University of Basel

BIOZENTRUM
The Center for Molecular Life Sciences

2019

Biozentrum Highlights

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

Dear readers

“Fountains!” That’s my answer when friends ask me what I notice the most since coming back to Basel. As I am rediscovering my hometown, I see fountains everywhere.

Why do I notice fountains? There are the aesthetic and nurturing aspects of fountains – they are beautiful monuments that provide refreshment. But more importantly, fountains are symbols of the “common good” – something shared by and beneficial to most members of the community. Instead of each of us fighting for a fountain in our backyard, we share fountains in town squares. This principle of the fountain as a common good is also the source and the mission of the Biozentrum – our community supports our research and teaching through funds and infrastructure, and we support our community by creating knowledge and educating the next generation. To illustrate this give-and-give, I would like to draw attention to two highlights detailed in the following pages.

First, we obtained three grants from the European Research Council (ERC) and were designated a National Center of Competence in Research (NCCR). The ERC grants support foundational research, whereas the NCCR “AntiResist” aims to develop new antibiotics. We are grateful that the fountains of Swiss and European funding feed our research.

Second, we launched two public outreach activities. We shared our research in the lecture series “Einblicke”, and in the “Basel Summer Science Academy”, high school students got a taste of how to do research by discovering and characterizing viruses from the Rhine. Both programs were a huge success, and we are happy that the Biozentrum is a fountain that feeds the public’s fascination with research.

Fountains are also a symbol of renewal. As we enter this new decade, I am looking forward to the Biozentrum as a fountain of youth and us Biocentrics as fountains for our community. Or in the words of James Russell Lowell (1819-1891):

Glorious fountain!
Let my heart be
Fresh, changeful, constant,
Upward, like thee!

Prof. Dr. Alex Schier
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2019 at a glance.

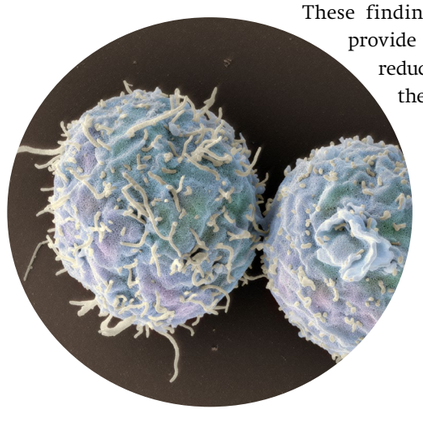
Biozentrum heads the new NCCR "AntiResist"

The University of Basel has received the grant to establish the National Center of Competence (NCCR) in Research "AntiResist", directed by Prof. Christoph Dehio from the Biozentrum. Researchers at the Biozentrum, the University Hospital Basel, the Department of Biomedicine and the D-BSSE will establish a unique interdisciplinary center for the development of new strategies in the fight against antibiotic-resistant pathogens. The Federal Government is supporting the program with 17 million Swiss francs in its initial funding phase.

Susan Mango, Professor of Molecular and Cellular Biology, has been elected as a new member of the prestigious European Molecular Biology Organization.

Immunity: Engineered T cells promote long-term organ transplant acceptance

Organ transplant rejection is a major problem in transplantation medicine. Suppressing the immune system to prevent organ rejection, however, opens the door to life threatening infections. A team of researchers led by Prof. Jean Pieters has now described a way to selectively suppress the immune reaction of the body against the donor organ by modulating the protein coronin 1. By blocking this protein in T cells, these immune cells do not attack the transplanted organ anymore, but still keep viruses, bacteria and fungal infections in check. These findings could potentially provide new approaches for reducing graft rejection in the future.

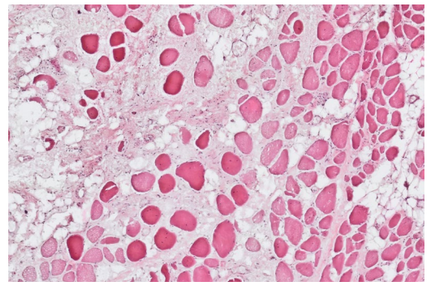


Silvia Arber receives the International Prize of the Fyssen Foundation

With the International Prize 2018, the Fyssen Foundation honors Prof. Silvia Arber for her scientific achievements in the field of neurobiology, in particular, for her work on the development and function of neuronal circuits involved in motor control. Her research has significantly advanced the understanding of neuronal circuit organization and function, both at a cellular and molecular level.

