University of Basel **BIOZENTRUM** U1.197 The Center for Molecular Life Sciences 12 2023 Biozentrui Highlights

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

Dear readers

On June 23, 2023, I was delighted to welcome over 400 alumni back to the Biozentrum. Former students, postdocs, group leaders and staff members were here to reminisce, reconnect and relive some of the excitement they had when they were at the Biozentrum. Our alumni have pursued very diverse careers, ranging from research scientist, professor, high school teacher, Nobel laureate or biotech entrepreneur to consultant, politician or journalist. This variety reflects the broad impact of the Biozentrum, but as different as our alumni's paths have been, they are still all connected by the values our institute stands for: excellent research, inspiring teaching and generous collegiality.

As you will read in the following pages, several of our current and future alumni were in the news this year. Simon Ittig, a former graduate student, launched the biotech company T3 Pharma in the Biozentrum in 2015. Building on his expertise in bacterial secretion systems, his start-up designs bacteria that inhibit tumor growth by releasing immune-modulating proteins. The initial data looks so promising that the pharma company Boehringer Ingelheim recently acquired T3 Pharma. Simon's success illustrates the innovative and entrepreneurial spirit nurtured at our institute. The Biozentrum also helped lay the foundation for Prof. Torsten Schwede, currently Vice-Rector for Research at Uni Basel, to be elected as the President of the Research Council of the Swiss National Science Foundation. His experiences in research, administration and leadership will help guide the SNSF in new directions at a time of opportunities and challenges such as AI and human engineering. As a Biozentrum alumnus myself, I have also come to realize that the mentorship and training I received here as a student was the best foundation for a life in biological research. The Biozentrum opened the world to me, both geographically and scientifically.

Just as the Biozentrum helped Simon, Torsten and me define our paths, it is currently doing the same for more than 250 young Biocentrists. I look forward to them becoming alumni who will look back at their time here with fond memories, gratitude and pride. Or as the poet John Donne* might have said more than 400 years ago:

In this present breath, our future's seed is sown, What now we live, in later thoughts full-grown. One day, with pride, we'll look upon this hour, No bitter root, but memories in flower.

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

*as hallucinated by ChatGPT

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2023 at a glance.



The Biozentrum PhD Fellowships, launched in 2006, offer a unique opportunity for ambitious young scientists worldwide to pursue a PhD at the Biozentrum. With 95 PhD graduates from 30 countries, the prestigious program emphasizes scientific excellence and diversity. The fellowships are competitively awarded to up to ten distinguished candidates annually. The fellows benefit from a rotation-based selection of a research group and other incentives fostering their scientific career. The PhD Fellowships program plays a pivotal role in attracting outstanding junior scientists to the Biozentrum and enhances the institute's research diversity. Currently, the Biozentrum is home to 40 fellows.



Novel insights into behavior of bacterial communities

Researchers led by Prof. Knut Drescher made two significant discoveries about bacterial behavior. First, they found that cholera bacteria form a novel type of bacterial community on immune cells: an aggressive biofilm that is lethal for the cells. This finding provides new insights into the infection strategies of pathogens. In a second study, they demonstrated that bacterial communities cooperate and share nutrients across generations. Using a newly developed technique, the team has been able to track gene expression during the development of bacterial communities over space and time.

Vidakovic et al., Cell / Jeckel at al., Nature Microbiology



National Future Day

On Switzerland's National Future Day, the Biozentrum buzzed with excitement as many children explored the fascinating world of cells and molecules in our labs. Kids from 5th to 7th grade had the opportunity to get a taste of research and peek into different fields of work.

Tagged for arrest: "Barcode" determines receptor's fate

Odors, light, hormones, and a tremendous variety of signaling molecules are recognized by a large family of cell receptors, known as G protein-coupled receptors (GPCRs). Due to its crucial role in many physiological processes, this receptor family is implicated in many diseases. Prof. Stephan Grzesiek's team discovered a unique recognition pattern in GPCRs that works like a barcode and tags the receptor for desensitization. In their study, focusing on the CCR5 receptor, the researchers identified a specific phosphorylation motif that tightly binds arrestin 2, a protein important for receptor removal. The strong interaction tells the cell to degrade the receptor. By this mechanism, signaling in cells is rapidly switched off when it is no longer needed.

