IMP
Research Institute of
Molecular Pathology

RESEARCH REPORT
2015–2016

Cover:
Connective tissue cells of axolotl finger.
(see also p. 34)

CONTENTS

HIGHLIGHTS

As of late 2016, the IMP has a new home. The move marks the grand finale in a series of highlights that the institute enjoyed in 2015/16.

The scientific milestones of the IMP are often marked by publications, awards, grants and honours, or talks by distinguished guest lecturers in our on-going seminar series. Each of these items is emphasised by designated chapters in this report.

JANUARY 2015

Max-Birnstiel Lecture by James Allison of the MD Anderson Cancer Center in Houston, Texas: "Boosting the Immune System to Fight Cancer".

MARCH 2015

Dignitaries from IMP, Boehringer Ingelheim, the city of Vienna and others gather for the ground-breaking ceremony of the new IMP building. The construction of the new IMP building demonstrates Boehringer Ingelheim's continued commitment to support basic research in molecular life sciences.

IMP group leader Stefan Westermann is appointed professor for molecular genetics at the University Duisburg-Essen, Germany.

MAY 2015

IMP and IMBA scientists organise the 10th annual "Microsymposium on Small RNA Biology".

Max-Birnstiel Lecture by Christof Koch, President and Chief Scientific Officer at the Allen Institute for Brain Science in Seattle, Washington, USA: "Neuronal and Theoretical Foundations of Consciousness".

The IMP hosts the 3-day EMBO workshop on "SMC proteins – Chromosomal organizers from bacteria to human".

JUNE 2015

The biochemist Gottfried "Jeff" Schatz reads from his novel *Postdoc*. A former Scientific Advisory Board member of the IMP, Jeff Schatz also chaired the search committee for the first IMP Director in the 1980s. Jeff Schatz passes away not long after the lecture, in October 2015.

Max-Birnstiel Lecture by Ruslan Medzhitov, Professor of Immunobiology at Yale School of Medicine in New Haven, Connecticut, USA: "Inflammation, homeostasis and disease".

SEPTEMBER 2015

Max-Birnstiel Lecture by George Church of the Harvard Medical School in Cambridge, Massachusetts, USA: "New Technologies for Reading and Writing Biology".

OCTOBER 2015

Andrea Pauli joins the IMP as a new group leader. Following postdoctoral research at Harvard University in Cambridge, Massachusetts, USA, Andrea Pauli studies the functions of short translated open reading frames (ORFs) in the context of development in the zebrafish.

NOVEMBER 2015

The 13th International PhD Symposium of the Vienna Biocenter (VBC) looks at "Communication" on intra-cellular, inter-cellular, intra-organismal and inter-individual levels.

Max-Birnstiel Lecture by Robert Kingston of the Harvard Medical School in Cambridge, Massachusetts, USA: "Epigenetic mechanism during development: Polycomb and chromatin dynamics".

DECEMBER 2015

Max-Birnstiel Lecture by Nobel laureate Randy Shekman of the University of California, Berkeley, USA: "Biogenesis and function of the autophagosome membrane".

Anna Obenauf joins the IMP as a new group leader. Following postdoctoral research at the Memorial Sloan Kettering Cancer Center in New York City, Anna Obenauf studies the molecular mechanisms of metastasis in cancer.

JANUARY 2016

IMP Group Leader Andrew Straw is appointed professor at the Bernstein Center Freiburg of the University of Freiburg, Germany.

Max-Birnstiel Lecture by Judith Frydman of Stanford University in California, USA: "Protein folding in the cell and the proteostasis network: biological mechanism and disease implications".

APRIL 2016

Max-Birnstiel Lecture by Nobel Laureate Sir Paul Nurse of the Crick Research Institute in London, UK: "Controlling the Cell Cycle".

MAY 2016

IMP and IMBA scientists organise the 11th annual "Microsymposium on Small RNA Biology".

JULY 2016

Max-Birnstiel Lecture by Carol Greider of the Johns Hopkins School of Medicine in Baltimore, Maryland, USA: "Telomeres and Telomerase in Cancer and Stem Cell Failure".

SEPTEMBER 2016

Max-Birnstiel Lecture by Wolf Singer of the Max Planck Institute for Brain Research in Frankfurt, Germany: "The cerebral cortex, a substrate for computing in high dimensional dynamic state space".

NOVEMBER 2016

IMP Group Leader Anna Obenauf is awarded one of five grants for "Precision Medicine" by the Vienna Science and Technology Fund WWTF.

The internationally recognized biologist Elly Tanaka takes up a position as Senior Scientist at the IMP. Her lab will study the regeneration of injured body parts in different models, including the axolotl. Before moving to the IMP, Elly Tanaka was professor at the Technische Universität Dresden in Germany and director of the DFG Center for Regenerative Therapies.

Max-Birnstiel Lecture by Adrian Bird of the University of Edinburgh: "DNA sequence and the Epigenome".

The IMP moves to the new building at Campus-Vienna-Biocenter 1.

JAN-MICHAEL PETERS

MANAGING DIRECTOR/
SCIENCE

HARALD ISEMANN

MANAGING DIRECTOR/
FINANCE AND
ADMINISTRATION

A research paradise – IMP's changes, challenges and future

In the two years since the last Research Report, IMP has seen some big changes: new group leaders, changes in research topics, new technologies and now a new building. Here Dr. Jan-Michael Peters, Managing Director Science, and Mag. Harald Isemann, Managing Director Finance and Administration, talk about the last two years and look to the future of the IMP.

What changes have you seen in the research being done at IMP?

Peters: There have been some major changes in the directions of our research and the technologies we use in the last two years. The arrival of new groups has strengthened cancer research at the IMP and introduced exciting new topics in developmental and regenerative biology. Also, the discovery of immune checkpoint therapy has led to new investigations by different groups here.

Almost everybody's work at the IMP has been changed by new technologies. New methods have made it possible to analyze different features of the human genome through high-throughput sequencing approaches, which we not only use but also develop further here at IMP. We can now visualize cells and the molecules they are composed of at astounding resolutions: there have been important developments in light microscopy and the ability to image both fixed and living cells. And cryo-electron microscopy, which involves using very low temperatures to freeze and image molecules, is making it possible to analyze the structure of protein complexes with unprecedented detail.

What have been the biggest challenges?

Isemann: The IMP continues to be challenged to remain state-of-the-art in various fields – this is a broad challenge we have seen over the past two years and will continue to see in the future. We must allocate sufficient resources to emerging technologies like those Jan mentioned, while ensuring core facilities operate smoothly with existing technologies. This has always been a constant process, but the pace at which we are phasing in these new technologies has increased significantly.

We take a strategic approach to tackling future challenges, and there is a great degree of flexibility in the research being done here. As such, we organize resources around answering the most important questions in biology, and make available the technologies and infrastructure that are needed to do that.

One of the major lessons we have learned from operating the IMP over the last 30 years is that the research building needs to be flexible, just like the research. The flexibility of the building to adapt to new challenges is a very important detail, because we don't know what we will be facing in five or ten years. The new building is technically well equipped to deal with unknown future developments, and will provide an appealing environment that also enhances communication between scientists.

What impact do you hope IMP's work will have?

Peters: Our major aim is to make discoveries. We want to understand how cells function, how they divide, how they form tissues, how they function in organs as complex as the brain, how organisms develop and how the information in the genome is used to build such organisms.

The IMP is a place where this type of knowledge is created. Our work is curiosity-driven basic research – it satisfies our curiosity and gives us a better understanding of fundamental biological processes. But in some cases, our discoveries hopefully also provide the understanding that is needed to develop better therapies.

What role do the people have in the development of this knowledge?

Peters: The people here are absolutely fundamental. Changes in group leaders have resulted in a shift in research topics. Andrew Straw and Stefan Westermann left in the time period covered by this report, and Alipasha Vaziri moved to Rockefeller, but remains affiliated with the IMP. We have three new arrivals: Anna Obenauf, Andi Pauli and Elly Tanaka. Elly Tanaka and her group have joined us from the Center for Regenerative Medicine at the TU Dresden, bringing with them a whole new area of research for the IMP. They will be investigating how invertebrate tissues can be regenerated, particularly how stem cells are activated after wounding. This is very interesting biologically, but it also has important potential medical applications.

PhD students, postdocs and technicians are equally important members of our research community: they are the ones who do the experiments and thus ultimately make discoveries that can change how we think life works. Group leaders provide the strategic direction, guidance and intellectual input in terms of asking the right questions, choosing the right approaches and helping to interpret the results. But the PhD students, postdocs and technicians are the people who actually do the work and get the results, and thereby create new knowledge. That work can also really propel people's careers; some of our alumni are now directing research institutes internationally.

Isemann: We have a very attractive, internationally competitive PhD programme and we are committed to getting the very best people. Although we look for people who want to succeed in research, not everybody will decide to pursue a scientific career. The IMP is a good foundation at every level for a career in research and we also want to train, educate and prepare young scientists for world-class performance in different areas, be that academia, industry, administration or something else.

The IMP can also be a good starting place for those who are looking for a career in industry or biotech. For example, the Vienna Biocenter Campus already hosts a couple of companies set up by former IMP members. We are now working with the City of Vienna to establish an incubator for startups in the old IMP building, to support more such spinoffs.

What excites you about the future of research at IMP?

Peters: Research can be done here beyond limits; in many ways, I think it's our imagination and our ability to identify how to address problems that limits us more than anything else. Of course, the reality is that not everything can grow to the sky. But within reasonable limits, you have the freedom to fulfill your dreams here. In that sense, it's a research paradise.

I think it is particularly exciting to have a brand new, very inspiring building. It is a beautiful workplace, and it gets people talking to each other in a way that other, larger institutions don't. This gives the IMP an interactive, cooperative, collegial spirit that has a hugely positive impact on the work being done here. ●

FACTS & FIGURES

Fascinating facts about the IMP's research, scientists, new building and subjects

A ZEBRAFISH LARVA HAS ABOUT 100,000 NEURONS; 30 MINUTES OF VIDEO FOOTAGE OF ITS BRAIN PRODUCE 1 TERABYTE OF DATA.

THE AXOLOTL CAN REGENERATE A SEVERED SPINAL CORD.

By late 2016, the IMP had 15 principal investigators, 37 postdocs, 42 PhD students and 14 master students.

Around 250 employees from 40 different countries work at the IMP.

52 percent of IMP staff are female, 48 percent male.

IMP scientists published approximately 120 papers in peer-reviewed journals in 2015 and 2016, adding to more than 2,000 IMP papers published since 1986.

IMP scientists work on 15,000 square metres of floor space in the new IMP building.

Boehringer Ingelheim invested 52 million euros in the IMP's new home.

3,000 square metres of laboratory space in the new IMP building account for an increase of 35% compared to the old building.

The new IMP building offers 160 working desks for students and postdocs – an increase of about 50 percent.

1,400 scientists work at the Vienna Biocenter (VBC).

The new IMP lecture hall offers 275 square metres and seats 280 people – the biggest facility of its kind at the VBC.

TODAY'S IMAGING TECHNOLOGY CAN REACH RESOLUTIONS OF 2 ÅNGSTROMS – THE SIZE OF JUST A FEW ATOMS.

The four research institutes at the VBC organise a joint international PhD programme and a yearly summer school.

The VBC comprises 90,000 square metres of lab and office space, plenty of room for more than 100 research groups.

In collaboration with its neighbouring institutes IMBA and GMI, the IMP runs nine core facilities.

On campus, another twelve facilities are available to all scientists, including child care for the very young.

ONLY 10 PERCENT OF PROTEIN-CODING GENES CONFER A VISIBLE PHENOTYPE IN ZEBRAFISH.

THE NEMATODE WORM *C. ELEGANS* HAS EXACTLY 302 NEURONS.

Filter pipette tips
in container.

CURRENT RESEARCH

MEINRAD BUSSLINGER

MEINRAD BUSSLINGER

PHD:
UNIVERSITY OF ZURICH, SWITZERLAND (1980)

POSTDOCTORAL RESEARCH:
MRC, LONDON, UK

JUNIOR GROUP LEADER:
UNIVERSITY OF ZURICH
(1983–1987)

SENIOR SCIENTIST:
IMP, VIENNA (SINCE 1987)

DIRECTOR OF ACADEMIC AFFAIRS: IMP, VIENNA
(SINCE 2007)

SCIENTIFIC DEPUTY DIRECTOR: IMP, VIENNA
(SINCE 2013)

Control of B cell immunity

How do transcription factors control the development of B cells and plasma cells?

B cells are an essential part of the human immune system, producing antibodies – immunoglobulins – to protect the body from pathogens. Immature cells are guided along different pathways to become one of several types of B cell. But how is this controlled?

Dr. Meinrad Busslinger has been investigating this for many years, having identified the "B cell identity factor" – a transcription factor called Pax5 that is strictly and specifically expressed during B cell development, from early to mature B cells. Following this discovery, which showed how repressing alternative lineage possibilities is key to B cell development, he has continued to study Pax5 and related molecules to understand the control mechanisms behind B cell development.

"We think we understand certain processes, like how B cells develop, but there is still a lot we need to understand at the molecular level," said Dr. Busslinger.

In B cell development, the immunoglobulin genes are rearranged. The heavy chain gene is assembled at the first committed stage of B cell development. The cell is then sent to the next stage, in which the light chain gene is rearranged. Only then is the B cell receptor, used to recognize invaders, expressed on the cell surface. At this point, the cell leaves the bone

SENIOR SCIENTIST/
SCIENTIFIC DEPUTY DIRECTOR:
MEINRAD BUSSLINGER

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GRACE JIE LIU,
MARTINA MINNICH,
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(UNTIL 30.07.2016)
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QIONG SUN

marrow, where it developed, and moves to the spleen or a lymph node to mature. It then turns into a plasma cell: a cell that produces antibodies and becomes part of the immunological memory.

Pax5 is one of several transcription factors that have a role in B cell lineage commitment and development; E2A and EBF1 specify the lineage, Ikaros controls the signalling of the pre-B cell receptor, and Blimp1 controls differentiation to plasma cells at the final stage of development. All these factors are expressed in mature B cells, and Dr. Busslinger is now investigating what their roles are in controlling the way B cells work.

Ikaros, for example, plays a role in suppressing autoimmunity. Dr. Busslinger's team inactivated the gene for Ikaros *(Ikzf1)* in mature B cells in mice. This resulted in the B and T cells being constantly activated and leading to the secretion of autoantibodies – antibodies that attack the body itself, causing autoimmune conditions. This research has shown that certain signalling pathways were hyperactivated when cells lacking Ikaros were stimulated, so Dr. Busslinger is now looking more closely at the way Ikaros works to suppress these signalling systems.

He is also investigating the molecular wiring of antibody-secreting cells – short-lived plasmablasts and long-lived plasma cells – using conditional gene inactivation as well as CRISPR/Cas9. "There are many transcription factors that people think are important for plasma cell development, but what they do at the molecular level is not yet clear," explained Dr. Busslinger. "The idea is to use these kinds of tools to systematically ask what genes are essential for plasma cell development."

CRISPR/Cas9 is helping researchers gain new insights into well-known cellular processes and molecules, such as Pax5. The role of Pax5 is so crucial in controlling cell identity that the original publication – in *Nature*, in 1999 – has been reprinted recently in a different journal to bring it back to the forefront for those who want to dig deeper. Dr. Busslinger continues to build on previous findings, following the discoveries and asking new questions.

"When you're excited about a particular problem in biology, the most important thing is to always ask the pertinent next question; you cannot always do what you set out to do, you have to go with the questions."

One such question is how Pax5 is linked to a certain type of cancer. When Pax5 is mutated or translocated – linked to a different gene on another chromosome – it can be associated with B-cell acute lymphoblastic leukaemia (B-ALL). By studying mouse models, Dr. Busslinger and his group have shown that when combined with the protein Etv6, Pax5 is potently oncogenic. They are now investigating similar protein combinations to see how they work at a molecular level.

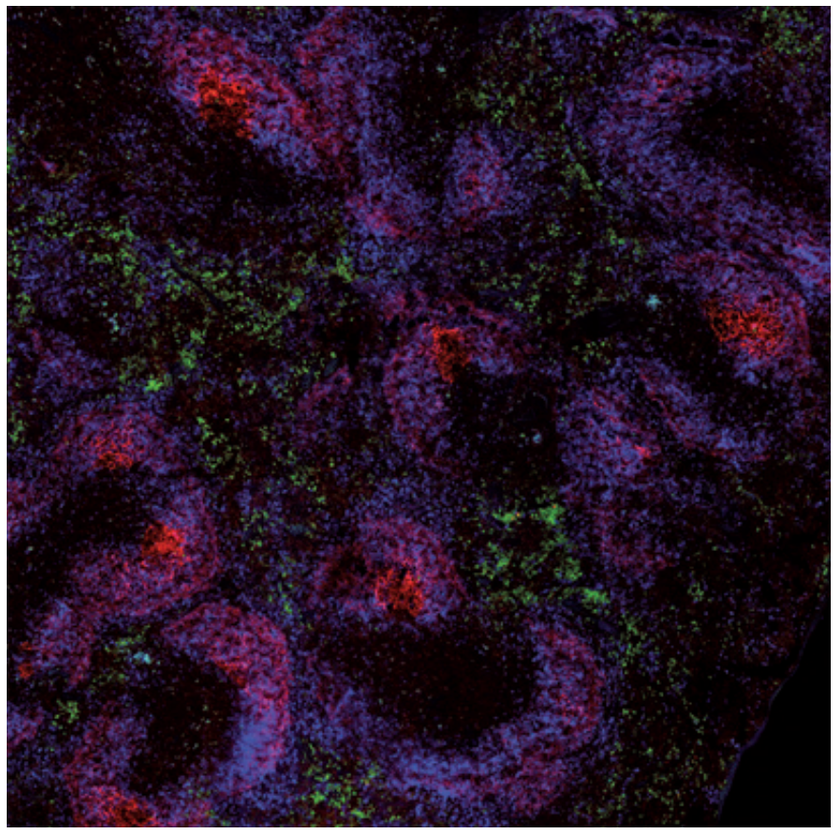

FIGURE:
B cell immunity provides acute and long-term protection of the host against infection by generating and secreting high-affinity antibodies that recognize a shear unlimited number of pathogens. The immune reaction against foreign antigens takes place in peripheral lymphoid organs such as the spleen. A section through a mouse spleen reveals the distinct locations of the different B cell types; B cells (blue) in the follicle, B cells (red) in the germinal center within the follicle and antibody-secreting plasma cells (green).

TIM CLAUSEN

TIM CLAUSEN

PHD:
TECHNICAL UNIVERSITY MUNICH, GERMANY
(1997)

POSTDOCTORAL RESEARCH:
MPI OF BIOCHEMISTRY, MARTINSRIED, GERMANY

GROUP LEADER:
MPI OF BIOCHEMISTRY, MARTINSRIED, GERMANY
(1999–2002)

GROUP LEADER:
IMP, VIENNA (2002–2009)

SENIOR SCIENTIST:
IMP, VIENNA
(SINCE 2009)

Controlling protein quality

How does the structure of chaperones and proteases that control protein quality relate to their function, and how could this be used to tackle disease and antibiotic resistance?