Flavio Donato starts his research group and the Schier lab moves in

In 2019, Flavio Donato joined the Biozentrum as Assistant Professor of Neurobiology and is establishing his first own independent research group. Here, he wants to explore how our brain learns and stores memory and how this ultimately shapes our personality. The Schier lab has also arrived at the Biozentrum. Once the lab is up and running, the researchers continue to study the molecular and cellular mechanisms underlying the development of complex living organisms.



Treating muscular disease – Santhera and Biozentrum join forces

Santhera Pharmaceuticals has started a collaboration with Prof. Markus Rüegg to advance gene therapy research for the treatment of type 1 congenital muscular dystrophy (MDC1A). This inherited disease is caused by a genetic defect leading to a loss of the laminin-alpha2, a protein important for muscle fiber stability. Previously, Rüegg's team has demonstrated that specifically designed linker proteins could compensate for the lack of laminin-alpha2. The gene replacement strategy aims to overcome the genetic defect by substituting laminin-alpha2 deficiency with these two linker proteins to re-establish muscle fiber integrity in patients. The Swiss Innovation Promotion Agency "Innosuisse" and Santhera will jointly invest 1.2 million Swiss francs in this research program.

Three Biozentrum scientists receive prestigious ERC grants

This year, the European Research Council (ERC) has awarded three researchers from the Biozentrum a highly endowed research grant. Prof. Alex Schier has received an “ERC Advanced Grant” for his project on the development of individual cells and the logic of governing cell differentiation. Prof. Flavio Donato has been awarded an “ERC Starting Grant” for his pioneering research project on infant memory. And finally, Prof. Marek Basler has been awarded a prestigious “ERC Consolidator Grant”. In his project, he will study ow bacteria aim their nanosized speargun, the so-called “type VI secretion system” (T6SS). Including these three scientists, there have been a total of twelve scientists from the Biozentrum distinguished with a prestigious and highly competitive ERC research grant.

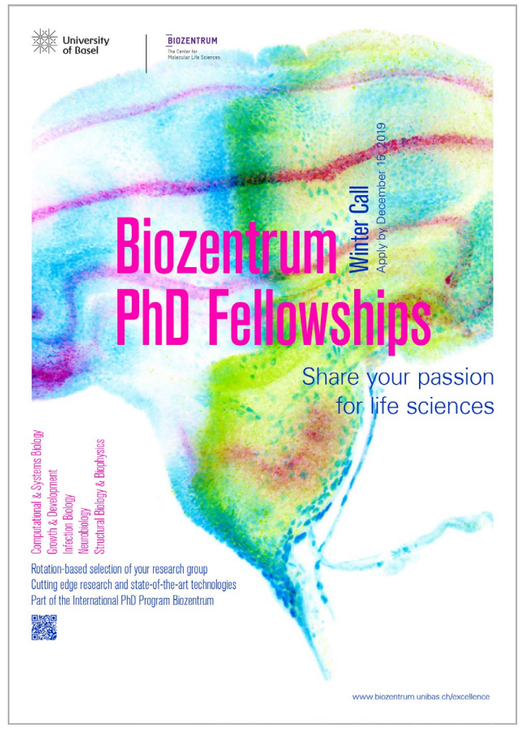
Michael N. Hall received the 2019 Nakasone Award, given by the Human Frontier Science Program (HFSP). “Michael Hall’s groundbreaking research has spawned a whole new field of inquiry and has far-reaching implications to advance scientific understanding and improve human health,” said Warwick P. Anderson, HFSPO Secretary-General.

Cell: Schizophrenia – 30 genes under suspicion

Schizophrenia is a psychosis that leads to a disturbed perception of reality. Previous studies have shown that several regions of the genome containing a variety of genes are associated with the disease. Prof. Alex Schier's team has now identified 30 genes in these regions and deciphered the function of the individual genes. The scientists have discovered that these genes have an impact on the structure and function of the brain as well as on various behavioral patterns. Furthermore, the team has been able to generate an atlas of all genes with their respective consequences for the brain.