Isaikina et al., Molecular Cell

Biozentrum Research Summer

With the Biozentrum Research Summer, we offer undergraduate students an exciting seven- to nine-week internship. This time, 13 participants engaged in real-life research projects, immersed into various scientific fields and enjoyed the social side program.







"Einblicke Biozentrum"

Our lecture series "Einblicke Biozentrum" for the general public was a complete success. More than 200 listeners followed the monthly lectures, offering fascinating insights into the world of science at the Biozentrum. Our group leaders took the audience on entertaining and enlightening journeys into their research. The high number of people attending the events reflects the unwaning interest in our research and institute.



Hospital germ's dual strategy

Infections are among the most frequent complications during a hospital stay. The group led by Prof. Urs Jenal uncovered why it is so difficult to combat the nosocomial pathogen *Pseudomonas aeruginosa*. It practices a division of labor: while some bacteria form a resistant biofilm on the lung mucosa, the others spread to distant tissue sites. This "stick and run" mechanism is regulated by different levels of the signaling molecule c-di-GMP. The team was also able to show that the anti-biofilm compound Disperazol targets this mechanism and flips the switch in favor of motile bacteria, leading to biofilm dispersal.

Manner et al., Nature Microbiology



Distinguished visitors

Throughout the year, our institute welcomed delegations from politics, business and culture to provide them with first-hand knowledge of scientific advancements and challenges. We received representatives from the Government of the Netherlands, the Department of Presidential Affairs of the Canton Basel-Stadt, the UK Ambassador to Switzerland and Liechtenstein at NCCR AntiResist amongst others. Furthermore, the newly elected Federal Councillor Beat Jans visited the Biozentrum. These visits are great opportunities to network and foster relationships.



Faster results and fewer animals thanks to new method

To study muscle diseases, scientists rely on the mouse as a model organism. Prof. Markus Rüegg's team developed an innovative method, enhancing efficiency while minimizing animal usage. Their new approach combines CRISPR/Cas9 with adenoassociated viruses to specifically alter gene function in muscle fibers. This technique not only opens new ways to investigate multiple genes simultaneously or even entire signaling pathways in adult skeletal muscle fibers, but also drastically reduces the number of laboratory animals needed.

Thürkauf et al., Nature Communications



Pregnancy remodels the brain

The ability of animal parents to recognize their offspring by smell ensures that they nurture their own young. Prof. Fiona Doetsch's team discovered that distinct pools of stem cells in the adult brain of mice are turned on during pregnancy and give rise to specific types of olfactory bulb neurons. These neurons prepare the animals for motherhood and are important for recognizing the odor of their own pups after birth. They are only temporarily formed and eliminated when pups are older. These on-demand adaptations of the brain underscore that brain plasticity is not only based on modifying synaptic connections between resident neurons.

Chaker et al., Science

Women in Science Day 2023

February 11th is celebrated globally as the International Day of Women and Girls in Science. This year, we featured three of our dedicated female PIs.



"This day is a great opportunity to celebrate the success of many outstanding female scientists and for girls around the world to get in touch with research, discover the fascination of scientific discovery, and explore science careers. It is obvious that, to this day, male faculty greatly outnumber female faculty in the natural sciences. But things have changed a lot in recent years – it is a core topic for many universities and research institutions to support and promote female talent!"

Prof. Maria Hondele



"Significantly more attention is given to gender equality today than when I started my lab about twenty years ago. My advice to young female scientists is: follow your dreams, be creative and bold. Being a scientist is a wonderful profession. And by making sure to encourage and promote excellent women to stay in academia, we can close the gender gap at the level of PIs or professors."

Prof. Silvia Arber

"Gender equality plays an important role in my team. Gender diversity is key to create a fair and productive work environment. I think that early exposure to science subjects as well as role models are very important in inspiring female high school students to pursue a scientific career. We are planning to host female high school students in the lab, for one week per year, to allow them to discover lab work and the scientific environment at the Biozentrum."

Prof. Anissa Kempf



Biozentrum Symposium

On June 22, 2023, the Biozentrum Symposium took place in the Kunstmuseum Basel – bringing together art and science. It was a great opportunity for our researchers to gain an overview of the projects carried out at our institute, as well as to discuss the latest results. Prof. Sonja Kleinlogel, Research Development Section Head at Roche, kicked off this event with a keynote lecture on designer optogenetic gene therapies for restoring vision, followed by a lively discussion on the potential and risks of this therapeutic approach. With the poster sessions and one-minute flash talks, young scientists were offered a platform to present and discuss their own work. This year, six young researchers from diverse fields were awarded a best poster prize. In his traditional "State-of-the-Union" address, Director Prof. Alex Schier embarked on a journey from the past to the future of the Biozentrum, highlighting the importance of a vibrant community. In a panel discussion, Profs. Anne Spang and Marek Basler discussed the trending topic of ChatGPT's role in research and teaching. The day filled with scientific discoveries and fresh insights came to a close with a convivial get-together.