When a cell's molecular machines build a protein, they have to piece it together and then fold it in a very specific way. Misfolding or stress, such as overheating, can cause proteins to unfold and group together. This aggregation can be dangerous biologically, and it could mean potentially vital proteins are not available to the cell. Aggregated proteins are implicated in several diseases, including Alzheimer's and Parkinson's disease.

To avoid misfolding and aggregation, cells have a process called protein quality control, in which molecules called chaperones and proteases monitor proteins to rid the cell of errors. Dr. Tim Clausen and his group analyse the relationship between the structure and function of these quality control molecules, with the aim of uncovering new ways to tackle related diseases.

"It's not completely clear why misfolded and aggregated proteins are dangerous," Dr. Clausen explained. "It could be that by accumulating proteins you miss the ones you need. It could also be that the aggregate itself is physically bad for the cell. Luckily, chaperones and proteases can deal with them."

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MASTER STUDENT:
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RESEARCH ASSOCIATE:
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Chaperones are proteins that can prevent aggregates from forming and even reverse the aggregation process, and proteases are enzymes that can chop up damaged proteins that cannot be saved. One such protease in eukaryotes is the proteasome, one that Dr. Clausen calls a "radical protein shredder."

Similarly radical chaperone machinery that interests the lab is the "heat-shock protein" Hsp104. Made up of six units, the protein is a hexamer that forms a barrel with a pore in the middle. The Hsp104 protein grabs the substrate – an aggregated protein, for example – and threads it through the pore, pulling it out of the aggregate.

In general, proteases and chaperones work together to monitor stressed and misfolded proteins, determining whether they can be refolded correctly and, if not, whether they need to be chopped up. Sometimes chaperones and proteases also join together to form complexes – large, complicated molecular machines – removing damaged proteins from the cell.

This kind of machinery is also found in bacteria, many of which have evolved to withstand extreme environmental stresses, from the acid in a person's stomach to the heat of a deep-sea vent. These bacteria have very efficient protein quality control systems, which several antibiotics target.

Recently, Dr. Clausen's group found that when a protein is misfolded or aggregated, it is marked for degradation: an arginine residue of the protein is phosphorylated. A specific protease complex, a simple bacterial version of the proteasome, recognizes this degradation tag, and shreds the protein into tiny peptide pieces.

"Previously it wasn't clear how the molecular machine selects which proteins to deal with," Dr. Clausen commented. "The system we have identified is essential for bacteria to survive stressful situations. Targeting this pathway could give us a new approach for developing novel antibiotics."

Dr. Clausen is also looking at whether phospho-arginine only occurs in bacteria; other organisms have the receptor for recognizing phospho-arginine so it could be that it is used more widely. And if phospho-arginine can have such an impact on a bacterial cell, are there other modifications involved in protein quality control?

Looking for other exotic protein modification is a new direction for the lab. Curiosity-driven research can lead scientists down exciting new paths like this; it is the surprises in this process that drive Dr. Clausen.

"I'm fascinated by how intricate these kinds of molecular setups are; we all take this for granted but as a scientist I think it's important that you can lean back and enjoy it. When you work with a protein and you see the structure, you might be the first person in this world to see it, and then you can start to think, 'Wow, what does it mean?' Making this kind of connection is something real that you see. If you're open minded the research can take you to surprising places." ●

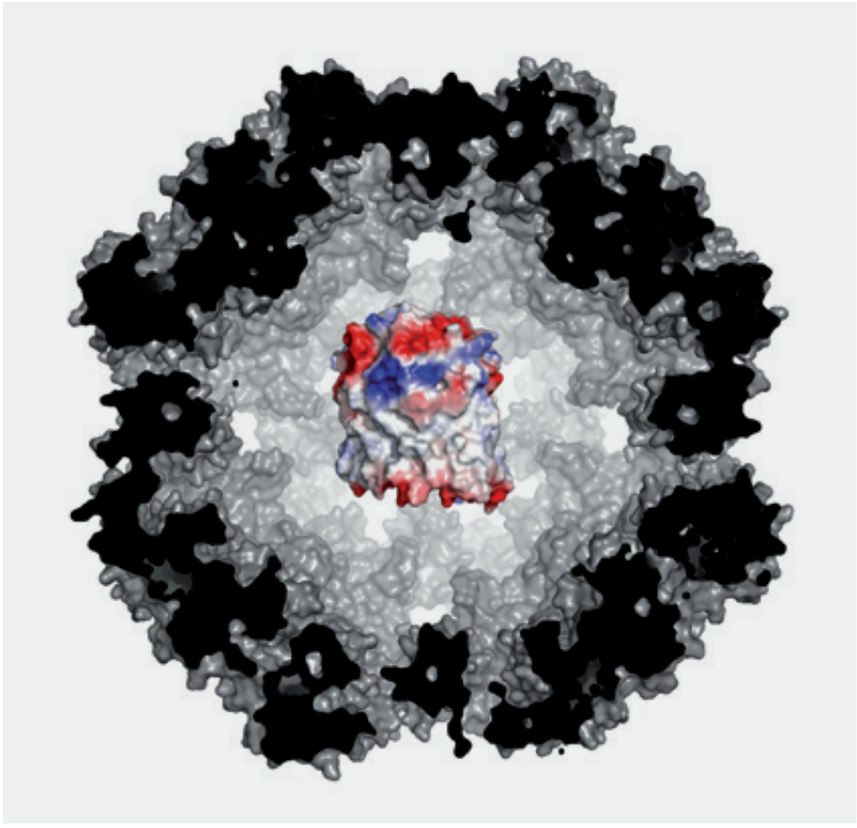

FIGURE:
Monitoring protein function in a case-by-case manner: the illustration shows the surface of the half-sliced DegP chaperone with a captured substrate. Of note, DegP is able to distinguish between proteins that can be refolded from hopelessly damaged proteins. In the latter case, DegP gets nasty, switches into a protease and digests the aberrant molecules.

LUISA COCHELLA

LUISA COCHELLA

PHD:
JOHNS HOPKINS SCHOOL OF MEDICINE, BALTIMORE, USA (2006)

POSTDOCTORAL RESEARCH:
COLUMBIA UNIVERSITY, NEW YORK, USA

GROUP LEADER:
IMP, VIENNA (SINCE 2013)

Understanding biological mechanisms with precision

How do microRNAs contribute to cellular diversity through the regulation of gene expression?

A single cell gives rise to many different cell types – muscle, skin, neurons, gut – and this differentiation is controlled by gene expression. Dr. Cochella wants to understand the mechanisms that switch certain genes off progressively during the early stages of development starting with the fertilized egg, then in specific groups of cells that become tissues and organs. To do this, she works with the tiny nematode worm *C. elegans*.

"Development is when gene expression is most dynamic; this seemed like the perfect setting where there would be a lot of interesting molecular mechanisms and where I could study something that has an impact on a beautiful biological process," explained Dr. Cochella. "*C. elegans* has a level of complexity that is sufficient for learning something about how higher animals work but it's still simple enough that we can ask questions at a very precise level."

Because it is transparent and very small, she and her group can identify each of the worm's 959 cells, which are invariant in every animal, and see which genes are expressed in each cell. They are also able to do a variety of genetic manipulations to delete, introduce or express genes where they are not meant to be.

A lot of the Cochella group's focus is on the nervous system, as roughly one-third of the worm's cells – 302 cells – are neurons. While the animal's skin cells are all quite similar, the neurons are not: *C. elegans* has more than 100 different classes of neuron. Sensory neurons are used to sense changes in the environment, interneurons compute what the response should be and motor neurons make the worm move toward or away from the stimulus. What makes all of these neurons different is which subsets of genes they each express.

Gene expression can be controlled at the level of transcription into mRNA, but also post-transcriptionally, before the mRNA is translated into protein. One such class of post-transcriptional regulators is composed of microRNAs or miRNAs. Dr. Cochella aims to understand how miRNAs contribute to creating cellular diversity during development.

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Specifically, Dr. Cochella and the team are looking at where miRNAs are expressed in *C. elegans* at single cell resolution – using reporter molecules they can light up the cells in which certain miRNAs are expressed. One miRNA they identified is only produced in three pairs of neurons in the worm's head that sense carbon dioxide. Removing the gene that encodes the miRNA affected the ability of the worm to sense carbon dioxide – a vital ability in the wild.

"Of course on our plates in the lab it doesn't really mean that much, but in the wild this is a response that basically can determine whether the animal survives and produces offspring or not. We found that this microRNA plays a role in the function of these particular neurons and we wanted to understand how it does that."

What they found was unexpected: the miRNA improves the sensing property of these cells by repressing two "housekeeping" genes that are expressed everywhere else, highlighting the importance of knowing which genes are specifically turned off in a specialized cell. They think this may be a general strategy employed in other systems and other animals.

Dr. Cochella and the team are now studying other miRNAs in *C. elegans*; they are also developing a method to extract and sequence all the miRNAs from a single neuron, to help them understand better the function of the miRNAs in different cells.

"The precision and depth with which we can address questions that are relevant to biology is really quite spectacular. We can find out how a particular gene is expressed in a certain cell, what it does in that cell and what the impact of that is on an organism that has hundreds of different cells, each one with its own function within that animal." ●

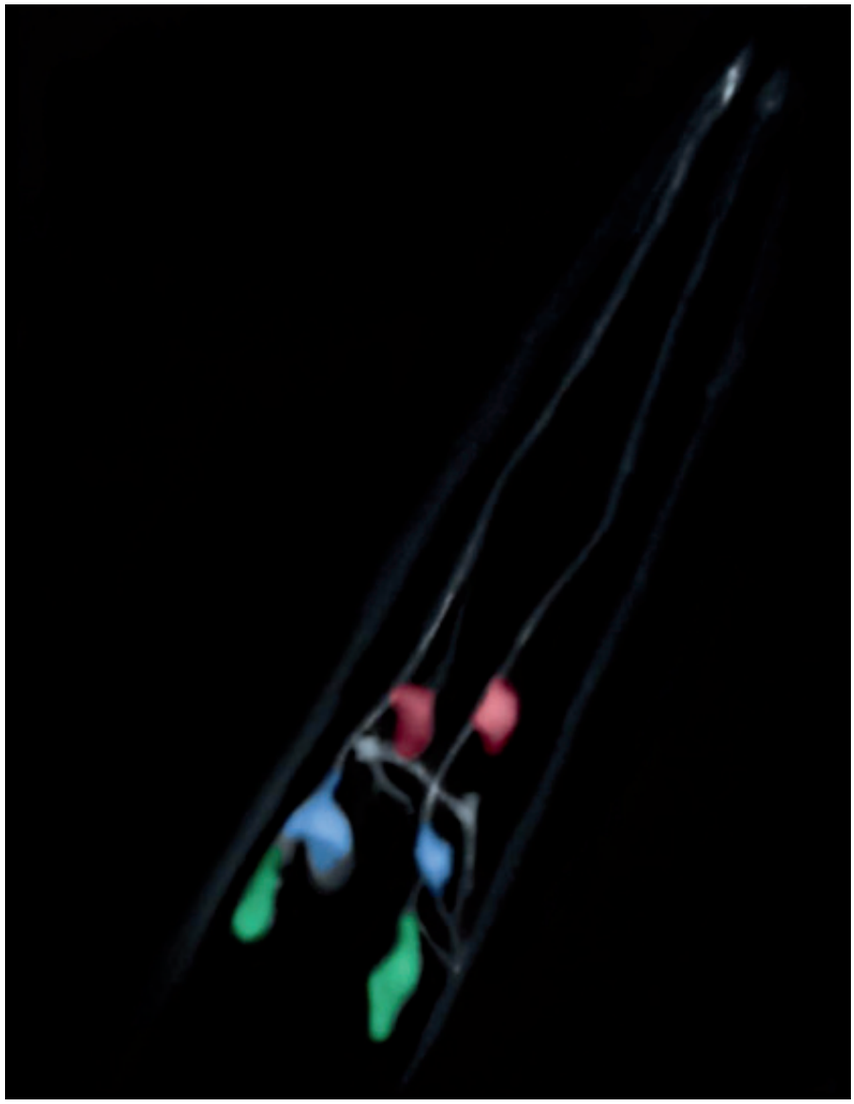

FIGURE:
C. elegans mir-791 is expressed in the main carbon dioxide sensing neurons and is necessary for the behavioral response of the worms to increased CO_2. Shown here is a fluorescence image of a live *C. elegans* larva expressing a GFP-based transcriptional reporter for *mir-791*, in the context of a large genomic clone. GFP labels the cell bodies of three bilateral pairs of neurons in the head of the worm, as well as their axons and dendrites, the latter of which can be seen extending to the tip of the animal's nose. The soma of the three pairs of neurons have been false colored in red, blue and green.

WULF HAUBENSAK

WULF HAUBENSAK

PHD:
MPI FOR MOLECULAR CELL BIOLOGY AND GENETICS, DRESDEN, GERMANY (2003)

POSTDOCTORAL RESEARCH AND STAFF SCIENTIST:
CALTECH, USA

GROUP LEADER:
IMP, VIENNA (SINCE 2011)

Connecting brain, mind and behaviour

What is the neural basis of emotions and how do genes and drugs control them?

If there was a spider in the corner of the room, would you to be scared? What if it moved closer; would you be more scared? How should you respond to it? It is your emotions that help you successfully cope with such challenges – or seize opportunities.

Dr. Haubensak and his group investigate how the brain helps us to navigate these types of situations. Using techniques like calcium imaging and optogenetics, which uses light to activate neurons, they can observe and manipulate the emotional parts of the brain. Ultimately, their aim is to understand how molecular and genetic interactions control the activity of neuronal circuits, emotional states and behavioural responses.

"In exploring basic emotional behaviours we learn first of all about the neuronal basis of emotions as a central part of our mind," Dr. Haubensak explained. "But we also learn about how the brain extracts important information and computes the correct

GROUP LEADER:
WULF ECKHARD HAUBENSAK

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BARBARA WERNER

behavioural responses. And this is what I am ultimately interested in: understanding how the brain makes sense of the world."

One aspect he is studying is temporal control of emotional responses. Sometimes, obtaining future rewards requires you to wait before reacting. How is this impulse control encoded in the brain? In another project he investigates response control in space. Think again about the spider; what is the mechanism that controls our fear in space? There seems to be an inhibitory mechanism in the brain that is controlled by space: the smaller the space, the lower the inhibition. So as the spider approaches, the space decreases and the fear increases.

"An important biomedical aspect of our research is that by investigating emotion-related processes, we might also better understand current treatments or one day even develop new therapies," said Dr. Haubensak.

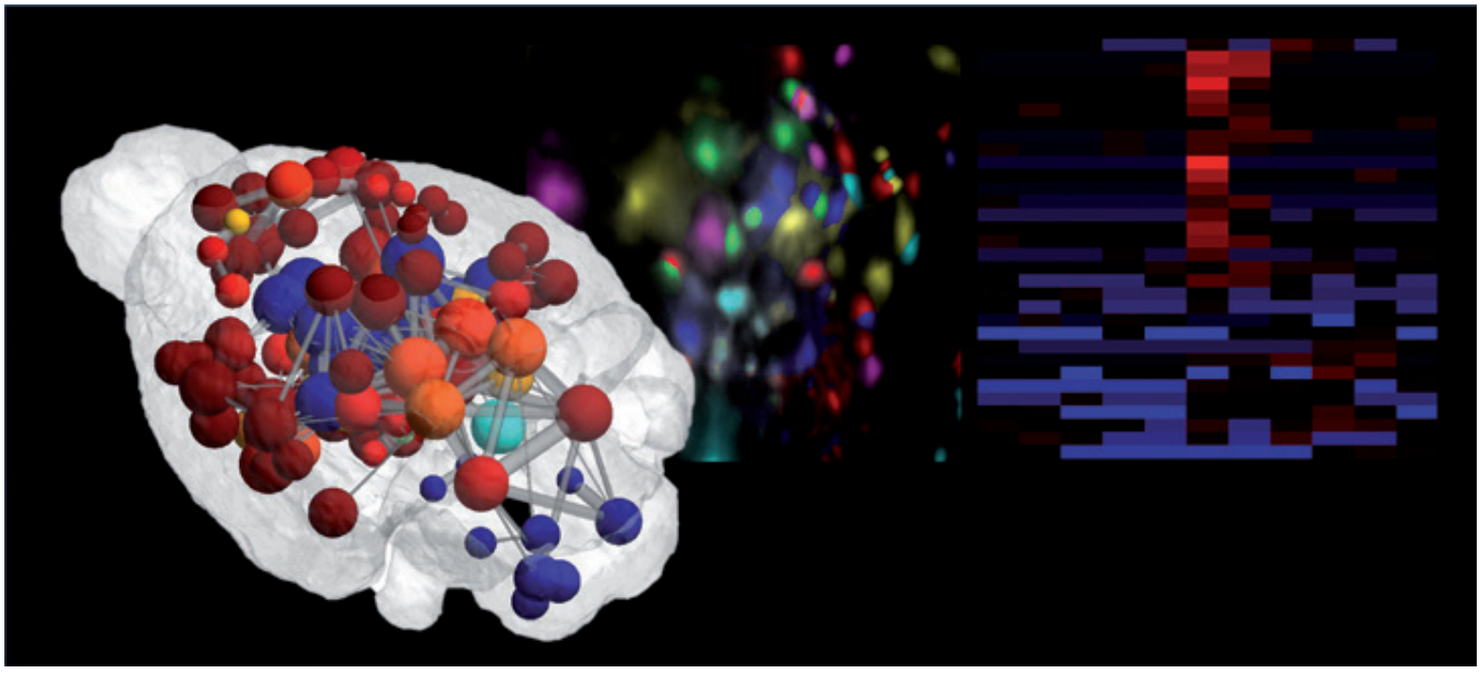
Take benzodiazepines for example; these sedatives have been widely used for more than 50 years. We have a relatively good understanding of their molecular receptors and their effects on the activity of individual neurons. However, how their interactions with complex neuronal networks flip the brain from an anxious to a neutral state is not fully understood. By studying the role of these drugs in modulating neuronal activity, brain states and emotional responses, Dr. Haubensak aims to shed light on some of these unknowns.

To do this, it is vital to have a comprehensive understanding of the brain's circuitry. Neuroscience is a fast-moving field, and there are several major international projects mapping genes and circuits in the brain. This creates the opportunity to mine the available data and explore the functional organization of the brain computationally.

Dr. Haubensak recently started an initiative to fuse brain data with genome wide association studies (GWAS) to investigate how genetic interactions control brain circuitry and behaviours. This traces a functional map of the brain that shows where the group should look using experimental techniques like optogenetics.

"We use many different technologies to identify circuit motifs the brain uses to solve a specific behavioural problem," Dr. Haubensak said. "Ultimately, I think all of us have an inherent drive to learn something about ourselves. We try to do this by exploring the building blocks of emotions, which I think is the most fascinating part of human psychology."