Biozentrum PhD Fellowships

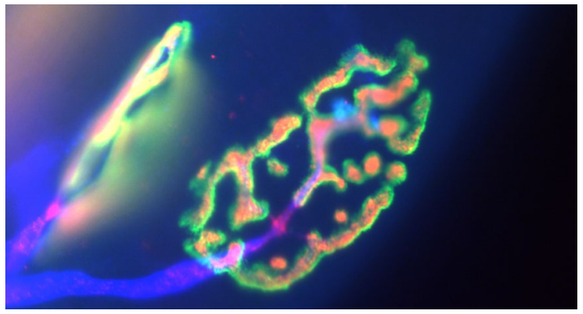
With its prestigious PhD Fellowships, the Biozentrum enables ambitious young scientists to do their PhD at one of the world’s leading institutes in the life sciences. The special feature of these fellowships is that the students are tied neither to a research group nor to a project but can select a group after a rotation. The fellowships are therefore particularly suitable for candidates who are open to a wide range of research and want to broaden their horizons. There are currently 41 fellows conducting research at the Biozentrum.



Nature Communications: Learning fine motor coordination changes the brain

Simply grasping a coffee cup needs fine motor coordination with the highest precision. This required performance of the brain is an ability that can also be learned and trained. Prof. Kelly Tan’s research group has investigated the red nucleus, a region of the midbrain that controls fine motor movement, and identified a new population of nerve cells which changes when fine motor coordination is trained. They have also been able to demonstrate that training of fine motor tasks promote plastic reorganization of this brain region. In a second study, published in “Cell Reports”, Tan’s team has identified and characterized two cell populations in the Substantia Nigra and has been able to assign an exact function to each of them. The researchers could show that one population is responsible for initiating a motor task, whereas the second group of nerve cells ensures the continuity of a desired movement. The findings are also important in regard to Parkinson’s disease, caused by the degeneration of neurons in the Substantia Nigra.

Prof. Peter Scheiffele has been elected member of the National Research Council at the Swiss National Science Foundation (SNSF).



Nature Communications: How neuromuscular connections are maintained after nerve lesions

The protein complex mTORC1 promotes muscle growth and is important for the self-cleaning process of the muscle cells. After nerve injury, mTORC1 takes over an important function in skeletal muscle to maintain the neuromuscular junction, the synapse between the nerve and muscle fiber. The team led by Prof. Markus Rüegg has shown that the activation of mTORC1 must be tightly balanced for a proper response of the muscle to nerve injury. The study opens new insights into muscle weakness related to neuromuscular diseases or caused by ageing.

Randy Schekman receives honorary doctorate

The University of Basel awarded Nobel laureate Prof. Randy Schekman, who has been closely associated with the Biozentrum for many years, an honorary doctorate at this year's Dies academicus.

"Summer Science Academy" for high school students

This year, the first Basel Summer Science Academy took place at the University of Basel. In a two-week course, sixteen high school students from various gymnasiums in the region had the opportunity to get a taste of research life and immerse themselves into invisible worlds at the Biozentrum. In the search for new types of bacterial viruses, the students collected samples from both the Rhine and at our doorstep and examined them microbiologically. Apart from research, there was also time for discovering the Life Sciences hub Basel and for social activities.

Launch of public lecture series "Einblicke Biozentrum"

What happens during human and animal development? What is muscle training good for and why do our cells age? On November 5, 2019, the Biozentrum launched "Einblicke Biozentrum", a new public monthly lecture series on current research topics. The broad audience will become acquainted with exciting fields of research and new discoveries in an easy-to-understand way.

T3 Pharmaceuticals: Lead product expected to enter clinical phase

The joining of forces with two experienced and specialized investors, the Boehringer Ingelheim Venture Fund and Reference Capital SA, and the closing of the second financing round of over 12 million Swiss francs, as well as the strengthening of the development team, provide an excellent position for T3 Pharmaceuticals to complete preclinical activities for its lead candidate. The Biozentrum spin-off is developing a protein delivery technology based on live bacteria expressing the "type 3 secretion system". The company has engineered the bacteria to grow selectively within solid tumors where they produce and deliver therapeutic proteins. T3 Pharma's lead product is expected to enter clinical testing in the middle of 2020. Furthermore, T3 Pharma has won the W.A. de Vigier Foundation's highest endowed award for startup companies in Switzerland.