Paired proteins give you wings

For hands, feet, or wings to develop the correct shape and size, harmonious interaction of a complex orchestra of proteins is essential. The research team led by Prof. Markus Affolter discovered that two proteins. the morphogens Dpp and Gbb, form a closely connected duo in this interplay. Only together do they ensure the proper development of the fruit fly wing.

Bauer et al., Developmental Cell



How cells kill themselves

Every day, millions of cells die in our body. Until recently, it was assumed that cells simply burst and die at the end of their life. In their study, researchers led by Prof. Sebastian Hiller provided new insights into the final step of cell death. Instead of bursting like a balloon, the protein ninjurin-1 provides a breaking point in the cell membrane. The protein assembles into filaments that work like a zipper and open the membrane, thus leading to the disintegration of the cell. The new insights are an important milestone in understanding cell death.

Degen et al., Nature

German pharma company acquired T3 Pharma

The biotech company T3 Pharmaceuticals, a spin-off from the Biozentrum, was acquired by the German pharmaceutical company Boehringer Ingelheim for 450 million Swiss francs. T3 Pharma has developed a novel technology that uses live bacteria to deliver therapeutic proteins to cancer cells and the tumor microenvironment.

Structural and functional map for forelimb movement

The motor cortex projects to diverse regions of the motor system processing information relevant to execution and learning of movements. Researchers led by Prof. Silvia Arber revealed a fine-grained anatomical and functional map between anterior cortex and medulla in mice, thus clarifying the interaction principles between these two key structures. In their study, they demonstrate the precisely matched functional organization between different cortical regions and brainstem centers involved in the regulation of skilled forelimb movements.

Yang et al., Cell









Biozentrum World Alumni **Day 2023**

On Friday, 23 June 2023, the doors of the Biozentrum swung open for our very first World Alumni Day a unique event that bridged the past, present and future. The air was filled with excitement and nostalgia as the alumni gathered for their reunion. The Alumni Day was kicked off with a welcome speech by Director Prof. Alex Schier followed by heartfelt talks by some of our renowned alumni: Nobel laureate Prof. Eric Wieschaus, Prof. Susan Gasser, Prof. Amy Gladfelter, and Prof. lain Mattaj. The four distinguished speakers were touched when presented with a special personal gift: a stone from the staircase - the last remains of the old Biozentrum building. More than 400 alumni from all over the world, who walked the halls of the Biozentrum during the past five decades, didn't miss the opportunity to visit the new building, meet old friends and lab mates, reconnect with former colleagues, share anecdotes from their time at the

"Great to be back at my academic cradle, the Biozentrum. for the Alumni Day! Feels weird to be back as a mere guest after spending so much good time here"

Biozentrum as well as reminisce about experiences and memories which shaped their lives and careers. The program featured a diverse range of activities, from scientific lectures, guided Biozentrum tours to trips and individual programs organized by the research groups. In the evening the crowd of alumni regathered for dinner, continued their conversations and visibly had a blast, many of them partying until late at night. Alexander Harms, who just recently moved his lab to ETH Zurich, commented on twitter: "Great to be back at my academic cradle, the Biozentrum, for the Alumni Day! Feels weird to be back as a mere guest after spending so much good time here, from BSc to habilitation, but it's wonderful to meet so many old and new friends!" This first Biozentrum Alumni Day fostered and renewed connections and left a lasting impression on all attendees.

Torsten Schwede: News and Views



Since the end of 2022, the artificial intelligence tool ChatGPT has been making headlines. We featured Prof. Torsten Schwede, computational scientist at the Biozentrum and Vice President for Research at the University of Basel, in an interview discussing the impact of AI systems on research and teaching. He highlighted that AI has long been part of daily life in various forms, from speech recognition to text correction, and explained the training and output of AI systems.