FIGURE:
Global brain network (fMRI, left) and local neuronal ensembles in one of its nodes (Ca^{2+} imaging, middle, right) encoding aversive experiences.



DAVID KEAYS

DAVID KEAYS

PHD:
UNIVERSITY OF OXFORD, UK (2006)

POSTDOCTORAL RESEARCH: WELLCOME TRUST TRAINING FELLOW, UNIVERSITY OF OXFORD, UK

IMP FELLOW, VIENNA (2008–2012)

GROUP LEADER:
IMP, VIENNA (SINCE 2013)

The search for nature's compass

How do animals sense the earth's magnetic field, and can this be used to study the brain?

Homing pigeons have been known to travel distances of 1,800 kilometres in a race, finding their way home using a complex navigation system. Like many other animals, including birds, turtles, lobsters and whales, pigeons use the earth's magnetic field to navigate. Dr. David Keays is trying to understand how this mechanism works, and if it's possible to harness it to activate specific regions of the brain.

For more than a decade Dr. Keays has studied the genes that are mutated in different brain abnormalities in humans and mice, but a chance encounter with Professor Gero Miesenboeck led him down a completely new path. Professor Miesenboeck pioneered a technique called optogenetics, allowing scientists to activate neurons by shining blue light on them. This is effective in organisms such as *C. elegans*, which are transparent, but is much more challenging in mice, which have opaque skulls. "What if it was possible to do something similar but using magnetic fields instead of light?" mused the Australian scientist.

"The idea was we could take nature's magnetoreceptor, genetically express it in neurons, then expose the animals to magnetic fields," explained Dr. Keays. "I started reading more about this and it turns out

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(UNTIL 30.09.2016),
ROBERT HICKMAN
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MARIA INES LECA,
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that we really don't understand how animals detect magnetic fields. It's clear that animals do detect magnetic fields, but the critical question is how do they do this?"

One idea is that cells that can detect magnetic fields – magnetosensitive cells – have an internal compass. This can be seen in certain aquatic bacteria, which have small crystals made of an iron oxide called magnetite – the same metal used in compasses. Might higher organisms have co-opted this strategy? Dr. Keays and his team recently discovered that sensory hair cells in the pigeon's inner ear contain iron balls.

Dr. Keays and his group are now working on an experiment to look at brain regions that are activated when the pigeon is exposed to a magnetic field; if the hair cells are associated with magnetic sensors, they expect to see activation in the acoustic or vestibular regions of the brain. But this poses a challenge: we are surrounded by magnetic contamination. Their solution? A fully custom-built magnetically shielded room at the IMP.

"It's a very difficult problem because we're working with pigeons which are not genetically so amenable, and contamination is unavoidable in most settings. It's also a conceptually challenging problem; whereas it's easy to wave your hand in front of your eyes and understand that's where your photoreceptors are, or play music into your ear to locate the sound receptors, magnetism is different – detector cells could really be anywhere, making them hard to find."

In tackling such a formidable scientific problem, Dr. Keays, has decided to hedge his bets. While half his lab delves into pigeon magnetism, that other half aims to understand how neurons migrate in the developing brain. Tubulin, a protein that makes up the cell skeleton, plays a key role in neuronal migration, and mutations in the tubulin genes can cause neurological diseases. To understand how, Dr. Keays and his group use the mouse as a model system and employs next-generation sequencing to study the exomes of patients with neuronal migration disorders.

Mouse brain genetics and pigeon magnetosensing are undeniably different, but there are many connections, as Dr. Keays explained:

"The methods we use are very similar – we're very focused on anatomical studies using all the latest tools in cellular and molecular biology to answer a specific question. We adopt a reductionist mind-set where we try and perform experiments in a blinded, controlled way, ideally changing one thing at a time and incrementally building on a foundation."

FIGURE:
The Keays lab employs pigeons as a model system to understand the molecular and cellular basis of the magnetic sense.

THOMAS MARLOVITS

THOMAS MARLOVITS

PHD:
UNIVERSITY OF VIENNA, AUSTRIA (1997)

POSTDOCTORAL RESEARCH: UNIVERSITY OF VIENNA, MPI OF BIOPHYSICS AND YALE UNIVERSITY, USA

GROUP LEADER AT IMP AND IMBA, VIENNA (SINCE 2005)

PROFESSOR OF STRUCTURAL AND SYSTEMS BIOLOGY (SINCE 2013)

DEPUTY DIRECTOR OF CSSB-CENTRE FOR STRUCTURAL SYSTEMS BIOLOGY, HAMBURG, GERMANY (SINCE 2014)

Life at a molecular scale

What does the molecular machinery that transports bacterial toxins into cells look like, and how does it function?

A *Salmonella* cell glides around between host cells until it lands on one and secretes proteins through the membrane. The proteins cause the host cell to ripple and swallow the bacterium – the cell has been infected. The bacterium used specialized machinery to secrete its ripple-inducing proteins, but what does this machinery look like, and how does it work?

Dr. Thomas Marlovits is interested in understanding this, so he visualizes the molecules that do the job. The *Salmonella* protein-delivering machine – the injectisome – looks and works like an injection device. Many of the experiments done to determine the structure and function of cellular machinery like the injectisome involves taking indirect measurements and accumulating evidence; Dr. Marlovits and his group just want to look at it directly.

"We are biochemists and structural biologists, we like to uncover the underlying molecular mechanisms that give rise to certain biological outputs," said Dr. Marlovits. "It's really mind-blowing what one can do – it's possible to get deep, atomic information from just a handful of individual molecules that you're looking at."

To do this they use a technique called cryo-electron microscopy. The first step is to isolate the molecular machines, then shock-freeze them in a very thin layer of ice or buffer. Freezing them very fast prevents the water from forming crystals – something that

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MASTER STUDENTS / ROTATION STUDENTS:
GEORGI NIKOLOV, TOBIAS THÖNI

ROTATION STUDENTS:
LUCAS GUENTHER SCHOLL, MARIJA SIMONOVIC, GREGOR WEISS

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LAB MANAGER:
JULIA MAYR

STUDENT ASSISTANT:
NICOLE NUSSBAUM (UNTIL 31.12.2015)

can cause the molecules to distort through sheer force. This technique also avoids staining, which has a major impact of the structure of molecules.

Imaging through a sample provides a two-dimensional image, but Dr. Marlovits and his group want to look at cellular machinery in three dimensions. To achieve this, they record images of different molecules from different orientations. With conventional mathematics they can produce a three-dimensional reconstruction.

With this method they can see the underlying three-dimensional structure of the amino acids and how they are positioned – they can see helices and sheets, and look in detail at how they are organized and folded.

Looking directly at the structure of a molecular machine also provides clues as to how it works. In the case of the injectisome, Dr. Marlovits was able to hypothesize that there is a specific tunnel within the structure through which proteins are transported. This was an idea indirect measurements would not have inspired. The images also revealed something puzzling: the tunnel through the injectisome was smaller than some of the proteins it was meant to transport.

For a clearer picture, he needed to see the transfer in action. This meant shock freezing a whole bacterium, putting that sample into the microscope and recording images from different angles by turning the stage. Doing this, he could see, for the first time, what was really happening inside the cell. The imaging revealed that the proteins being delivered were completely unfolded to fit through the tunnel.

"It's astonishing to see such a static, beautiful assembly of molecules. This *in situ* imaging is even more thrilling, because you're not taking things out of their context – you're observing those molecules and how they work in action."

When Dr. Marlovits started in the field 20 years ago, it was possible to reach resolutions of 25 angstroms – about the width of a DNA molecule – but today's technology can reach resolutions of 2 angstroms – the size of just a few atoms.

In addition to building our understanding of fundamental molecular mechanisms, in the future knowledge at this level of detail could be applied to designing antibodies against supposedly undruggable targets. The secretion power of the system could be harnessed to deliver antibody therapy directly into particular cells.

In the meantime, there is much to be discovered, according to Dr. Marlovits. "There are still many questions. How are the substrates selected? How are they recognized? How are they transported? We have come so far in structural biology and with continuing advances in technology we will be able to continue answering more and more complicated and detailed questions." ●

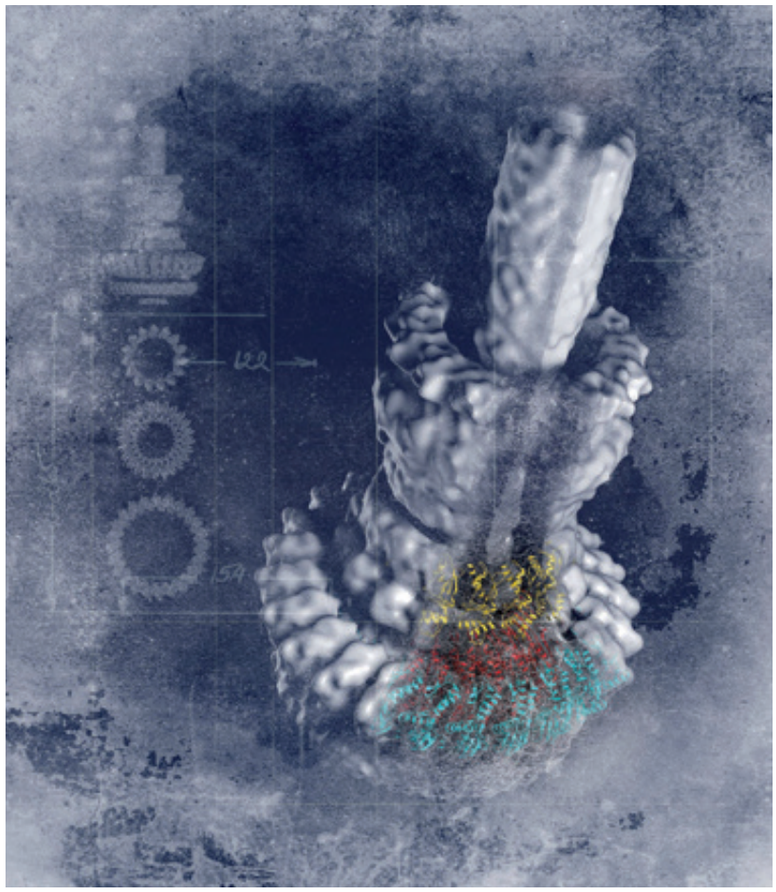

FIGURE:
Three-dimensional reconstruction of the needle complex that is used by *Salmonella* to make contact with the host cell.

ANNA OBENAUF

ANNA OBENAUF

PHD:
MEDICAL UNIVERSITY OF GRAZ, AUSTRIA (2010)

POSTDOCTORAL RESEARCH: MEMORIAL SLOAN KETTERING CANCER CENTER (MSKCC), USA

GROUP LEADER:
IMP, VIENNA (SINCE 2015)

Exploiting cancer cells' vulnerabilities

What are the molecular mechanisms behind cancer? How can we exploit the vulnerabilities of cancer cells to find opportunities for new therapies?

After months in remission, a cancer patient receives the news that the cancer has spread to other organs. This is not an uncommon story – cancer cells leave the primary tumor, where they may have been for years, overcome many obstacles and stresses, metastasize throughout the body, and take over vital organs such as the liver, the lung, or the brain.

Only the most resilient cells manage to form metastases; these cells are also well equipped to withstand other stresses, such as pressure from therapeutic drugs. Consequently, metastases frequently become rapidly drug resistant, limiting the efficacy of current therapies. Metastases are ultimately responsible for more than 90% of cancer-related deaths.

How do cancer cells overcome the obstacles to metastasize? Dr. Anna Obenauf believes the mechanisms and pathways behind metastasis are important to tackle alongside classical proliferation driving genes and pathways.

"It's really interesting to figure out how cancer cells metastasize and become resistant to the therapies that have been developed to target them," she said. "In theory, cancer cells are disadvantaged – the body has put so many control mechanisms in place to make sure cells function how they should function and die, if they don't fulfill these functions any more. Cancer cells have found innovative ways to overcome these control mechanisms and hijack many processes to their advantage."

By identifying specific "driver mutations" in tumors, it can be possible to develop tailored, mechanism-based treatment strategies. Several such "targeted therapies" are already being used in the clinic but very small fractions of the tumors they are designed to treat can be resistant or are prone to develop a resistance mechanism. Dr. Obenauf looked at what happens to resistant cells when the tumor falls apart around them as a result of treatment.

"The tumor doesn't go down without a fight; drug resistant cells secrete hundreds of different factors that signal to neighboring cells. This secretome helps the non-resistant cancer cells to survive and potentially develop resistance mechanisms, and it gives pre-existing drug resistant cells a growth boost as they thrive on the goodies in the micro-environment."

GROUP LEADER:
ANNA CHRISTINA OBENAUF

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IZABELA KRECIOCH

The result of the drug-responsive cells' therapy-induced secretome (TIS) is that the resistant cancer cells metastasize heavily. Dr. Obenauf showed in animal models that the cancer cells can colonize regressing tumors in different parts of the body, which act as "magnets," attracting resistant cells that are in circulation. Because of this, a pocket of resistant cells in one tumor could be enough to make other tumors resistant, potentially explaining why the cancer often recurs during treatment in several metastases simultaneously.

Understanding how highly metastatic, drug-resistant cells emerge and targeting them before they take over the metastases could lead to longer-lasting treatment responses.

One strategy could be to harness the immune system. Cancer cells are known to protect themselves by blocking immune cells' checkpoint proteins – off-switches that stop the immune cells from attacking. Recently developed immunotherapies reactivate the immune cells and have led to durable responses in a small subset of patients. The challenge is now to extend these successes to more patients; Dr. Obenauf believes combining immunotherapies with a therapy that targets the cancer cells could be a successful strategy.

"By studying the changes in the tumor during therapy, we are trying to systematically identify the best therapy combinations and schedules," she said. Dr. Obenauf is now examining three main areas: identifying mechanisms that lead to the emergence of drug resistant cells; analyzing the effect the TIS has on cancer and immune cell populations; and integrating clinical and experimental data to pinpoint vulnerabilities of cancer cells. These three areas will all contribute to developing more effective combination therapies.

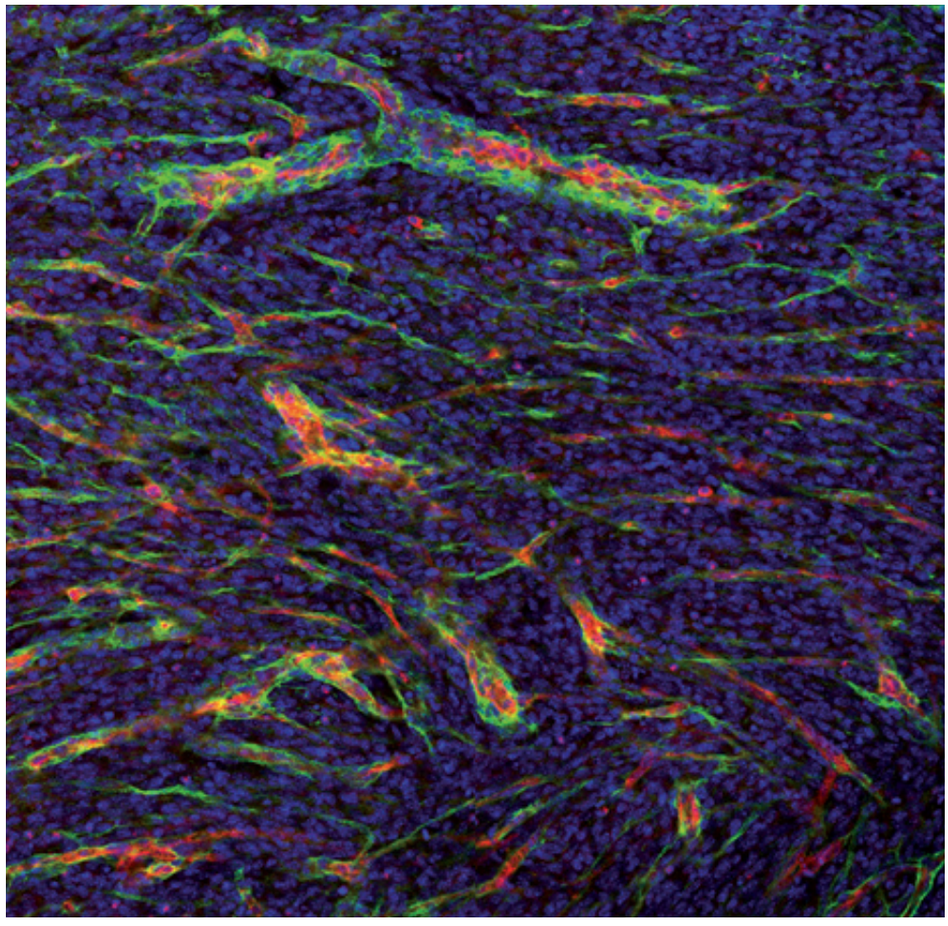

FIGURE:
Section of a tumor (mouse melanoma) interwoven with blood vessels.

ANDREA PAULI

ANDREA PAULI

PHD:
OXFORD UNIVERSITY, UK
(2009)

POSTDOCTORAL
RESEARCH: HARVARD
UNIVERSITY, USA

GROUP LEADER:
IMP, VIENNA (SINCE 2015)

Found in translation

What is the function of short open reading frames in embryonic development?

There are many short open reading frame (ORF)-containing transcripts that researchers previously thought to be noncoding. But when Andrea Pauli started looking at one of these more closely in zebrafish, she made a surprising discovery: not only was the region transcribed, but it also encoded a protein essential for zebrafish embryogenesis.

"I was interested in finding out whether these novel transcripts matter – we didn't know if they would have a function or if transcription just happens because chromosomal regions are accessible," she explained. "We discovered something exciting: many regions not known to encode proteins are in fact translated, and some encode short proteins."

The first short protein she characterized in her postdoctoral time at Harvard University was Toddler (also known as Apela or ELABELA). Toddler signals mesendodermal cells to move, and it is essential in zebrafish embryogenesis – without it, the embryos do not have a functioning heart and die quickly.

Since joining IMP in 2015, Dr. Pauli and her group have continued to study how Toddler controls cell migration during gastrulation, a time when the three germlayers form. They use genetic, molecular, cellular and genomics methods in zebrafish embryos to investigate this question.

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ANDREA PAULI

PHD STUDENTS:
LUIS ENRIQUE CABRERA QUIO, SARAH HERBERG, JESSICA STOCK

BIOINFORMATICIAN:
TOMAS KAZMAR

TECHNICAL ASSISTANT:
KARIN PANSER

TRAINEE:
NINA EL-ASRAG

In addition to Toddler, the group has been working with several of these short ORFs to determine their function in the context of zebrafish embryogenesis. It is known that only about 10 percent of protein-coding genes confer a visible phenotype. Consistently, mutating 12 of these ORFs has already revealed one additional ORF that has an essential function during zebrafish embryogenesis.