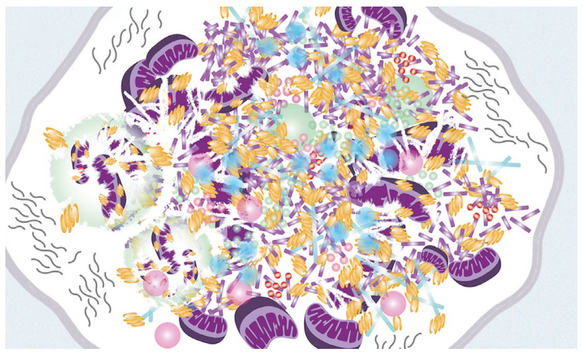
Nature: Development of a novel class of antibiotics

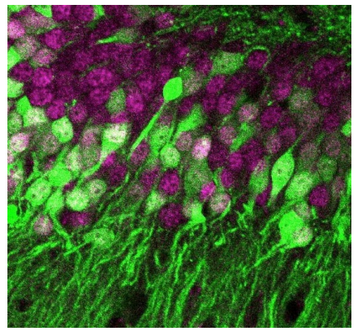
A number of pathogens protect themselves with an outer membrane that makes it difficult to combat them with antibiotics. In addition, the widespread use of antibiotics promotes the development of resistant bacteria. In collaboration with academic partners including Prof. Sebastian Hiller, the Allschwil-based Polyphor AG has now discovered a new class of antibiotics known as OMPTA (Outer Membrane Protein Targeting Antibiotics). These drugs target important components in the outer membrane of Gram-negative bacteria. Antibiotics of this new class have the potential to successfully fight difficult-to-treat infections, even if the pathogens are already resistant or multi-resistant to conventional antibiotics.

On June 3, 2019, Prof. em. Werner Arber celebrated his 90th birthday. In his honor, the Biozentrum held a scientific symposium.

Nature Neuroscience: Neuronal Parkinson inclusions are different than expected

For decades, it was assumed that Parkinson's disease is caused by deposits of insoluble fibrils consisting of the protein alpha-synculein in the Lewy bodies. An international team of researchers, including Prof. Henning Stahlberg refute this long held common thesis. The researchers have shown that the inclusions in the brain's neurons, characteristic of Parkinson's disease, are comprised of a membranous medley rather than protein fibrils. With their work, the researchers raise many new questions regarding the role of the Lewy bodies in the etiology of Parkinson's disease.





Nature Neuroscience: What makes nerve cells unmistakable?

Our brain consists of hundreds, if not thousands, of different types of nerve cells that control our brain functions due to their individual characteristics. But how do the different cell types manage to develop their diverse traits? In a genome-wide analysis, the team led by Prof. Peter Scheiffele has now discovered that alternative splicing leads to a broad range of variants of individual proteins, which ultimately allows to distinguish types of nerve cells. This process allows organisms to build a highly complex neuronal network with only a limited number of genes. In collaboration with the "Center for Scientific Computing" (sciCORE), a user-friendly website has been set up which allows scientists worldwide to investigate the role of individual splice variants in brain function.

Nature: Resistance can spread even without the use of antibiotics

Antibiotic resistance does not spread only where and when antibiotics are used in large quantities, conclude researchers from laboratory experiments. Reducing antibiotic use alone is therefore not sufficient to curtail resistance and should be done in conjunction with measures to prevent infection with resistant germs. In this study led by Prof. Wolf-Dietrich Hardt, ETH Zurich, and Prof. Médéric Diard from the Biozentrum, the researchers have discovered an additional, previously unknown mechanism that spreads resistance in intestinal bacteria that is independent of the use of antibiotics.

PNAS: Speed controllers for protein production

The growth, differentiation and functions of cells are intimately coupled to their protein synthesis activity, which translates the genetic code into proteins. The research team led by Prof. Mihaela Zavolan has investigated thousands of genes in growing yeast cells and uncovered determinants affecting the speed with which different proteins are synthesized. The results serve as a basis to better analyze translational control in a wide range of cell types.