Regarding AI text generators, he rather sees them as opportunities and beneficial for science, for example, assisting in literature reviews and translations and reducing the workload. In academia, Torsten Schwede mentioned that ChatBots raise several challenges, particularly in teaching. The university set up the working group "AI in teaching" to discuss how AI systems can be used in teaching and integrated into modern curriculums, emphasizing the importance of understanding AI's workings and limitations. Torsten Schwede concluded that we should learn how to use these new, powerful AI tools appropriately to benefit from them.

Also in research, AI has been regularly used for many years. As a bioinformatician and structural biologist, Torsten Schwede, along with numerous scientists worldwide, has been using the AI tool "AlphaFold" to predict 3D protein structures with high accuracy. The success of AlphaFold led to the modelling of an astounding 215 million proteins last year, providing insights into the shapes of almost any protein.

Employing such Al tools, Schwede's team was able to uncover a treasure trove of uncharacterized proteins. Embracing the recent deep learning revolution, they discovered hundreds of new protein families and a novel predicted protein fold. The researchers constructed an interactive network of 53 million proteins with high quality AlphaFold structures. This network served as a source for theoretically predicting unknown protein families and their functions on a large scale. Building on their expertise in developing and maintaining the leading software SWISS-MODEL, the team made the network available as an interactive web resource, termed the "Protein Universe Atlas".

Last but not least, the Committee of the Foundation Council of the Swiss National Science Foundation (SNSF) elected Torsten Schwede as the new President of the SNSF Research Council. The renowned bioinformatician and current Vice President for Research at the University of Basel will take office on 1 January 2025.

Durairaj et al., Nature

How muscles change during endurance training

Researchers led by Prof. Christoph Handschin gained new insights into how muscles adapt to endurance training. They investigated in mice how gene expression changes in response to exercises and revealed that depending on the training state, the muscles respond differently to physical stress. In untrained muscles, endurance training activates inflammatory genes, while in trained muscles protective genes are activated, making them more efficient and resilient. Moreover, they discovered that endurance training alters the epigenetic pattern in muscles, priming them for better performance during prolonged workouts.

Furrer et al., Nature Metabolism



Molecular switch controls lipid metabolism

Our body's fat metabolism plays a vital role in energy production in our body. The team led by Prof. Anne Spang investigated lipid metabolism more closely in both yeast and human cells and discovered that a protein called Arf1 works like a molecular switch that controls the storage or conversion of lipids into energy. When the body signals a need for energy, Arf1 allows lipids to enter the mitochondria by changing the contact site between the lipid droplets and mitochondria. The results indicate that Arf1 coordinates fatty acid metabolism and mitochondrial homeostasis.



EMBO Membership for Marek Basler

Prof. Marek Basler was elected as a new member of the renowned European Molecular Biology Organization (EMBO). Basler is one of a selected group of more than 2,000 leading life scientists in Europe and beyond who have been honored by EMBO for their outstanding achievements. Including Basler, a total of 33 scientists have been recognized with an EMBO Membership since the foundation of the Biozentrum.

New SNSF Ambizione Fellows

In 2023, three young scientists from the Biozentrum received a prestigious Ambizione Grant from the Swiss National Science Foundation (SNSF). Florent Waltz will explore the biology and evolution of mitochondria in photosynthetic organisms like plants and algae. Amir Saei is investigating how polyamines, natural metabolites found in human cells, promote tumor growth. Marc van Oostrum, who joined the Biozentrum in December 2023, will work on the proteome diversity and plasticity of the thalamocortical synapse. The Ambizione Fellowships give young scientists the opportunity to carry out their own research project.

Biozentrum meets partner institutes

In a joint meeting, 40 group leaders and heads of core facilities from the Biozentrum and the Department of Biomedicine shared expertise and innovative techniques. The Biozentrum also invited the research group leaders from the Roche Institute of Human Biology (IHB) to discuss future collaborations. The newly founded institute is dedicated to research in organoids, human model systems and translational bioengineering. In this kick-off meeting, a new project grant was launched, aiming to create synergies between the two institutes. Furthermore, Prof. Michael N. Hall started as a new group leader at IHB, while maintaining his lab at the Biozentrum.

Knut Drescher awarded SNSF Consolidator Grant



Prof. Knut Drescher received a prestigious SNSF Consolidator Grant of about 1.7 million Swiss francs. Over the next five years, the biophysicist will study bacterial communities, how they develop and form resistant biofilms. The SNSF Consolidator Grant is a transitional measure to replace EU funding programs within "Horizon Europe" of the European Research Council.