The zebrafish is an ideal model system for this work. Its embryos are transparent and develop outside of the mother, which means they are accessible for imaging and other assays. Hundreds of eggs are produced a day and embryogenesis happens fast, making them what Dr. Pauli calls a very powerful "*in vivo* test tube" system. And, importantly, because it is a vertebrate, understanding how a conserved protein like Toddler functions in the zebrafish could also tell us something about how this molecule works in humans.

"Embryogenesis as a process is fascinating. Scientists have studied it for years so we know quite a bit, but we still don't understand exactly how it works. It's such a fundamental process with so much still to be discovered. It's exciting to investigate the mechanisms in zebrafish so we can understand more about how it possibly works in humans."

Another, even less explored territory Dr. Pauli and her group are focusing on is regulatory translation. While some of the newly detected translated regions are predicted to encode short conserved proteins, most are found in protein-coding transcripts upstream of the regions that are known to encode proteins and lack a conserved translated amino acid sequence; some are in fact only a few amino acids long. Research so far suggests they could be involved in regulating access of the ribosome to downstream protein-coding regions.

"This could be important during embryogenesis, where there are particularly rapid developmental transitions that mean the cell needs to switch very quickly from expressing one set of transcripts to another," explained Dr. Pauli.

To address these questions, the group uses high-throughput genomic technologies like ribosome profiling and RNA-Seq, combined with computational analyses and CRISPR/Cas9 technology, enabling them to analyse, test and reveal the importance of translational regulation during embryogenesis.

Dr. Pauli and the group's ultimate goal is to find mechanisms and regulatory principles that are required for the orchestration of embryogenesis to happen in a normal way – including those that involve short peptides. Researching translational regulation during embryogenesis provides a different angle on the topic, supported by powerful molecular tools that can reveal details explaining the transition from a single cell to an organism. ●

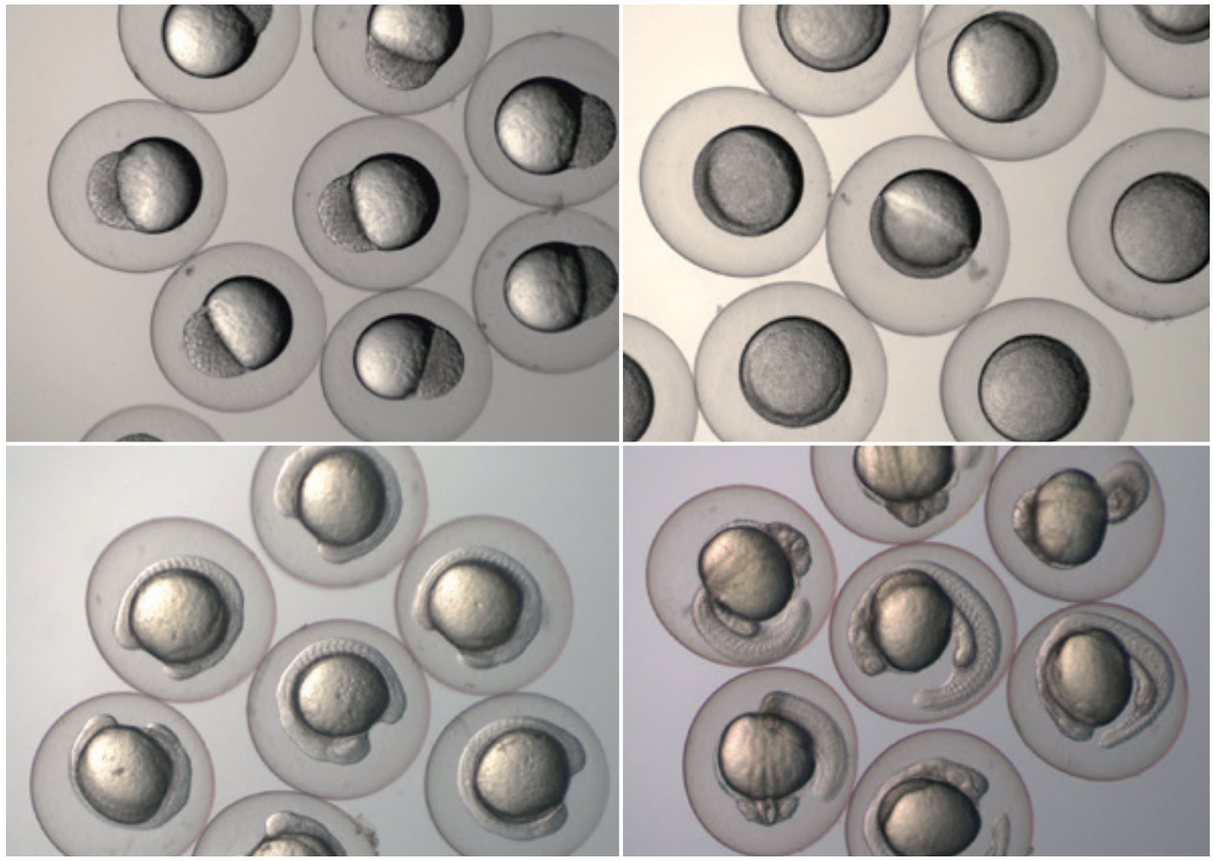

FIGURE:
Zebrafish are ideal model organisms to study embryogenesis in a vertebrate: empryos are abundant, translucent and develop rapidly. Here, the first 24 hours in the developing zebrafish embryo are shown.

RUSHAD PAVRI

RUSHAD PAVRI

PHD:
UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY, USA (2006)

POSTDOCTORAL RESEARCH: ROCKEFELLER UNIVERSITY, NEW YORK, USA

GROUP LEADER:
IMP, VIENNA (SINCE 2013)

Probing mutation hotspots in B cells

How do B cells control targeted mutation in the antibody genes to generate a vast repertoire of high-affinity antibodies?

Our long-term immunity relies on mutations – lots of them, in fact. Random changes in our DNA that lead to changes in our antibodies enable the immune system to build up an arsenal of B cells that produce highly specific antibodies to keep pathogens at bay. Through a process of mutation and selection, the B cells that produce the best antibodies are chosen and stored, ready for action should a pathogen present itself.

Our bodies encounter an almost continuous stream of antigens – bacteria on our hands, viruses we breathe in or fungal spores that irritate our eyes – so our B cells need to produce a diversity of antibodies to tackle all the invaders. How does the immune system generate this diversity? Dr. Rushad Pavri and his group are addressing a specific part of this question, by studying a hotspot of mutation in B cells.

"Targeted mutation happens at the late stages of B cell development when B cells first 'see' the pathogen," Dr. Pavri said. "It's tightly regulated in order to protect the rest of your genome but it's fundamental to your immune response and immune memory. When you just think of it in that way it's fascinating."

GROUP LEADER:
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MASTER STUDENTS:
TOBIAS KORNTHALER (UNTIL 14.05.2016), **MONIKA STEININGER**

SENIOR RESEARCH ASSISTANT:
EVA-MARIA WIEDEMANN

There are two major phases in the development pathway of B cells where the antibody genes are rearranged and recombined. At the first stage of recombination, the locus of the heavy chain of the antibody – the immunoglobulin – is rearranged. The second stage, antibody maturation, involves a very unique kind of targeted mutation, which ultimately determines which antigen or pathogen the antibody will target. The B cell appears to be the only cell in the body that undergoes this kind of mutation at very specific points.

It is this mutation process that Dr. Pavri and his group study – the mechanisms of how these mutations come about and the factors that regulate the discrete nature of the mutation pattern. Although the mutations themselves are random, they happen in very specific and controlled loci – hotspots of mutation – where the rates are at least a million fold higher than what you would expect from a random mistake.

"When the enzyme that carries out the mutations has been unleashed in the nucleus, somehow it rarely targets the rest of the genome, only the loci that encode the antibodies. One of the most fascinating and unanswered questions is how the cell controls this mutagenesis," Dr. Pavri commented.

Evolutionarily speaking, this targeted mutation is beneficial because it produces antibodies that have a high affinity for their target, so are better able to fend off infection. The random mutations change the antibodies, and the best are selected for and mass-produced in a process called clonal expansion. Over time, the B cells produce better and better antibodies through mutation and selection. After the pathogen is cleared from the system, the B cells that produce the high-affinity antibodies against the pathogen are stored "in memory," ready to attack the pathogen if it appears again, even decades later.

Dr. Pavri knew the process was coupled to transcription but questions remained, as only part of the transcribed region was mutated. One factor he investigated – Spt5 – is tightly associated with RNA polymerase, the enzyme that transcribes DNA into RNA.

Spt5 appeared to stall RNA polymerase along its transcription journey, and mutations occurred at the points at which the enzyme stalled. But mutations do not occur at all stalled sites in the genome, so it seems Spt5 is not the answer to all the questions that surround this targeted mutation.

"Although this mechanism sort of explains how the enzyme gets there, it doesn't explain the rates of mutation," explained Dr. Pavri. "This is still a big mystery. We try to do many different things, to see if we can approach the problem using different techniques. We try not to shy away from something just because it's new for us." ●

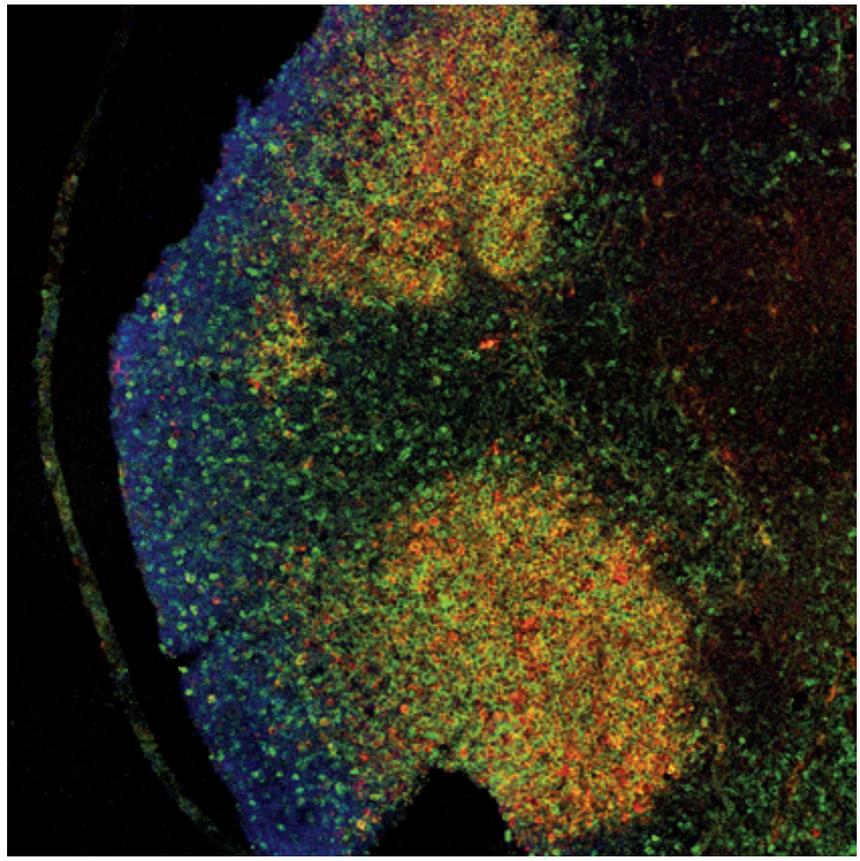

FIGURE:
A peek at the humoral immune response in action. Seen here is a cross-section of a mouse lymph node showing B cells (in red) undergoing antibody diversification after immunization. These B cells are experiencing accelerated Darwinian clonal evolution characterized by cycles of mutation and selection that will ultimately generate clones with high affinity for the foreign antigen.

JAN-MICHAEL PETERS

JAN-MICHAEL PETERS

PHD:
UNIVERSITY HEIDELBERG, GERMANY (1991)

POSTDOCTORAL RESEARCH:
DKFZ HEIDELBERG, GERMANY AND HARVARD MEDICAL SCHOOL, USA (1992–1996)

GROUP LEADER:
IMP, VIENNA (1996–2001)

SENIOR SCIENTIST:
IMP, VIENNA (SINCE 2002)

SCIENTIFIC DEPUTY DIRECTOR:
IMP, VIENNA (2011–2013)

SCIENTIFIC DIRECTOR:
IMP, VIENNA (SINCE 2013)

Unpicking precision in cell division

How can one cell divide into two identical daughter cells in a way that ensures the genome is precisely copied and partitioned?

When a fertilized egg – a zygote – develops into an organism, it divides many times through a process called mitosis, in which a mother cell divides into two identical daughter cells. In each of these divisions, the entire genome must be replicated accurately and passed on in its complete form.

The human genome is gigantic. A single cell nucleus, with a diameter of less than 10 micrometers, contains about two meters of DNA. Cells in our bodies are dividing all the time, which involves replicating this DNA; the DNA produced in an average human body in 50 years has been estimated to have the length of a light year – almost 10 trillion kilometers of DNA.

Dr. Jan-Michael Peters is interested in understanding how the whole genome can be copied and divided perfectly.

First, the genome is duplicated through DNA replication. A human cell has 46 chromosomes, each containing a single long DNA molecule; all of these are duplicated, resulting in chromosomes that contain two identical DNA molecules, called sister chromatids. These are physically connected until the cell divides, so that each daughter cell can receive a complete copy of the genome.

The connections between sister chromatids are mediated by a protein complex called cohesin. Dr. Peters' lab is interested in understanding how cohesin establishes these connections, and how they are removed to allow the separation of sister chromatids during cell division.

When DNA replication is complete, each of the sister chromatids is attached to opposite poles of the mitotic spindle – a large structure that can move chromosomes. For this, the chromosomes are lined up in the "equator" of the cell, so that when the cell divides in the middle the two sister chromatids are pulled apart into the two forming daughter cells. For this to happen in a way that each daughter cell receives identical sets of chromosomes, the sister chromatids must not be separated before spindle assembly has been completed.

The correct order of these two events is ensured by a mechanism called the spindle assembly checkpoint, or SAC. This checkpoint regulates a large protein complex called the anaphase-promoting complex/cyclosome, or APC/C, the activation of which leads to

SENIOR SCIENTIST
SCIENTIFIC DIRECTOR:
JAN-MICHAEL PETERS

POSTDOCS:
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BIOINFORMATICIAN:
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the removal of cohesin from chromosomes and thereby to the separation of sister chromatids. For Dr. Peters, the big question here is how does the SAC control activation of the APC/C to make sure sister chromatids are separated exactly at the right time?

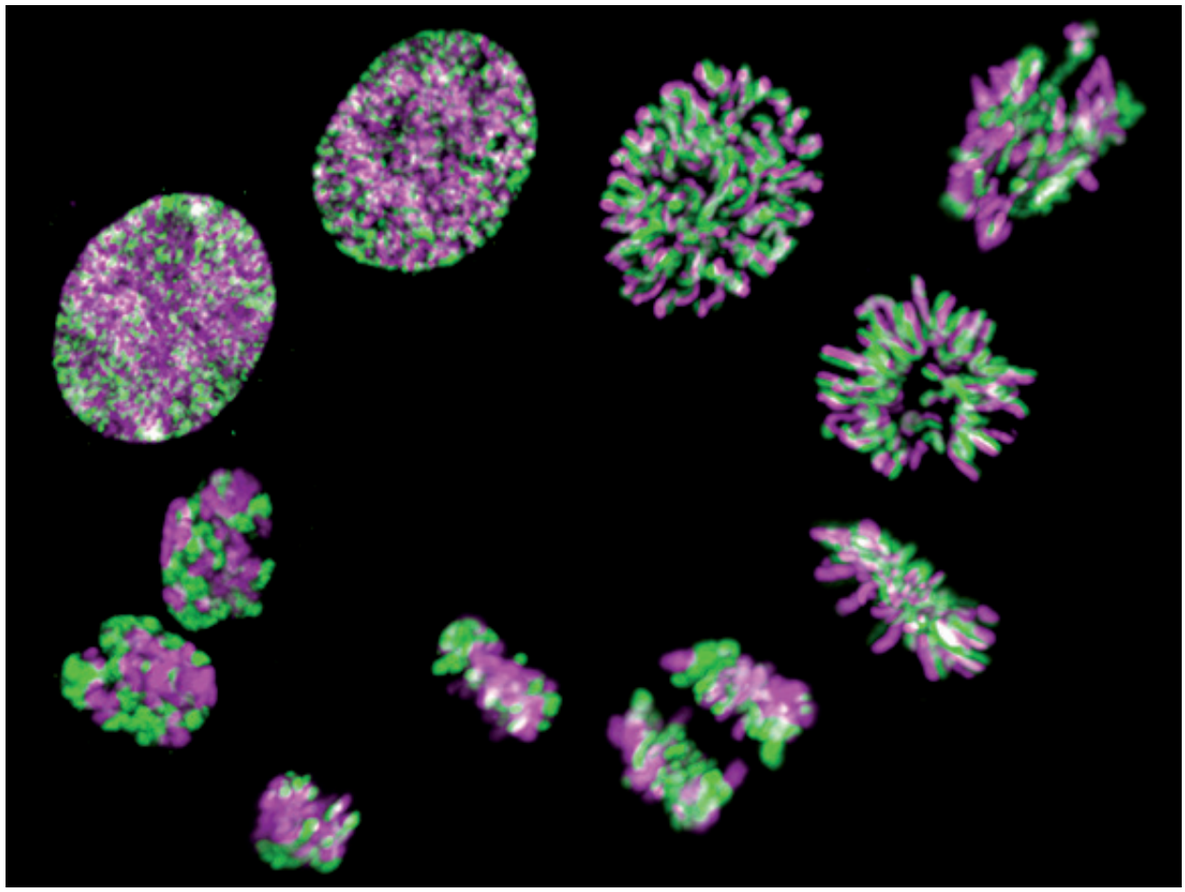
The group's work in these areas also led them to a third aim. Many years ago they found that cohesin complexes are not only present in cells undergoing division, but also in cells that will never divide again, like neurons, and which will therefore never need sister chromatid cohesion again. This implied that cohesin could also have functions other than mediating cohesion. Interestingly, the group also discovered that increasing the levels of cohesin on chromatin led to chromosome compaction, indicating that cohesin also controls chromatin structure.

Cohesin complexes form peculiar ring-like structures, which resemble cherries connected by a stalk. To mediate cohesion, these rings enclose the two sister DNA strands to connect them. However, Dr. Peters suspects that these rings can also form around a single strand of DNA, entrapping it twice to make a loop. This looping is required for transcription and gene expression, and also to keep the DNA in a compact, well organized form.

The Peters lab discovered that cohesin is found at the same locations in the genome as a DNA binding protein called CTCF, and suspects that CTCF determines where cohesin is forming chromatin loops. The group wants to find out if this is the case and, if it is, how cohesin and CTCF form chromatin loops.

"Science is all about the moment you realize all the things you don't know," said Dr. Peters. "It's about trying to understand the unknown, not understanding the known. When you get to the point where you begin to realize there's a whole universe of things out there which we do not understand, you can begin to ask questions; that's what we are doing here."

FIGURE:
Human cultured cells (HeLa) at different stages of the cell cycle. Sister chromatids were stained in different colours as described in Nagasaka et al., Nat. Cell Biol. 18,692–699, 2016 (courtesy of Kota Nagasaka).