A springboard into research for Bachelor students

Sixteen Bachelor students were selected from over 60 applicants for the "Research Summer 2019". They represented a colorful mix with regard to both scientific background and origin. With the "Research Summer" program the Biozentrum offers Bachelor students the opportunity to immerse themselves for several weeks in cutting-edge research projects, learn new lab techniques, how to document and present research results and train scientific thinking.

Pestalozzi Schulcamp

The Biozentrum cooperates with the educational program "Pestalozzi Schulcamps" for Swiss primary schools in districts with a high proportion of migrants. The foundation aims to promote the personality development of children in the long term. The Biozentrum provides a follow-up program for selected children.

ARTIDIS joins world's largest medical center

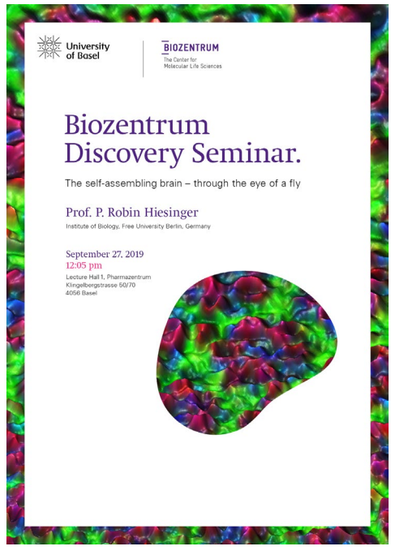
ARTIDIS announced its successful integration in the highly competitive international Medical Device Cohort 2019 at the Texas Medical Center's Innovation Institute. The company, a spin off from the lab of Argovia Prof. Roderick Lim at the Biozentrum and the Swiss Nanoscience Institute, is developing a medical device based on nanotechnology for clinical application in cancer diagnostics. The TMC Innovation Accelerator (TMCx) is a program that aims at impacting the healthcare industry by fostering integration of cutting-edge technology in the clinics. Furthermore, ARTIDIS announced the successful closure of a CHF 8.8 million seed financing, securing early clinical validation and the next development phase towards market entry in 2021.

Nature: Molecular bodyguards against Parkinson's disease

The causes of the Parkinson's disease, which leads to the progressive death of nerve cells in the brain, are still not well understood. In their current study, the team led by Prof. Sebastian Hiller has shown that chaperone proteins in human cells dynamically interact with the protein alpha-Synuclein, which is strongly associated with this most common neurodegenerative disorder. A disturbed relationship to these "bodyguards" leads to cell damage and the formation of Lewy bodies typical for Parkinson's disease. Using state-of-the-art NMR technology, the structural biologists have discovered a specific pattern that determines the exact interaction site of alpha-Synuclein with chaperones.

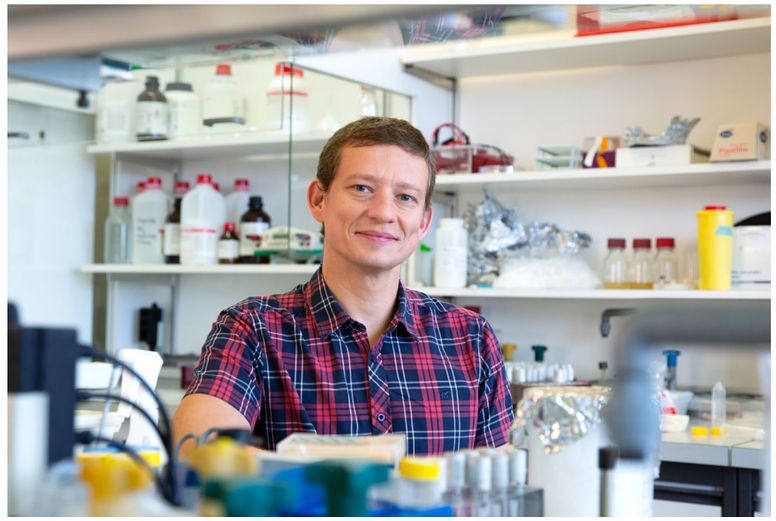
One year Biozentrum Discovery Seminars

The Biozentrum Discovery Seminar series has been a success since its start in fall 2018. The series alternates between talks given by graduate students and postdocs from the Biozentrum and by invited scientists from institutions worldwide.