Research on metabolic changes

Obesity is a well-known risk factor for diabetes and fatty liver disease. The research group of Prof. Michael N. Hall discovered that a high-fat diet alters the function of adipose tissue, thus impairing its ability to regulate blood sugar. The researchers found that a high-fat diet induces the loss of the enzyme hexokinase 2, thus leading to reduced sugar disposal in adipose tissue and disturbed sugar metabolism in the liver. The combined effect of these metabolic changes in the two tissues inevitably leads to permanently elevated blood sugar levels and ultimately to diabetes. In a second study, the team investigated liver tumor samples from mice and human patients and discovered that high levels of arginine drive metabolic rewiring in liver cancer cells. The tumor cells accumulate arginine by increasing its uptake and suppressing its consumption. At high concentrations, arginine binds to a specific factor, which triggers metabolic reprogramming and promotes tumor growth by regulating the expression of metabolic genes. As a consequence, tumor cells revert back to an undifferentiated embryonic cell state, in which they can divide indefinitely. This study also suggests new avenues to improve liver cancer treatment.

Shimobayashi et al., eLife / Mossmann et al., Cell



Basel Summer Science Academy

The "Basel Summer Science Academy" offers high school students from the Basel region the opportunity to work as scientists at the lab bench and to enjoy a program of social activities. In the 2023 summer course, 19 high schoolers were hunting for bacteriophages in the Rhine River and embarked on a thrilling scientific journey at the Biozentrum, immersing themselves in the phage world and unraveling its secrets.



Biozentrum Discovery Seminars

Our Biozentrum Discovery Seminars, with talks given by both in-house PhD students and postdocs as well as internationally renowned guest speakers, were held regularly throughout the year. Launched in 2018 to promote scientific exchange and strengthen our community, this seminar series has become a permanent fixture in the calendar of the Biozentrum scientists. The seminars cover a wide range of research topics and provide a platform for networking.

Two Biozentrum scientists among the world's most cited

Profs. Alex Schier and Torsten Schwede are among the most frequently cited scientists worldwide. To determine the "Highly Cited Researchers", the USbased company Clarivate evaluates the Web of Science database annually, which records scientific publications from a variety of disciplines. For the current list, publications from 2012 to 2022 were evaluated, and 6,849 researchers from 67 countries in 20 fields were recognized.

Biozentrum in brief.

People

Members of staff in total

32 Research groups and professors

Nationalities

Junior researchers

112 Postdocs, 137 PhD students, 42 Master students

.

Staff 46 Scientific staff, 132 Lab staff, 36 Administration

Finances

67.5 Million Swiss francs total expenditure

66.1 % University of Basel

19.9 **Swiss National Science**

Foundation

2.2 % Swiss Institute of

Bioinformatics

11.7 % Misc. third party grants

Awards, Grants & Fellowships for PhD students and Postdocs

Gustavo Aguilar Ortega, Gottfried Schatz PhD Student Prize for the Best Thesis, Biozentrum, and Prize of the Science Faculty, University of Basel Don Gary Benjamin, Innosuisse, Swiss Innovation Agency Carlos de Bento Flores, Human Frontier Science Program Fellowship Amirata Saei Dibavar, SNSF Ambizione Fellowship Patrick Fischer, EMBO Postdoctoral Fellowship Enea Maffei, J.C.W. Shepherd PhD Student Prize for Scientific Excellence, Biozentrum Eleonora Maino, AFM-Telethon - Plateforme Maladies Rares Annika Nichols, SNSF Spark Grant Marc van Oostrum, SNSF Ambizione Fellowship Joana Soares Pereira, Novartis Foundation for Medical-Biological Research Konstantin Schneider, Freiwillige Akademische Gesellschaft Basel, Grant Elisa Venturini, SNSF Spark Grant Florent Waltz, SNSF Ambizione Fellowship

Research groups 2023

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. Knut Drescher Prof. Benjamin Engel Prof. Stephan Grzesiek Prof. Michael N. Hall Prof. Christoph Handschin Prof. Sebastian Hiller

- Prof. Maria Hondele
- Prof. Urs Jenal
- Prof. Anissa Kempf
- 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. Torsten Schwede
- Prof. Anne Spang
- Prof. Erik van Nimwegen
- Prof. Mihaela Zavolan