ALEXANDER STARK

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Reducing complexity in gene regulation

How is gene regulation and therefore the development of our bodies encoded in our DNA sequence?

When you write a sentence, the different words it contains each have their own meaning; you can remove certain words and retain the meaning of the sentence but take away others and you change or even lose the meaning entirely. Something similar happens in our DNA, according to Dr. Alexander Stark.

"All animals have a genome that contains all the genetic information needed to build that organism," he explained. "The DNA sequence in this very simple four-letter alphabet somehow specifies how to build every cell type, what genes to activate and which functions each type of cell should have."

Dr. Stark has two main goals related to this. He wants to understand how the information about when and where each gene is activated – in the brain or in muscle, for example – is encoded in the DNA. He also wants to know how our cells read this information and which mechanisms they use to activate genes. But how is it possible to decipher the patterns encoded?

It is a task similar to understanding text written in an unknown language: sequences of DNA can be seen as sentences, built up of sections that are like words, and with a function – such as gene expression – that is like meaning. It is possible to investigate different

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sequences that have a similar functions for shared sections. Computational analysis can reveal sections that are very strongly correlated with a certain function, such as a gene expression pattern, then experiments can determine whether removing those sections kills the function of the sequence.

Dr. Stark does this work in *Drosophila* embryos, looking at different patterns of gene expression, for example in the central nervous system. Overall, he focuses on three particular features of gene regulation: enhancers, promoters and regulatory proteins – and how they all work together.

An enhancer is a short section of DNA that encodes these patterns, boosting the transcription of a gene into mRNA in a particular cell or tissue. An enhancer can sit between two genes, making it difficult to see immediately which gene it regulates. Promoters are regions of DNA where gene transcription starts.

Recently, Dr. Stark and his group investigated how the DNA sequence leads to an enhancer's choice of promoter. They found that some sequences could exclusively activate transcription by the promoters of housekeeping genes required by every cell and other sequences could exclusively activate the expression by promoters of developmental genes.

"The result was surprisingly clear; it suggested that the enhancer sequences have a section that aims the enhancers specifically towards either one or the other promoter," Dr. Stark said. "This means the way a cell or an entire organism regulates its housekeeping genes is different from the way it regulates its developmental genes – two different approaches in the same cell."

This is essentially how cells can express certain genes that all cells need while independently superimposing cell-specific functionality without the possibility of interference.

Dr. Stark also looks at the proteins that mediate communication between the enhancers and promoters – called transcription factors and cofactors – to understand how they activate or repress gene expression. He found that some factors can activate transcription strongly on their own, some could only work in combination with other factors, and some were specific to either the housekeeping or the developmental promoter.

"We approach this almost as physicists, taking a reductionist approach. Methods like next generation sequencing often reveal confusing complexities when studying gene regulation. We develop dedicated assays to remove the complexities of regulation while maintaining the core functions of the sequences or proteins that we are interested in. This can take us to very strong conclusions."

Dr. Stark and the group are currently investigating the strength of different promoters. In a living organism, this can be complex as a promoter's apparent strength may actually be attributed to one or more enhancers. By taking them out of context and combining all candidate promoters with the same enhancer – investigating the biology as physicists – they can see clearly which are stronger.

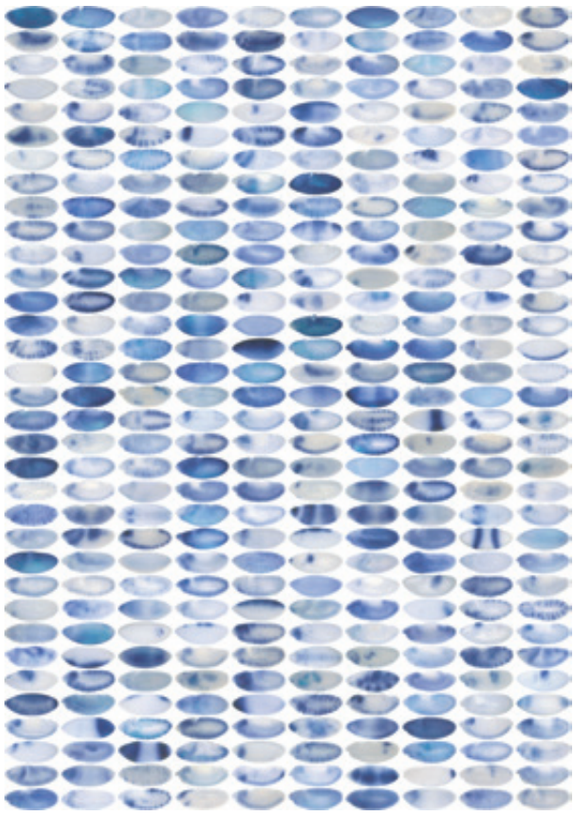

FIGURE:
Drosophila embryos with diverse enhancer activity patterns visualized by *in situ* hybridization (blue stain; from Kvon et al., *Nature* 2014).

ANDREW STRAW

ANDREW STRAW

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Flying in virtual reality

How does activity in the nervous system create sophisticated, adaptive goal-directed behaviour?

A fruit fly – *Drosophila* – moves through the air in a figure of eight, as its surroundings twist and turn to guide its endless path. Dr. Andrew Straw and his group are controlling the surroundings to study how the fly's tiny brain processes visual signals and turns them into behaviour.

"Flies are highly visual – when they fly around the room, the major sensory feedback they get is their visual feedback, which tells them about everything that's there," Dr. Straw explained. "But what does it get from these signals; how does it know there are objects in the room and how does it then avoid them?"

These are questions Dr. Straw and his group are trying to answer, with a custom-built virtual reality system that can be altered to make the flies behave in different ways. "It's essentially a holodeck for flies," Dr. Straw added.

With the virtual reality system, Dr. Straw can show images that make the flies think they are turning to the left, which makes them compensate by turning to the right; the result is the flies move in endless loops. Using effector molecules that can kill, hyperpolarize or block communication between cells, Dr. Straw can turn off very specific groups of neurons in the fly brain and see how their behaviour changes as they fly around.

This kind of lesion study can reveal how the different cell types in the fly brain contribute to their overall visual navigation behaviour. For example, the research showed that a certain group of neurons is fundamentally responsible for many more behaviours than people had thought.

New insights like this are the result of a fairly new approach: Dr. Straw's targeted lesion studies give him the ability to link specific neuron types with

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behaviour directly. Previously, scientists correlated neuronal responses and behaviours. While this is suggestive, by blocking neurons directly it is possible to see the resulting behaviour change.

Dr. Straw and his group custom-built another instrument, the Fly Mind-Alteration Device, or FlyMAD, to carry out thermogenetics experiments in freely walking flies. Optogenetics uses blue light to activate neurons, but it can damage the fly's vision – not something conducive to the vision studies the group works on. With thermogenetics they can use infrared lasers to heat up the fly for a fraction of a second and activate the neurons with no damage to its vision.

He has a big question to answer using these techniques: "How does a fly combine all of its sensory signals, its internal state and what it wants to do in order to do what it actually does?"

In related research, Dr. Straw and his group have shown that enhancers – short regions of DNA that encourage transcription – define brain regions in *Drosophila*. Looking at the patterns of where these enhancers are expressed can help identify different functional units in the brain, such as neuropils. In a recent paper, they used this technique to identify 14 novel types of neurons involved in vision using bioinformatic analysis of the fly's DNA sequence – a technique that could lead to deeper insights into how the fly's brain activity leads to behaviour.

The group has moved to the University of Freiburg in Germany, where they are continuing the lesion studies and the work on enhancers. Dr. Straw plans to develop the work further, making it possible to study naturalistic fly behaviour with the same level of rigor as simpler behaviours often studied in the lab. He is also interested in tools that would enable labs to share data and build a more complete picture of how the brain works in *Drosophila*.

"I'd like to build databases that are useful for individual labs, but then make them collaborative across labs," he explained. "Historically, we have a few data curators employed worldwide to collate data from multiple sources but to make this really scalable and fast paced, we would like to complement this work with scientists directly sharing and collaborating on that information themselves."

FIGURE:
A virtual reality arena for fruit flies.

ELLY TANAKA

ELLY TANAKA

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Revealing the secrets of regeneration

What gives a stem cell its ability to regenerate into a whole limb, and why is that ability lost in mammals?

The axolotl – an almost alien-looking amphibian – can regenerate a whole limb in its lifetime; it can even regenerate a severed spinal cord. This regeneration happens through stem cells: amputation switches on certain cellular mechanisms that tell stem cells to rebuild the limb. This does not happen in mammals, so why in the axolotl?

This is one of the questions Dr. Elly Tanaka and her group are working to answer. They have been mapping the stem cells that regenerate tissues in the axolotl, with a view to understanding regeneration, and perhaps harnessing it in the future for regenerating or healing human tissues.

"I was always interested in the polarity of tissues and how tissues recognize and replace what's missing," Dr. Tanaka explained. "Limb regeneration seemed like a very fascinating, unsolved problem. The axolotl has tremendous regenerative capabilities, something mammals have lost in the course of evolution, so comparing the two could give us some insights."

Stem cells have the potential to turn into different cell types, such as muscle, skin or heart cells, in a process called differentiation. Different stem cells are programmed to turn into a range of cell types.

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JUTTA DAMMANN

Dr. Tanaka and her group have been trying to identify the extracellular signals that are switched on by limb amputation, which are thought to promote the growth of these stem cells. They are also mapping the differences between mouse and axolotl stem cells, to explain the difference in regenerative ability and show how the cells have changed.

The revolution in analytical methods over the last decade has transformed the way Dr. Tanaka and her group can study regeneration. At IMP, Dr. Tanaka and her group will be looking more closely at the nuclei of regenerating cells, studying the molecular mechanisms of cell division and how gene expression is controlled.

"It's a very exciting time to be working on this. For a long time, people told me limb regeneration was very fascinating but hopelessly complicated. Now we really have the possibility to understand the principles of how complex tissues and organs are organized; understanding regeneration is within grasp."

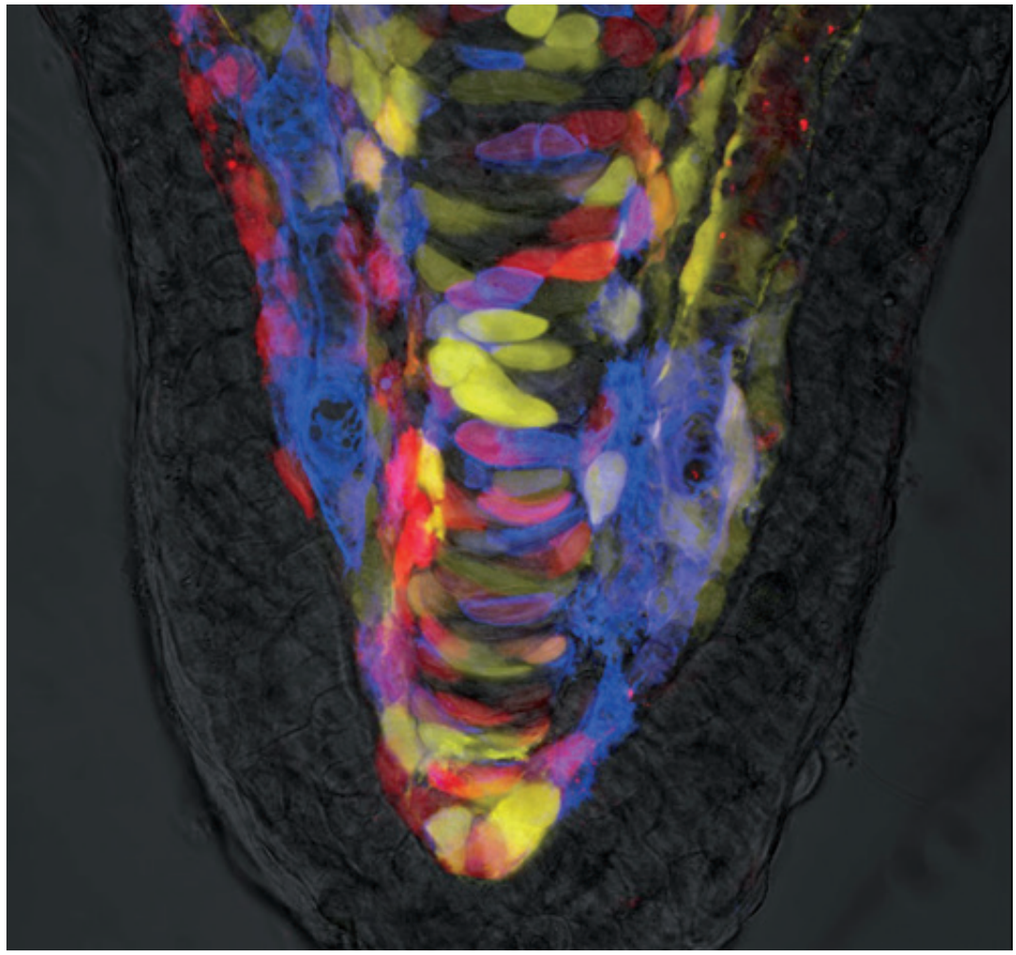
In the mouse or human, relatives of these regenerative stem cells tend to form scar tissue. Dr. Tanaka is interested in what is different about the internal circuitry of a cell that can regenerate a limb versus a cell that makes scar tissue. In the future, this knowledge could potentially be applied to switch the cells back to a different state so they can heal skin more effectively.

The group is applying the principles they learned from regeneration to engineer complex organs from embryonic stem cells: organoids such as three-dimensional parts of the spinal cord and retinal tissue. One thing that surprised Dr. Tanaka was the ability of the cells to self-organize to form the tissues.

Generating these tissues helps them understand the principles of how the spinal cord develops and the mechanisms of retinal disease. The protocol they developed for turning mouse stem cells into spinal cord cells turned out to be the fastest and most complete protocol for turning human embryonic stem cells into a certain cell type in the eye. Taking advantage of that, they are now looking for molecules that help improve the function of the eye cells as they age, which could ultimately help delay blindness diseases.

"This whole area of research started from studying limb regeneration, and then thinking about engineering tissues, and then ending up in retina," Dr. Tanaka commented. "It's been very exciting; if you follow interesting observations and ideas, it can take you to surprising new places." ●

FIGURE:
Limbow transgenic axolotl finger showing multicolour labelling of connective tissue cells undergoing regeneration.



ALIPASHA VAZIRI

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Imaging the impossible

How can imaging technologies for the brain-wide recording and manipulation of neural activity be developed to understand how brain structure leads to function?

Imagine being able to simultaneously record the activity of millions of neurons as they signal and form connections in a live brain. This is something that would help neuroscientists understand the way the brain works, but today it remains out of reach. Physically imaging such a large volume of tissue and being able to handle the enormous amount of data such a recording would produce are two of the many challenges involved.

Despite the difficulty, this is a goal Dr. Alipasha Vaziri is working towards. "If we want to understand how the brain works, we need to be extremely creative and come up with methods we may not even be thinking about right now," he explained. "If we want to ever figure out how our brain works – how it transforms information from inputs to outputs – we need to image the whole brain."

Given the sheer size and complexity of the brain, it has been hard to understand how information is handled by the activity of neurons or how their activity leads to behaviour in model systems. Existing tools enabled scientists to look at very small portions of the brain, but this did not give a broad enough picture; information is distributed on a large scale in the brain, so it also needs to be imaged that way.

The first step was to determine what brain size would be feasible. At that time, nobody had been able to record from the whole brain of *C. elegans* – one of the simplest model organisms, with 302 neurons. Dr. Vaziri and his colleagues came up with a volumetric imaging technique called light sculpting, which involves exciting neurons lined up on a single plane and recording their activity, then rapidly moving the plane so the camera records the activity of the whole

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brain. Using this technique, they recorded the activity of the whole *C. elegans* brain for the first time.

The next step was to increase the volume of what they recorded. The zebrafish larva has about 100,000 neurons – the brain volume is orders of magnitude larger than that of *C. elegans*. Using light field microscopy they could record the activity of the neurons by capturing different views and putting the images together to get a three-dimensional view. They used a micro lens array – a number of small lenses in different positions, each capturing an image at a slightly different angle. With a single snapshot, they could capture information from the entire volume of the brain.

Dr. Vaziri's next frontier is extending these imaging capabilities into rodents, which have a more complicated cortex. Unlike those of *C. elegans* and zebrafish, rodent brains are not transparent, so this presents a bigger challenge: imaging through scattering tissue. The volume of data produced, which would need to be analysed and stored, is also challenging; just half an hour of footage of a zebrafish larva's brain produces close to 1 terabyte of data.

"This calls for new ways of being able to make sense out of the data so it can answer the question you have. There are two philosophies: you can do hypothesis-driven research, which is traditionally done in biology, or you can take an unbiased approach and identify patterns in the data. For this, we are applying methods from machine learning and computer vision to find patterns that may be related to linking the behaviour of the animal with the activity patterns in the brain."

With detailed information about how every element works in real time, would it be possible to reverse engineer the brain? Could computers working on that principle be as powerful as the human brain? And if it were possible to predict when and how actions unfold in the brain just by watching neuronal activity, could neurological diseases associated with memory loss be treated more effectively?

Whatever the future possibilities, it is the interdisciplinary collaboration that helps propel the field. "If you think about a biological problem as a physicist, you tend to approach it in a different way than a biologist would, so it can be fruitful to have biologists and physicists thinking about solutions to a biological problem together." ●

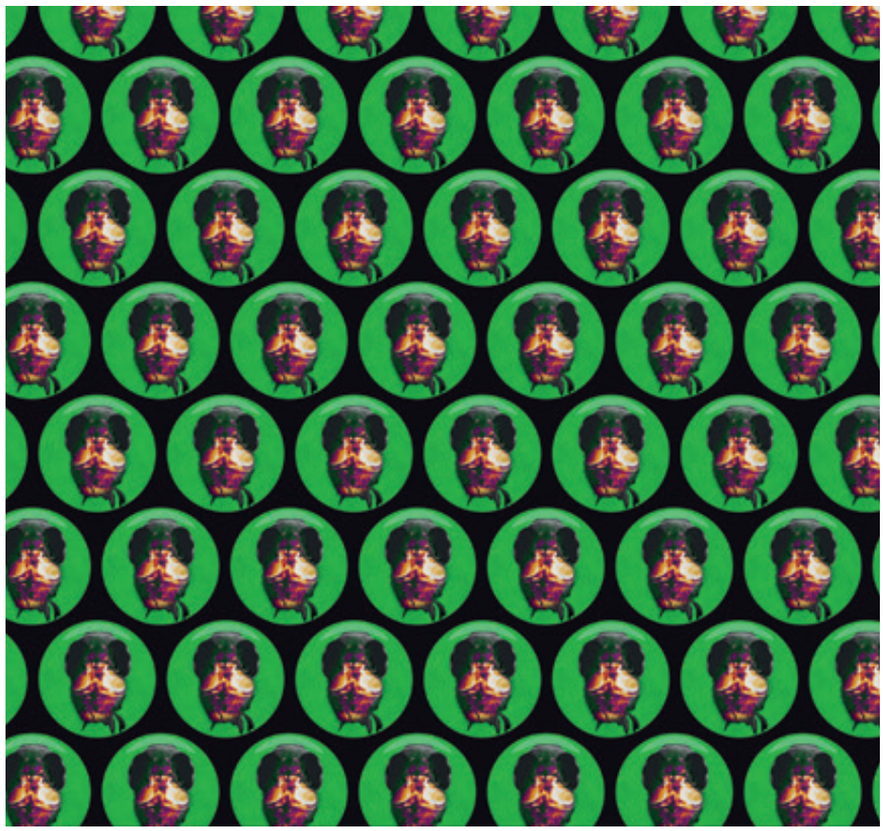

FIGURE:
Multiple images of the head region and brain of a zebrafish larva, as recorded and reconstructed using the light-field microscope (artistic rendering). Parts of the brain show pronounced neuronal activity and are artificially coloured in magenta to white, proportional to the strength of the activity.