Science: Magnesium deprivation stops pathogen growth

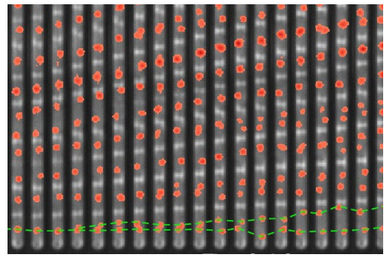
When pathogens infect an organism, the defense system immediately starts to fight the bacteria. To escape the patrolling immune cells, some bacteria invade and replicate inside host cells. However, the host has developed various strategies to keep the intracellular bacteria under control. Prof. Dirk Bumann's team has now discovered that magnesium is crucial for bacterial growth inside host cells. Magnesium starvation is a stress factor for the bacteria, which stops their growth and replication. The host cells limit magnesium supply to these intracellular pathogens using a transport protein called NRAMP1. If the pump in the host cells is defective, magnesium is available in sufficient quantities to enable rapid *Salmonella* growth.



Prof. Marek Basler is one of three scientists to be awarded this year's Sanofi-Institut Pasteur International Junior Award.

PNAS: Why strength training might come at the expense of endurance muscles

In their recent work, Prof. Christoph Handschin's team has more closely studied strength muscles and the myokine brain-derived neurotrophic factor (BDNF), which plays an important role in the formation of strength muscle fibers. The researchers have demonstrated that this factor is produced by the muscle itself and remodels the neuromuscular synapses, the neuronal junctions between the motor neurons and muscle. BDNF not only causes the strength muscles to develop, but at the same time leads to endurance muscle fiber number decline. The findings provide new insights into age-related muscle atrophy.



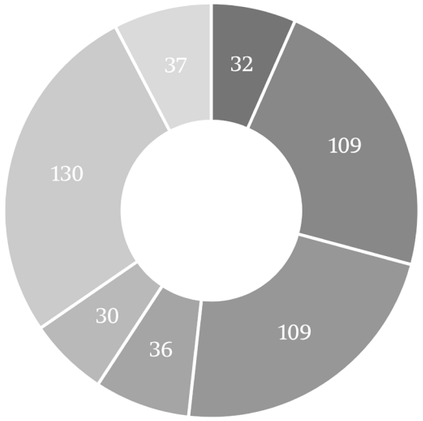
eLife: How bacteria control their cell cycle

The cell cycle describes a periodic repetition of two coordinated cycles: the duplication of a cell's genetic information on the one hand and cell division on the other. Although it is natural to think that the cell cycle begins with the birth of the cell and ends with the next cell division, the researchers led by Prof. Erik van Nimwegen argue for a major shift in this concept. Their findings show that, in bacteria, the cell cycle starts and ends with the initiation of DNA replication, with the cell division event occurring between two DNA replication events. The current study uses a new approach in which analysis of the subtle fluctuations that normally growing cells exhibit is used to infer how the underlying process is controlled.

Facts & Figures.

Members of staff

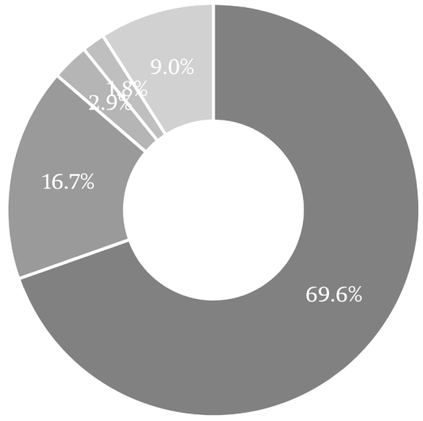
Total members of staff: 483
Scientists from over 50 countries



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

Annual financial statement

Sources of funding of the budget of 63.8 million Swiss francs:



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

Research groups 2019

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Prof. Markus Affolter
Prof. Silvia Arber
Prof. Marek Basler
Prof. Attila Becskei
Prof. Dirk Bumann
Prof. Christoph Dehio
Prof. Médéric Diard
Prof. Flavio Donato
Prof. Fiona Doetsch
Prof. Stephan Grzesiek
Prof. Michael N. Hall
Prof. Christoph Handschin
Prof. Sebastian Hiller
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
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Prof. Tilman Schirmer
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Prof. Erik van Nimwegen
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