial statement

Sources of funding of the budget of 65.4 million Swiss francs:



- University of Basel
- Swiss National Science Foundation
- EU/ERC grants
- Swiss Institute of Bioinformatics
- Misc. third party grants

Research groups 2020

Prof. Jan Pieter Abrahams
 Prof. Markus Affolter
 Prof. Silvia Arber
 Prof. Marek Basler
 Prof. Attila Becskei
 Prof. Dirk Bumann
 Prof. Christoph Dehio
 Prof. Médéric Diard
 Prof. Fiona Doetsch
 Prof. Flavio Donato
 Prof. Stephan Grzesiek
 Prof. Michael N. Hall
 Prof. Christoph Handschin
 Prof. Sebastian Hiller
 Prof. Maria Hondele
 Prof. Urs Jenal
 Prof. Roderick Lim

Prof. Timm Maier
 Prof. Susan Mango
 Prof. Richard Neher
 Prof. Camilo Perez
 Prof. Jean Pieters
 Prof. Markus Rüegg
 Prof. Peter Scheiffele
 Prof. Alex Schier
 Prof. Tilman Schirmer
 Prof. Torsten Schwede
 Prof. Anne Spang
 Prof. Martin Spiess
 Prof. Henning Stahlberg
 Prof. Kelly Tan
 Prof. Erik van Nimwegen
 Prof. Mihaela Zavolan

Awards, Grants & Fellowships for PhD students and Postdocs 2020

- Layara Abiko, SPARK SNSF Grant
- Emily Bayer, Jane Coffin Childs Memorial Fund
- Karolin Berneiser, Boehringer Ingelheim Fonds
- Anastasiya Börsch, Novartis University of Basel Excellence Scholarship for Life Sciences
- Jakob El Kholtei, Boehringer Ingelheim Fonds
- Elisabetta Furlanis, Swiss Society for Neuroscience Best Publication Award and J.C.W. Shepherd PhD Student Prize of the Biozentrum
- Regula Furrer, Gottfried & Julia Bangerter-Rhyner Stiftung and Swiss Life Jubiläumsstiftung Grant
- Souvik Ghosh, Research Fund Junior Researchers University of Basel
- Asier González, Technology for the next generation prize from HEJUBA
- Alexander Harms, Emilia-Guggenheim-Schnurr-Stiftung
- Stefan Imseng, Technology for the next generation prize from HEJUBA
- Rajesh Jayachandran, Swiss Transplantation Society Award and Propelling Grant University of Basel
- Steffen Kandler, Marie Skłodowska-Curie Individual Fellowship
- Maxim Kolesnikov, Boehringer Ingelheim Fonds
- Oded Maysel, EMBO Postdoctoral Fellowship
- Annika Nichols, SPARK SNSF Grant
- Raul Ortiz, EMBO Postdoctoral Fellowship
- Sujin Park, Research Fund Junior Researchers University of Basel
- Madalena Madeira Reimão Pinto, EMBO Longterm Fellowship and Marie Skłodowska-Curie Individual Fellowship
- Parthasarathi Rath, Research Fund Junior Researchers University of Basel
- Ahilya Sawh, Research Fund Junior Researchers University of Basel and SPARK SNSF Grant
- Max Shafer, SPARK SNSF Grant
- Mitsugu Shimobayashi, EFSD/Novo Nordisk Future Leaders Award
- Amandine Thomas, Marie Skłodowska-Curie Individual Fellowship
- Lisa Traunmüller, "Gottfried Schatz" PhD Student Prize of the Biozentrum, inaugural FENS-Kavli Network of Excellence PhD Thesis Prize and Faculty of Science prize of the University of Basel for her PhD thesis
- Yinan Wan, EMBO Postdoctoral Fellowship