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The macromolecular mystery of cell division

What is the structure, function and regulation of the kinetochore and how does this control the propagation of genetic material during cell division?

When researchers first investigated cell division – mitosis – at the end of the 19th century, they realized the chromosomes had to be moved correctly in order to ensure the two daughter cells had identical copies. Fast-forward more than a century and modern techniques are continuing to reveal more detail about the kinetochore – a complex of protein structures that join the chromatids in dividing cells to the parts of the cellular skeleton that pull them apart.

Dr. Stefan Westermann and his group study the kinetochore, which he considers one of the most fascinating but complicated macromolecular machines in the cell. "We are dealing with fundamental problems of how the cell propagates its genetic information during cell division," he said. "The kinetochore is amazingly complex: it has to distribute the genetic material with extremely high precision so it cannot have any errors."

As such, the kinetochore has evolved to ensure high fidelity. This means it is made up of different building blocks, each one having multiple copies that must come together at precisely the right time, which requires careful regulation. It is still one of the least understood complexes in the cell; only now do we have the full "parts list" of the kinetochore, so focus is on completing the puzzle of how these parts work together.

To do this, Dr. Westermann and his group use a combination of approaches in biochemistry, genetics and microscopy. They are investigating individual parts biochemically to reconstitute complexes – or ideally, kinetochores – and look at them structurally *in vitro*. And they test mutations and other predictions made using biochemistry *in vivo* in yeast, to look at the consequences for cell division.

Working in yeast enables them to manipulate the architecture of kinetochores and ask what impact it has on chromosome segregation during cell division. And with microscopy they can study the behaviour of individual components of the kinetochore after connecting with microtubules.

"It's very exciting at the moment because we're really starting to understand mechanistically what individual parts of the kinetochore do," commented Dr. Westermann. "Look at a biology textbook and

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you may think we understand the whole process of cell division already; that's not the case, there is still so much for us to learn about fundamental processes like this."

During his work at IMP, Dr. Westermann discovered that there is a surprisingly strong similarity between human and yeast kinetochores, which were thought to be quite different. That gave him confidence that yeast is the best model organism for studying the kinetochore to learn basic principles about how things work.

He found that a component of the yeast kinetochore called the Dam1 complex forms a strong ring around the microtubule to attach the complex, even when the microtubule is being disassembled. The next challenge is to work out how this component is connected to the rest of the kinetochore.

His work continues at University Duisburg-Essen (UDE) in Germany, where he is hoping to understand even greater mechanistic detail of how kinetochores work as dynamic connectors, but also as sensors. He wants to determine how they bind and influence dynamic microtubules, and also how they can sense the presence of other molecules and relay that information to the machinery involved in the cell cycle.

Combining information from a variety of methods is key, and this information will continue to become more detailed as the different technologies improve over time. The enormous improvements in electron microscopy, for example, will help Dr. Westermann image the kinetochore at higher resolution and combine the information with single molecule visualization.

"I think that technology is always pushing the boundaries of what you can do. It used to be that you had to build microscopes for single-molecule imaging yourself to be able to do these experiments. But now with the advancement of the technologies, they have become more and more accessible for more labs. We are certainly benefiting from that."

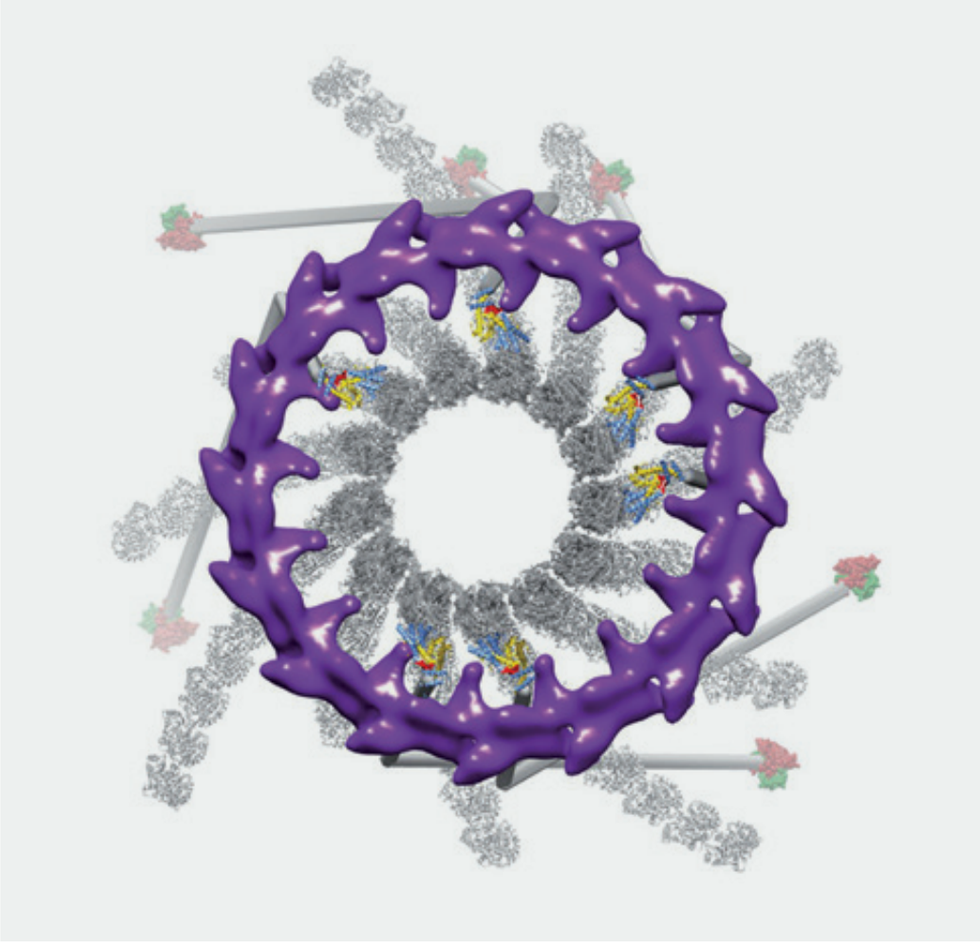

FIGURE:
Model of the Dam1-Ndc80 interface. A Dam1 ring (purple) seen in "end-on view" associating with six Ndc80 complexes (grey). The microtubule-binding CH domains of the Ndc80 complex are shown in yellow and blue.

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Watching the brain generate behaviour

How can neural circuits in the brain encode behaviour?

Behaviour, thoughts and sensations are controlled by a network of billions of neurons spanning the entire brain. Understanding how this network functions is one of the major challenges facing neuroscientists. For example, in humans, functional MRI (fMRI) scans can show the regions in which the brain is active in certain conditions, but this does not provide insights at a cellular level to mechanistically explain circuit function.

It is possible to reach this level of detail, just not in such a complex brain. Dr. Manuel Zimmer studies the behaviour and neural networks in a model organism: the small nematode *C. elegans*. With exactly 302 neurons, it is possible to image the worm's brain and track the activity of individual neurons, helping explain how neuronal networks lead to behaviour.

"*C. elegans* is the only model organism for which we have a complete circuit board written down for the anatomy of an entire nervous system," Dr. Zimmer commented. "Given the huge size and complexity of other brains, it will still be decades before we have such detailed information for larger organisms."

It may be small, but the *C. elegans* brain is not simple. The neurons are connected in a very complicated network, comparable to the internet or social networks. Because of this it is not possible to read function from a static map of connections without additional input; a map is useful, but not sufficient alone.

So in collaboration with Dr. Alipasha Vaziri, Dr. Zimmer pioneered a technique to capture, in real time, the activity of an entire brain at the resolution of individual neurons. A combination of Dr. Alipasha's microscopy innovations and Dr. Zimmer's biological samples with calcium indicators localized to the

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neuronal nuclei resulted in recordings that tracked individual neurons, which led to a whole host of exciting discoveries.

One such discovery is that if you look at the brain of a worm that is not being acutely stimulated, a large proportion of the neurons are always active. And the activity is not random, it is highly coordinated: most neurons actually work together to coordinate their activity; almost none of the neurons work in isolation. This collective action of many neurons can be mathematically described as an overall brain state.

Dr. Zimmer and his team wanted to know what this meant. In the experimental approach for visualizing the activity of the whole brain, animals need to be immobilized to a fixed microscope stage, so they took some representative neurons from the collective brain states and recorded their activity individually, in completely freely moving animals. This meant they could track the neuronal activity of the nematodes while they behaved normally. In order to search for food, the worm has a particular action sequence: it moves forward, backward, it turns in one direction, then in the other direction. They could see instantaneously how neural activity relates to the animals' actions.

Their revolutionary discovery resulted from the synthesis of both approaches. If you look at brain activity, you see a continuous transition from one brain state to another, which follows this action sequence. The neurons are highly coupled with each other, communicating via synapses and neurotransmitters, and seem to be dictating to each other what to do next.

Dr. Zimmer and his team are now effectively able to read the worms' minds and understand how particular behavioural strategies are established in the brain – something that had never been possible in this way in any model organism before.

Dr. Zimmer believes that from this model in *C. elegans*, models could be developed for people studying more complex brains. The idea is that if you can record many neurons from different brain regions over long time periods, a similar network structure should be seen in other animals.

"One can learn a lot about the general principles of biology, like brain function, if one chooses the right model. It doesn't have to be human to ask questions that are relevant for the human brain. By studying simple model organisms, like these tiny wriggling worms, we can discover principles that are applicable to other more complex systems."

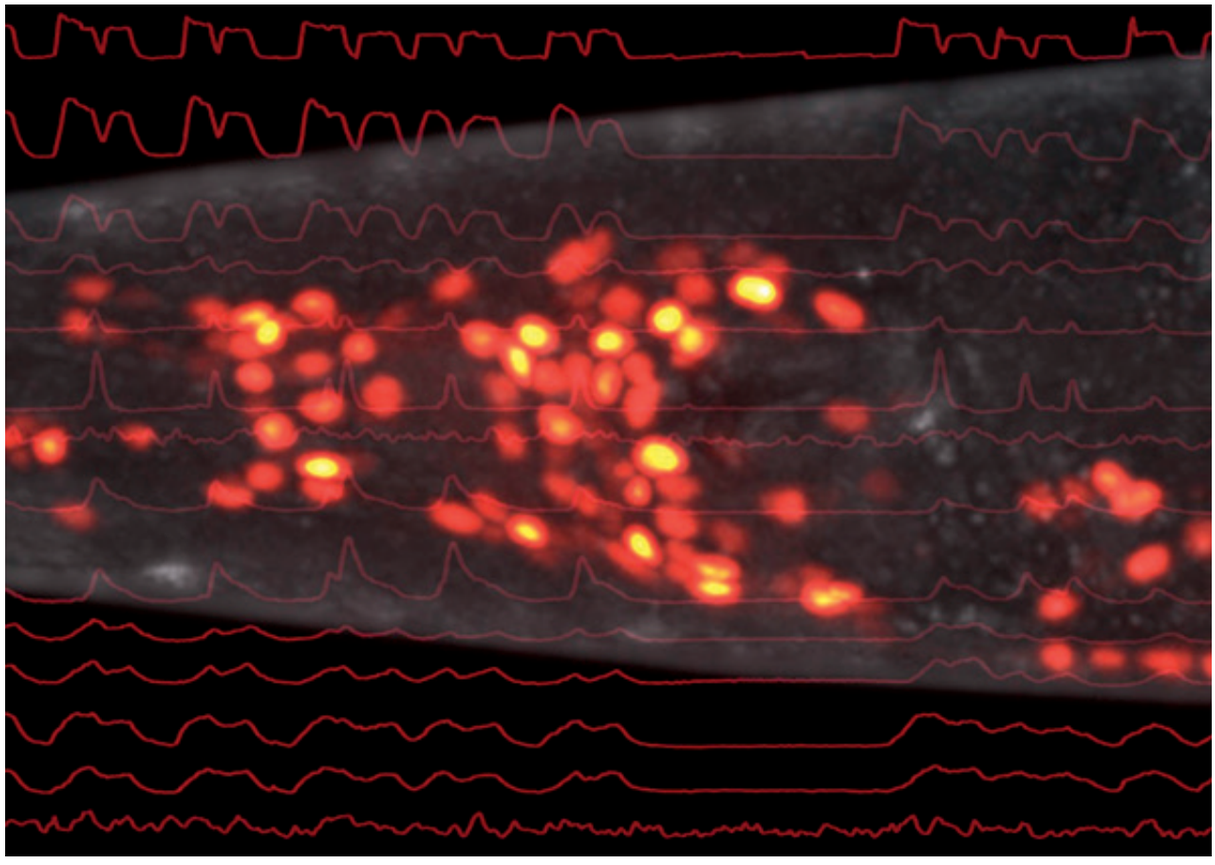


FIGURE:
The image shows a head of a roundworm whose nerve cells have been genetically modified to glow under the microscope when they are active. The traces in the background are typical activity measurements from some of these cells.

JOHANNES ZUBER

JOHANNES ZUBER

MD:
HUMBOLDT-UNIVERSITY OF BERLIN, GERMANY
(2003)

POSTDOCTORAL RESEARCH AND CLINICAL FELLOW:
COLD SPRING HARBOR LABORATORY, NY, USA

GROUP LEADER:
IMP, VIENNA
(SINCE 2011)

Killing cancer cells

Why are cancer cells immortal, what genes do they depend on, and how can we exploit cancer-specific vulnerabilities for cancer therapy?

By 2030, cancer will be the leading cause of death in Europe. Cancer arises from complex patterns of mutations that can affect more than 500 genes. This poses a daunting challenge for the development of targeted therapies.

Despite their complexity, individual mutations dysregulate basic cellular processes such as growth control, differentiation, metabolism and interactions with surrounding cells in similar ways. These changes ultimately enable cancer cells to grow indefinitely, invade tissues and escape the immune system, but alterations of these basic cellular processes also lead to vulnerabilities that can be exploited for cancer therapy.

Dr. Johannes Zuber and his team search for and study these vulnerabilities in genetically defined cancer models. To do this, they develop and employ new genetic tools, such as advanced RNA interference (RNAi), CRISPR/Cas9 and inducible protein degradation systems.

"Previously, cancer research focused a lot on what turns a normal cell into a cancer cell, but now we have the tools to answer the most important question: 'what kills a cancer cell?'" said Dr. Zuber. "In genetic screens we can systematically switch off genes in cancer cells and ask which ones are required for their survival. Once a gene is identified as a weak spot of

GROUP LEADER:
JOHANNES ZUBER

POSTDOCS:
MARTIN AICHINGER,
SUMIT DESWAL,
KATRINA JOY FALKENBERG
(UNTIL 31.08.2016),
THOMAS HOFFMANN,
JULIAN JUDE,
PHILIPP RATHERT
(UNTIL 15.09.2015),
MARKUS SCHÄFER

PHD STUDENTS:
INES AMORIM MONTEIRO BARBOSA,
MATTHIAS MUHAR,
SARAH CHRISTINE RIESER,
MAREIKE ROTH

MASTER STUDENTS:
KATRIN BERTRAM
(UNTIL 31.05.2016),
MATTHIAS HINTERNDORFER,
ROBERT WOLFGANG KALIS

BIOINFORMATICIAN:
JESSE JONATHAN LIPP,
TOBIAS NEUMANN

RESEARCH ASSOCIATE:
ANJA EBERT

TECHNICAL ASSISTANTS:
MICHAELA FELLNER,
BARBARA HOPFGARTNER
(UNTIL 15.09.2015),
MARTINA WEISSENBÖCK

cancer, we use genetic tools to study its function and its potential to serve as a drug target. In this way we can simulate a drug without having it."

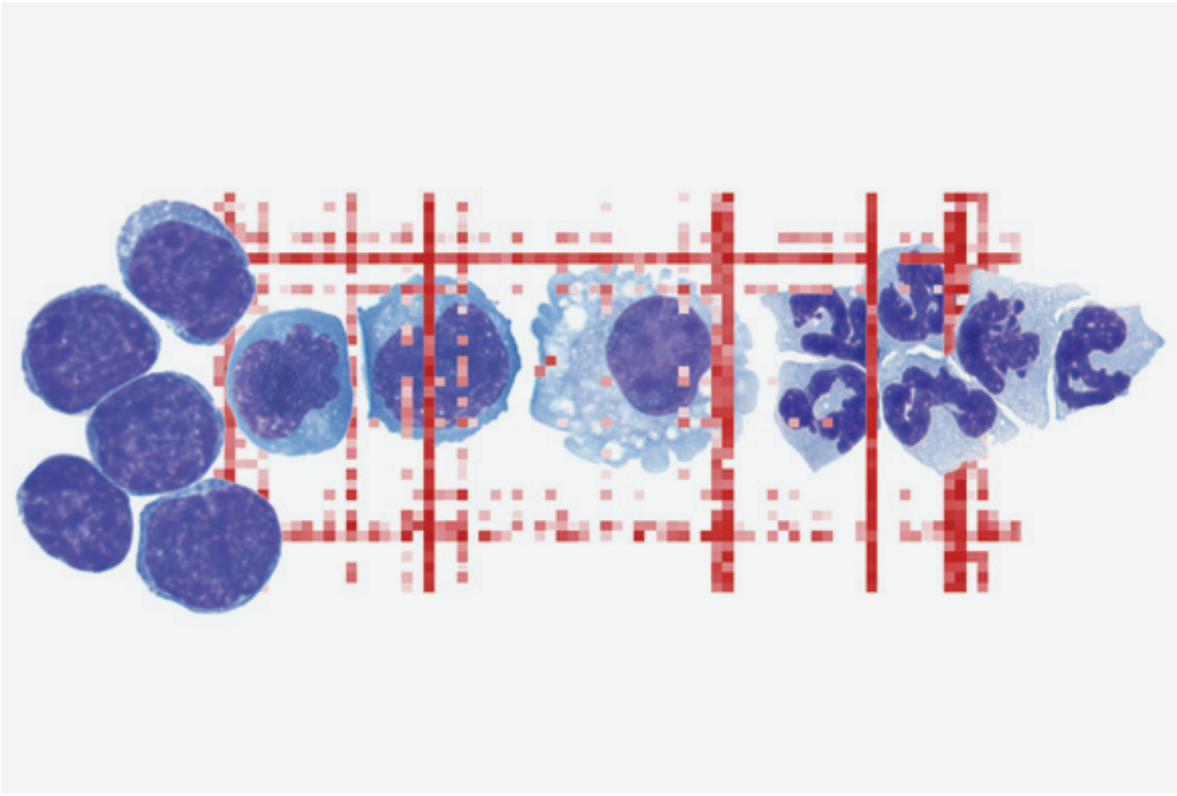
A major focus of the lab's on-going research is what makes cancer cells immortal. With the exception of stem cells, most cells in the body divide only a few times before they become a specialized tissue cell – their final destiny. "The tight link between cell division and a limited life-span is a fundamental protection mechanism against cancer," explained Dr. Zuber. "The ability to break this link and divide forever is one of the most fascinating traits of cancer cells. We want to find out how they do this and how we can break this cycle and force them to re-enter their original fate."

As a first step, the team is performing focused and genome-wide genetic screens to identify factors that maintain immortality in leukaemia. A particular focus has been the exploration of chromatin regulators, which govern the epigenome and, thereby, the identity and fate of a cell. Using these genetic screens, Dr. Zuber discovered the epigenetic reader BRD4 as a vulnerability and candidate drug target in various types of leukaemia. Only four years later, the first BRD4 inhibitors have shown promising effects in clinical trials.

More recently, the team has also discovered how leukaemia cells can adapt to and ultimately become resistant to BRD4 inhibitors, which is a common problem in cancer therapy. "Even for therapies that have very strong initial effects, cancer cells often find ways to escape them," explained Dr. Zuber. "It is very clear that effective cancer therapies will require drug combinations, and to find those we need to understand how cancer cells respond to drugs and which escape routes they use."

Beyond exploring vulnerabilities in cancer cells, Dr. Zuber's team has recently started to apply the same genetic tools to search for cancer therapy targets in immune cells. The immune system can be very effective at killing cancer cells, but cancers often find ways to evade this defence, for example, by triggering so-called checkpoints that paralyze anti-cancer immune cells. Drugs that block these checkpoints have recently led to a major breakthrough in the treatment of malignant melanoma. Recently developed genetic screening techniques, which so far have mainly been applied in cancer cells, now open great opportunities to search for and investigate candidate therapeutic targets in tumour-specific immune cells.

Dr. Zuber envisions that innovative genetic tools will ultimately provide a fascinating approach to identify and study therapy targets in both cancer and immune cells in an integrative way. "With the advent of powerful genetic tools, cancer research has entered a new era. Genetic screens will yield a plethora of new candidate targets, and genetic tools will also help to characterize them in great detail and select the most promising ones for drug development." ●



WHAT THE GROUP LEADERS SAY

Funding and Facilities

"There is a lot of core funding here, so if you can justify your needs, most things are possible. This makes a big difference in respect to, say, working with mice. There are so many people who never had – and probably never would have – worked with mice until they came here but at IMP they had the opportunity."

RUSHAD PAVRI

"Everybody is always jealous about this working relationship we have with Boehringer Ingelheim. They don't tell me what I should do but they are a big partner for me. They wouldn't do the kind of risky science that we sometimes do, but once we have something in our hands that looks real, they can become a very powerful partner in validating and doing analyses, and, ultimately, building a drug. It's a great and very unique setup."

JOHANNES ZUBER

Diversity and Collaboration

"All the facilities we have are quite unique and so is the career structure that we have here – there are a lot of junior research groups that come and go, a lot of PhDs. This is a very collaborative, interactive environment, and as a young Group Leader at IMP, I talk to my peers at IMBA and GMI as if they were colleagues at the same institute. It's very intertwined and very interactive. This one doesn't find necessarily in so many other places in the world."

MANUEL ZIMMER

"The advantage of the IMP is that there is a lot of diversity in technical skill, and a great infrastructure. You really don't feel inhibited to try something new because it's all there, and it's there to be used. I think I'm not the only one, everyone does this – we make use of the fantastic facilities that we have."

RUSHAD PAVRI

"For me, one of the great things about this campus is that we represent a broad diversity of research topics, while also having a critical mass for specific areas of research. For example, for us the strong RNA biology community is extremely important, but so is the possibility of unexpected connections and inspiration from people asking different questions and using different approaches."

LUISA COCHELLA

"Before I joined the IMP I was at a cancer center, where more than 100 groups shared a common goal: to understand and control cancer. The science at IMP is less focused on the translational aspect and is more diverse, spanning various research fields. This can sometimes be challenging, but is also very inspiring and sparks new ideas."

ANNA OBENAUF

Opportunity

"The IMP has been very supportive. When I came here eight years ago, I wanted to build up a wet lab after doing an exclusively computational PhD and postdoc. I think the IMP is probably one of only a handful of places in the world that would have allowed me to do so, but also probably one of the few places where this would have worked because the institute is very open. You find this openness both at the level of the services and also across the different scientific groups – people share products, ideas and staff resources."

ALEX STARK

"The IMP has been absolutely crucial for the discoveries we have made. Without it, it would not have happened. I wasn't a mouse geneticist, but because we have good animal facilities and colleagues who knew how to do it, I went into mouse genetics, which is now the most important aspect of our research. We are very well-known for what we are doing in this field."

MEINRAD BUSSLINGER

"You can do crazy science at the IMP, and we do do crazy science. We're doing more adventurous work than I would be able to do at a cancer research institute. We come up with small, creative ideas about how to approach a problem. We can take technologies from very different fields and just make them a cancer technology."

JOHANNES ZUBER

Infrastructure

"Having access to the outstanding core facilities, with cutting-edge technologies and expertise, enables scientists to embark on projects that are outside of their comfort zones. Many of our core facilities provide their service free of charge, which permits young scientists to freely test their hypotheses and explore new ideas."

ANNA OBENAUF

"The IMP's mechanical workshop was fundamental to our work in building virtual reality arenas. In the lab, we even invented a new verb, 'to Colombini' something – derived from the head of the workshop. That means that you take some kind of chicken scratch design that a scientist gives you and you turn it into a beautiful, precisely engineered product."

ANDREW STRAW

Centrifuge rotor.

Folded filters, latex gloves.

IN-HOUSE SERVICES

BioOPTICS

Light microscope.

FACILITY MEMBERS

HEAD OF BIOOPTICS:
KARIN AUMAYR

MICROSCOPY:
TOBIAS MÜLLER, PAWEL PASIERBEK

MICROSCOPY / FLOW CYTOMETRY:
GABRIELE STENGL

FLOW CYTOMETRY:
MARIETTA WENINGER

FLOW CYTOMETRY / IMAGE ANALYSIS:
THOMAS LENDL, GERALD SCHMAUSS

Life through a lens

Flow cytometry, microscopy and image processing and analysis

Looking at the fine detail of cells and cellular structures can provide valuable insights into their function and interaction with other cells and molecules. With state-of-the-art machines and skilled experts, the BioOptics lab supports research groups by helping them analyse and visualise cells.

The lab has eight flow cytometry machines – four to analyse cells and four to sort cells – which researchers can get training and support to use. With these machines it is possible to count and sort cells and detect biomarkers using lasers.

The facility also runs more than 25 microscope systems, which are specialized in imaging a variety of things.

Wide-field microscopy can be used to visualize all kinds of things, from detail in cells to large tissue samples, and confocal laser scanning microscopy (CLSM) can be used to look at whole cells in three dimensions. Two-photon (2P) microscopy can image deep into tissues while total internal reflection (TIRF) microscopy can be used to observe a very thin segment of a specimen; with lightsheet fluorescence microscopy (LSFM) you can see cells, whole organs and even embryos, and structured illumination microscopy (SIM) provides super resolution.

BioOptics has experts in all these systems, who can support the research groups with everything from planning experiments to analysing results, including training them to use the equipment. Once they have the images, the facility has computer workstations with specific software and people with the right skills to process and analyse the images.

But projects are not necessarily limited by the lab's equipment and skills; Karin Aumayr, Head of BioOptics, is keen to try new things. "I'm interested in the technology and how it changes, and what you can do with these fascinating instruments; I think we all are," she said. "Our main interest is how we can push the technology – and with it the science – to the border. We're happy to try absolutely everything, we are really excited about finding ways to get things done."

This is certainly valued by the research groups. "If someone comes up with a new project that involves a specific type of microscope or imaging technique that doesn't exist or needs an additional device, the facility would try to get it," said Group Leader Dr. Rushad Pavri. "Because of this flexibility, people are doing experiments they were never doing before. I think this is one of the big advantages that attracts all of us to IMP." ●

Computer keyboard, array of pipettes.

BIOINFORMATICS

ALEXANDER SCHLEIFFER

COMPUTATIONAL BIOLOGISTS:
THOMAS BURKARD, MARIA NOVATCHKOVA, ALEXANDER SCHLEIFFER

SOFTWARE DEVELOPER:
MALGORZATA GOISER
(01.01.–31.12.2016)

Analysing data to answer questions

Analysing biological data: protein sequence analysis, high-throughput screening and next generation sequencing (NGS) data analysis

Molecular biology generates enormous amounts of data that need to be read, understood, analysed and interpreted. Bioinformatics is therefore needed in almost every field of biology today. The Bioinformatics facility provides specialist services in next-generation sequencing analysis and protein sequence analysis.

"The research groups are asking classic biological questions," said Dr. Alexander Schleiffer, head of Bioinformatics support. "When they contact us before they start their experiments, we can discuss how best to design experiments and manage the data that will help them find the answers they need."

For example, if research groups want to see the transcriptome of a cell line – all the RNA produced in that cell – next generation sequencing (NGS) can help. NGS data analysis is particularly popular, and can also be used to explore the binding sites of regulatory factors on genomic DNA.

Analysing DNA and RNA sequencing data is one of the more straightforward services the facility provides; with an enthusiasm for trying new things, the team of three also carries out nonstandard analyses using custom designed workflows. For example, they developed a method to characterize particular modifications of micro RNAs using NGS.

High-throughput experiments like this often result in large datasets, which are hard to interpret. Such data needs tools for processing, visualising, and reducing the complexity to reveal statistically significant characteristics. Dr. Schleiffer and the team help put gene sets into their functional context, looking for common biochemical activity, pathways or diseases.

Protein analysis produces equally complex data. By combining evolutionary and structural information, the team can gain insight into the activity and function of these cellular machines, benefiting from the work the scientific community has done to sequence and annotate thousands of genomes and resolve just as many molecular structures.

For Dr. Schleiffer and the team, bioinformatics is a tool for answering research questions. When a research group comes up with a question and a project, they embark on an unknown journey through the data. This can be straightforward but it can also require them to combine tools – such as pattern matching, complexity analysis and homology searches – to create a new approach.

"What we do always starts with the research group that has a specific question," Dr. Schleiffer said. "Our work is very widespread because the groups have many different kinds of questions and model organisms; if it's an organism that we don't know a lot about, our expertise is needed even more. It's always a challenge when you don't know what is coming up." ●

Background: Celera Human Genome Assembly.

HEAD OF FACILITY: **HARALD SCHEUCH**

SEQUENCING SPECIALISTS: **ZUZANA DZUPINKOVA, MARKUS HOHL, CAROLINE SCHUSTER**

PROTEIN EXPRESSION SPECIALIST: **KRISTINA MARINOVA UZUNOVA, BORIL BOCHEV**

MOLECULAR BIOLOGY SPECIALIST AND ANTIBODY SPECIALIST: **ROBERT HEINEN, SABINA KULA**

TECHNICAL ASSISTANT: **SUSANNE ZICH**

TEAM MEDIA LAB: **CHRISTA DETZ-JADERNY, CHRISTINE GIESEL, JISS JOHN, JENS SCHAICH**

TEAM STERILE PROCESSING DEPARTMENT: **BETTINA RADICH, SVETLANA PEKEC-NIKOLIC, NURAY KILIC, ASEL AYKUT, SULTAN CAN, NORBERT DEMETER**

Sequencing DNA, making proteins

Sequencing DNA, producing proteins, producing media and buffers and sterilizing equipment

To study the molecular mechanisms behind biological phenomena, IMP's researchers need high quality proteins, the ability to sequence DNA, services and access to automated liquid handling; this is where the experts of the Molecular Biology Service are needed.

The molecular biology portfolio includes two Sanger DNA sequencers that are capable of analysing 48 and 96 samples at a time. The lab provides a "Speed Congenics Service" and produces monoclonal antibodies and about 30 different competent *E. coli* strains. Since 2012, it has also offered a weekly routine mycoplasma testing service.

The lab's other major activity is protein expression. The expression of recombinant proteins – using bacteria and yeast – has become a rapidly growing activity. The lab has established routine production of more than 60 enzymes and growth factors that the researchers need in their daily work. Recently they have also started using a 20-liter fermenter to produce large quantities of protein.

"Protein expression has become an expanding task and we now have a comprehensive portfolio of proteins that we can produce for the research groups," said Harald Scheuch, Head of the Molecular Biology Services.

The lab has all the latest equipment the scientists need to work toward answering their research questions – including droplet-digital PCR, liquid handling robots and one clone picker, which can detect single clones and transfer to liquid culture media.

Using robots like this, the Molecular Biology lab provides a mini prep service, to extract the DNA from cultures and hand it straight over to the sequencing experts.

Automation in the Media Lab is helping IMP researchers save time too; a recently implemented online system allows the scientists to shop their media, buffers, sterile water and much more, just by clicking on what they want and specifying the amount. And in case of emergency, there is a fully stocked storeroom they can visit for some standard items.

The Sterile Processing Department makes sure everything is clean and sterile for use. "This is important as it's part of ensuring the quality of experiments," Scheuch said. "We see thousands of items go through our Sterile Processing Department every month, it's quite amazing how much they do!" ●

Science textbook.

LIBRARIAN:
KARLO PAVLOVIC

More than a reading room

Providing published content and scientometric information to support researchers and students

Libraries are changing. Gone are the days of kilometers of shelves full of dusty academic books, waiting to be perused by busy scientists. A modern academic reference library like IMP's Max Perutz Library is more likely to have computers than printed books, with millions of peer-reviewed research articles available at a click.

In fact, librarian Karlo Pavlovic has recently swept out the unused hard copy content of the library, donating three full trucks of books and periodicals. "I'm a one-person library," he said. "There are basically two things I do: the first is providing content and the second is providing services."

He buys preferably online books that researchers request or he thinks would be useful. He also negotiates licenses with publishers and collaborates with other institutions for consortial licensing – an unseen but vital part of the role.

In addition, he provides scientometric services: data that can be used to describe the research being done at IMP. For example, if a Group Leader is applying for a grant, they may need to show how many high impact publications they have had, their H-index or other metrics.

The library itself is a space for quiet reading and collaboration. There is a reading room with a binding machine and a scanner, where IMP scientists can go to read, think and come up with ideas.

Beyond this, the role of the library and librarian is changing further. As an expert archivist, Karlo is in an ideal position to help researchers organize and manage their extensive – and sometimes unruly – lab notebooks for documenting their work and data.

Karlo is evaluating a shortlist of electronic laboratory notebook solutions that will help preserve this information, and he is working with IMP researchers to test them for usability. This is an unusual task for a librarian today, but it is something that could be standard in a few years, according to Karlo.

"Things are always changing, but not always as we had planned," he said. "You have to be alert to see what's happening and hear signals from the researchers about what needs to change." ●

MASS SPECTROMETRY AND PROTEIN CHEMISTRY

Borosilicate glass beads, styrofoam flakes.

FACILITY MEMBERS

HEAD OF FACILITY:
KARL MECHTLER

DEP. HEAD OF FACILITY:
ELISABETH ROITINGER

POSTDOCS:
REBECCA BEVERIDGE, JOHANNES STADLMANN (WITTGENSTEIN FELLOW)

BIOINFORMATICIANS:
GERHARD DÜRNBERGER, JOHANNES DOBLMANN, SERGEY MALTSEV, ZSUZSANNA ORBAN-NEMETH, FLORIAN STANEK

TECHNICAL ASSISTANTS:
OTTO HUDECZ, RICHARD IMRE, GABRIELA KRSSAKOVA, MATHIAS MADALINSKI (PART TIME), **DOMINIK MAYER** (PART TIME), **SUSANNE OPRAVIL, MICHAEL SCHUTZBIER, INES STEINMACHER, KAREL STEJSKAL**

TRAINEES:
DANIEL LENGAUER

Discovering the proteome

Purifying, synthesising and characterising peptides and proteins

To understand basic biological processes, researchers often need to purify, synthesise and analyse proteins, building a clearer picture of the proteome. With expertise in protein chemistry and mass spectrometry, Karl Mechtler and his colleagues help IMP researchers investigate proteins, developing new techniques to help them answer specific research questions.

Using mass spectrometry, which measures the mass of molecules in a sample, Mechtler can identify and quantify the proteins in a sample, providing information about the proteome. But modern mass spectrometers generate huge amounts of data, which requires automated data processing. Therefore computational proteomics is used to quantify peptides and proteins and localise post-translational modifications.

For example, Mechtler and his colleagues recently developed highly specialized technology that enables them to analyse to a high degree of resolution proteins that have been modified by the addition of sugars to produce glycoproteins. They used the technology to determine the impact of a mutation in the gene *Jagn1* on glycoproteins in white blood cells. They were able to identify subtle, yet marked alterations caused by the mutation in glycoproteins known to be involved in cell adhesion and the functioning of white blood cells.

Developing new methods is one way to stay ahead of developments in the field, but the hardware also needs to be kept current. Mass spectrometry is a core analytical technique in protein chemistry, and it requires big, complex and expensive machines. Proteomics technology changes quickly and it is important to invest in the newest versions of the lab's machines, as Mechtler explained:

"The abundance of proteins is at ten orders of magnitude, which means you're sitting on the moon with a microscope and you can see the pea on the ground on the earth. Today no technique can resolve ten orders of magnitude. The most sensitive mass spectrometry machines like our Orbi-Trap Lumos can go deep inside the proteome, but we need good sample preparation and good chromatography to sequence complete proteome."

The technology will continue to develop and will undoubtedly shape the work of Mechtler's lab. As resolutions improve, in the future it will be possible to detect even more proteins and post-translational modifications, helping answer ever more complex research questions

"This would be a dream become reality, widening our knowledge of the proteome," commented Mechtler. ●

Zebrafish in beaker.

COMPARATIVE MEDICINE AND TRANSGENIC SERVICES

HEAD OF COMPARATIVE MEDICINE:
ANDREAS

HEAD OF TRANSGENIC SERVICES:
CHRISTIAN

Vital research models

Transgenic mice and animal husbandry for biological and biomedical research

Many biological experiments are carried out *in vitro*, for example, imaging cells grown in a petri dish. But to truly understand complex biological systems like the brain or immune system, they need to be studied in context, which means studying them in live animals.

The Comparative Medicine facility at IMP houses mice, pigeons, frogs, zebrafish and axolotls for researchers who need to study biology in context. All research is carried out in accordance with the strict Austrian laboratory animal act.

To work with live animals, researchers need to apply for a license for each project. Group Leaders have to give evidence that the procedure they are applying for cannot be replaced by *in vitro* research. The facility's experts advise the researchers on the legal requirements of their work and when approved, they look after the animals that arrive.

"When a scientist wants to carry out a procedure and needs a project license, we are between them and the authorities, it's our job to be familiar with the law," said Andreas, Head of Comparative Medicine. "As a veterinarian I'm interested in the technical side of animal husbandry, particularly for animals that serve a particular purpose. Here we have very high standards of care, which also translates into better research results."

From 2017 there are two facilities – one for mice and one for the other animals. The facility's biggest undertaking is mouse husbandry. Mice are vital for biomedical research, as they can be used as models of disease, growing particular tumours, for example.

For example, the immune system functions in the whole organism. For researchers working on this, it is impossible to study the complexity of the whole system in a petri dish, as Dr. Meinrad Busslinger explained: "Seeing the interaction between all the cell types in the immune system is so essential. That's why mouse genetics is the golden standard. Having a mouse facility means our research can be enormously competitive; if there is a project we want to work on we can do it, and that has always put us at the forefront."

Working with the Comparative Medicine facility, Transgenic Services develops transgenic mouse models for the research groups to use in their investigations. The researchers first produce the genome they want to use, incorporating certain mutations for example, and take it to the Transgenic Services facility to be injected into embryos. Once the mice are born and weaned they can then be studied.

"We are not doing research ourselves, we are helping scientists do their research," said Christian, Head of Transgenic Services. "It's a great service in that sense; it would take several months for a scientist to learn to do this, so we are taking this step out of the work they have to do themselves." ●

Petri dish, dry yeast.

Characters representing nucleobases.

A strong scientific community

The IMP has seeded the development of the Vienna Biocenter (VBC), which today unites 1,400 scientists from more than 40 countries. One of the most distinguished and dynamic life science centres in Europe, the VBC comprises four research institutes, 18 biotech companies and three universities. More than 100 research groups and 120 VBC-PhD students work across an area of 90,000 square meters of lab and office space.

Being located in close proximity to such a diversity of researchers means VBC scientists are rooted in a large, excellent scientific community. They have a broad exposure to topics across molecular biology, and access to expertise, giving them the opportunity to form collaborations.

Located in the third district of Vienna, the VBC is easily accessible to external researchers by public transport or from Vienna's airport, thereby fostering international collaboration and encouraging distinguished scientists at other institutions to visit. On campus, researchers can connect in shared social zones such as cafés and chance encounters in the many walkways, stairwells and shared grounds have resulted in fruitful partnerships.

The VBC also has a world-class research infrastructure, enabling scientists to tap into technical expertise, carry out high quality research and compete with leading researchers around the world. The IMP's scientists can use the Vienna Biocenter Core Facilities (VBCF) and the VBC International PhD Programme brings the best PhD candidates together to find the perfect placements.

The IMP's new building is an important addition to the VBC; the design lends itself even more strongly to encouraging collaboration and strengthening connections between the institutes.

SCIENTIFIC ADVISORY BOARD

Maintaining high standards

With world-class scientists, outstanding students and state-of-the-art technology, the IMP strives to maintain the highest standard of research. To ensure this, the IMP works with internationally recognized scientists from some of the world's top research institutes and universities to review and steer the IMP's research.

The Scientific Advisory Board (SAB) meets with IMP researchers every year to discuss the quality, significance and main focus of research conducted at the IMP. Through this process, the IMP gains important feedback on its work, which can then inform future decisions.

Erlenmeyer flask, aluminium foil.

PROF. LESLIE VOSSHALL (CHAIR)
ROCKEFELLER UNIVERSITY
NEW YORK, USA

PROF. ANGELIKA AMON
MIT CAMBRIDGE, USA

PROF. HANS CLEVERS
HUBRECHT INSTITUTE,
UTRECHT, THE NETHERLANDS

PROF. MICHAEL HÄUSSER
UNIVERSITY COLLEGE
LONDON, UK

DR. NORBERT KRAUT
BOEHRINGER INGELHEIM RCV GMBH
VIENNA, AUSTRIA

PROF. DAN LITTMAN
NYU LANGONE MEDICAL CENTER
NEW YORK, USA

PROF. RUSLAN MEDZHITOV
YALE SCHOOL OF MEDICINE/HHMI,
NEW HAVEN, USA

PROF. TOM RAPOPORT
HARVARD MEDICAL SCHOOL
BOSTON, USA

PROF. DIRK SCHÜBELER
FRIEDRICH MIESCHER INSTITUTE
FOR BIOMEDICAL RESEARCH
BASEL, SWITZERLAND

VIENNA BIOCENTER CORE FACILITIES (VBCF)

www.vbcf.ac.at

Safety glasses.

Supporting experimental research

IMP researchers have access to the Vienna Biocenter Core Facilities (VBCF) – shared facilities that are run by highly qualified experts. Available for IMP, IMBA, GMI and other institutions, VBCF provides a variety of resources and services, from scientific infrastructure like electron microscopy and CRISPR to social infrastructure such as the Child Care Center.

Advanced Microscopy

With an expanding inventory of the latest optical imaging technology and techniques, the Advanced Microscopy Facility (advMICRO) can visualise anything from single molecules to whole embryos. Cutting-edge technologies are frequently added to the existing portfolio of more than 15 microscopy and spectroscopy techniques, which includes 3D Structured Illumination Microscopy, Total Internal Reflection Microscopy and Brillouin Light Scattering Microscopy. As well as access to these techniques, the facility offers support in using the instruments and analysing the data. The dedicated team of physicists and biologists also develops custom and novel solutions when commercial technology is unsuitable.

Bioinformatics & Scientific Computing

The Bioinformatics & Scientific Computing Facility (BioComp) aims to develop advanced analysis tools and implement novel approaches for the analysis of high-throughput datasets, with a special focus on next-generation sequencing. The team helps researchers design experiments in areas such as transcriptomics, epigenomics and metagenomics, and gives them insights into their next-generation sequencing data by carrying out the data analysis. In addition, the facility develops image and video processing solutions and bespoke hardware, which biological experiments often require. The team also offers training and consultation in bioinformatics, statistics and programming.

Electron Microscopy

From preparing samples to producing images, the Electron Microscopy Facility (EM) helps researchers look closely at molecules, cells and tissues. Using scanning (SEM) and transmission electron microscopes (TEM) and a variety of techniques, such as negative staining, chemical fixation and cutting-edge cryo-EM, the EM facility can visualize the ultrastructure of a range of biological samples. They can examine the complex architecture of macromolecules, cells and tissues at nanometer resolution. Researchers can request to be trained in the techniques themselves or for the facility team to carry out the work directly.

HistoPathology

Combining expertise in histological techniques with scientific input from certified veterinary pathologists, the HistoPathology Facility (HP) provides researchers with high quality tissue analysis. Services include isolating embryos, which can later be fixed and stained; mouse perfusion and necropsy; trimming, processing and embedding tissue for sectioning; paraffin, cryo and vibratome sectioning; and the most common types of staining – including manual and automated basic staining and immunostaining. The HP team offers consultation before and during the experiment, and interprets and reports the results following the tissue analysis.

Metabolomics

The Metabolomics Facility (Metabol) provides quantitative data on the building blocks of life, through the comprehensive analysis of small biomolecules, such as sugars, lipids and nucleic acids, in biological samples.

The Metabolomics Facility aims to deliver state-of-the-art quantitative and qualitative analysis of small organic compounds to researchers. Opened in March 2016, the facility uses diverse methodologies based on liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS). Services include targeted analysis of compounds defined by the researchers and metabolite profiling to assess changes in various biochemical pathways in exploratory studies.

Next Generation Sequencing

Genome-wide studies have given researchers unprecedented insights into biological processes, accelerating discovery. The goal of the Next Generation Sequencing Facility (NGS) is to provide researchers with cutting-edge NGS technology, which has become a key analysis method for biological research. With a team that has years of experience with sequencing systems and sequencing data analysis, the NGS facility provides advice and guidance on sequencing projects and supports research from library preparation through quality control and sequencing to data analysis. The team offers all common sequencing applications and encourages the development of novel methods and protocols.

Plant Sciences

Research in plants has led to many groundbreaking discoveries about the molecular mechanisms of life. With 22 high-quality, state-of-the-art and highly specialised plant growth chambers, the Plant Sciences Facility (PlantS) can control environmental conditions precisely, reproducing plant stress conditions such as frost, drought and various light and gas conditions. The facility can help plant researchers answer complex questions by providing services like automated phenotyping for the objective, reproducible and high-throughput assessment of plant phenotypic traits and environmental simulation. The team also offers basic plant growth and digital phenotyping and image analysis.

Preclinical Phenotyping

Analysing genetically manipulated mice is complex and phenotyping is becoming increasingly important for linking molecular mechanisms to whole-body effects. The Preclinical Phenotyping Facility (pcPHENO) provides state-of-the-art equipment and services to test various aspects of the mouse phenotype. Services include behavioral tests and physiological assays, metabolic studies, motor coordination and balance, anxiety and depression-related behavior, learning and memory, pain studies, social interactions and (neuro)physiological analysis. Researchers are trained under expert supervision, so they can choose whether to plan and perform experiments and analyse and interpret the results alone or with support from pcPHENO.

Preclinical Imaging

The Preclinical Imaging Facility (pcIMAG) provides comprehensive multimodal magnetic resonance (MR) imaging, with a focus on *in vivo* mouse imaging and welcoming smaller model organisms. The facility offers state-of-the-art ultra-high-field magnetic resonance imaging using a 15.2 T Bruker magnet. Through MR imaging data acquisition and MR spectroscopy, the pcIMAG team can support researchers with anatomical characterisation of organ systems, axonal track tracing, quantitative perfusion measurement, angiography and proton magnetic resonance spectroscopy, providing top quality image analysis, data processing and 3D visualisation. The facility plans to establish a combination of functional MRI (fMRI) and optogenetics.

Protein Technologies

Two major experimental bottlenecks in molecular and cell biology, protein biochemistry and structural biology are protein production and purification; the Protein Technologies Facility (ProTech) aims to help researchers overcome these. With expertise in most protein-related technologies, the team offers services including molecular cloning, protein production and purification and the biophysical characterisation of proteins. They also offer services related to CRISPR/Cas9, providing knowledge and materials. Researchers use the proteins produced by ProTech in antibody generation, biochemical and cell biological assays, structural analysis and the study of biomolecular interactions and CRISPR/Cas9 experiments.

Vienna Drosophila Resource Center

Drosophila melanogaster is a model organism commonly used in genetics to provide insights into brain and behavior, among many other things. The Vienna Drosophila Resource Center (VDRC) aims to promote scientific discoveries in *Drosophila* by maintaining transgenic *Drosophila melanogaster* stocks and DNA resources for the use of researchers. VDRC maintains and distributes the largest collection of *Drosophila* RNAi lines worldwide, with more than 38,000 independent transgenic fly lines, nearly all in duplicate. VDRC offers a private stock keeping service and also runs the Fly Food Kitchen, for fly media. ●

VIENNA BIOCENTER TRAINING PROGRAMME

Read more about the VBC Summer School, VBC PhD Programme and other VBC training at: www.vbcphdprogramme.at

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Empowering curious students

At the IMP, PhD students and postdocs are at the heart of the research being done. As key people who carry out research, they work closely with the Group Leaders to design experiments, share their findings with the community and drive the future direction of the research.

The IMP's approach to training reflects this; the emphasis is on developing independent scientists. Vienna Biocenter (VBC) scientific training activities are organised jointly by the IMP, the Max F. Perutz Laboratories (MFPL), the Institute of Molecular Biotechnology (IMBA) and the Gregor Mendel Institute (GMI).

"I can go in whichever direction I want to here, which, to me, is the best training for someone who wants to be an independent scientist one day," said Harris Kaplan, a PhD student in the Zimmer Group.

"We think the best way to learn science is hands-on, by doing science yourself," explained Ines Crisostomo, VBC Scientific Training Coordinator. "We try to engage motivated and curious students who already have some research experience and give them the opportunity and resources to put their curiosity to work and do good, meaningful science."

In July and August, the campus is abuzz with enthusiastic undergraduate students from around the world. The Summer School is very popular among prospective students and IMP researchers alike, providing an injection of energy in the summer months.

Shortly after, the IMP welcomes prospective PhD students from around the world to meet Group Leaders and see if they can find the right fit for their training. Students are selected from a pool of highly qualified candidates who apply to the VBC PhD Programme.

Postdocs also play a vital role in the research done at the IMP. Rather than applying via a central programme, postdocs apply directly to the research group they would want to work with. They have access to a broad range of training opportunities, and are given an annual budget so they can direct much of their own training.

Flexible training

"We have a very diverse student community, all working on different topics, so we need to find clever ways of giving them the skills and training they need without formal training," said Crisostomo. "We run away from the traditional, formal classroom!"

There are three standard elements to the PhD Programme: an introductory course, Monday Seminars and on-going mentoring. The three-week introductory course "Priming Your PhD" sets the students off on the right track, strengthening their network on campus to give them a strong foundation for their work.

Every week, three different PhD students or postdocs present at the Monday Seminar, sharing their knowledge throughout the campus community and gaining a multidisciplinary view of science. Even though topics are diverse, attendees find overlap in techniques and technologies and form collaborations that take their research in new directions.

The Monday Seminars are popular beyond the PhD Programme, as Group Leader Dr. Rushad Pavri explained: "This is probably the best scientific activity that happens at the IMP, maybe even better than any invited lecture, for the simple reason that the work is so diverse, just sitting there for one hour every week you will learn something new about something completely different."

The students have regular meetings with the thesis committee throughout their time at the IMP, and there is strong emphasis on mentoring. The Programme provides guidelines to make sure everybody is aware of their responsibilities and can focus on empowering the students.

"It's very satisfying to supervise students, see them developing, see my first postdoc get a position as a professor," said Dr. Manuel Zimmer. "Working in a team like we do, you can discuss work with the students and coach them; they are not employees, they are people who work independently on their own projects."

Beyond these three elements, there is a lot of flexibility in how students navigate their time at the IMP. They are given a budget to organize a two-day symposium every year – they choose the topics and speakers, and organize the event themselves. And the annual career day features topics like interview training and assessment, applying for non-academic positions and career planning. PhD students can also make suggestions for workshops throughout the year, depending on their needs.

But the real training happens every day in the lab. The aim is for every student to have their own project and focus on research that will give them a first author publication by the end of their PhD. This is a huge advantage, as it helps them begin a career in the highly competitive world of academia.

Harris Kaplan was joint first author on a paper in *Cell* describing a method for whole brain imaging in the nematode worm *C. elegans*. For him, having the freedom to make decisions about his work has been hugely beneficial.

"The Programme is hands-off in the sense that you have a lot of your own freedom – it's you and your supervisor and your lab and that's your focus right from the beginning. Any time I need guidance and I need help I can go to Manuel or have a long discussion with anyone about the right direction. Otherwise it's pretty much up to me how I do it."

The social side of the VBC training also has a big impact on students. Arriving in the same group means prospective PhD students spend a week together during the selection and they get to know each other, forming connections that last throughout their time at the IMP.

"I chose to come here because I could do the research I wanted to do and I felt like it was a friendly place," said Pinelopi Pliota, a PhD student in the Haubensak Group. "I moved to Vienna from Greece and I didn't know anyone when I arrived. Through the selection I got to know some people, which helped me settle in."

Completing the VBC PhD Programme and other trainings at the IMP sets researchers off on the path to a successful academic career, and some, like Dr. Andrea Pauli, return as Group Leaders. But a career in research does not suit everyone; for those people, the training at the IMP serves as a good foundation for work in many other areas.

Pliota was working on the brain circuitry involved in anxiety and fear in mice when she decided she would move forward in a more technical facilities role. "I prefer the technical side of research rather than the writing and publishing, so I would like to support research instead, in a facility like the ones we have here at the IMP," she said. ●

Inflated latex glove.

Falcon tube holder, IMP-pin.

Sensational speakers

The quality of the IMP's seminars, talks and guest lectures are indicators of the institute's international recognition and academic excellence. Several different types of lectures are held regularly, most notably the Monday Seminars and Max-Birnstiel Lectures.

Every Monday, IMP researchers take their seats in the main hall for the Monday Seminar – one hour in which three speakers from the IMP and its partner-institutes talk about their research. This provides a unique learning opportunity – one that inspires new ideas and fosters collaboration. With such diverse skills and expertise, IMP's world-leading researchers and students talk from a broad variety of perspectives, often sparking an "aha" moment or helping their colleagues solve a tricky problem.

The IMP also invites distinguished speakers from around the world to give Max-Birnstiel Lectures, named after the late IMP founding director – regular seminars on hot topics in molecular biology. These lectures, held under the name of the IMP's founding director, underline the high academic standard and international scope of the science pursued at the Vienna Biocenter. Hearing from exceptional external speakers is inspiring for IMP researchers, enabling them to stay in touch with the latest developments in their fields and beyond.

19.12.16 / IMP GL Interview Seminar

STRUCTURAL DIFFERENCES IN TRANSLATION REGULATION BETWEEN EUKARYOTIC PARASITES AND THEIR MAMMALIAN HOSTS
Yaser Hashem / University of Strasbourg; Host: Daniel Gerlich

15.12.16 / VBC Regular Seminar

COMPUTATIONAL BIOLOGY IN CRISPR SCREENS AND CANCER IMMUNOLOGY
Xiaole Shirley Liu / Dana Farber Cancer Institute; Host: Johannes Zuber

09.12.16 / Impromptu Seminar

MOLECULAR AND NEURAL CIRCUIT MECHANISMS FOR SALT CHEMOTAXIS LEARNING IN C. ELEGANS
Yuichi Iino / University of Tokyo; Host: Manuel Zimmer

06.12.16 / Impromptu Seminar

GENETIC BUILDING BLOCKS OF NEURONAL CONNECTIVITY AND VISUOMOTOR BEHAVIORS IN ZEBRAFISH
Albert Pan / Augusta University, Georgia; Host: Andrea Pauli

05.12.16 / Impromptu Seminar

A 3D CODE IN THE HUMAN GENOME
Erez Lieberman-Aiden / Rice University and Baylor College of Medicine Impromptu Seminar; Host: Jan-Michael Peters

01.12.16 / VBC Regular Seminar

MOLECULAR MECHANISMS OF INTRACELLULAR MEMBRANE FUSION
Reinhard Jahn / Max Planck Institute for Biophysical Chemistry; Host: Gang Dong

28.11.16 / IMP GL Interview Seminar

CONFORMATIONAL DYNAMICS OF THE HUMAN 26 S PROTEASOME ANALYZED BY CRYO EM
David Haselbach / MPI for Biophysical Chemistry, Göttingen; Host: Tim Clausen

24.11.16 / IMP GL Interview Seminar

SINGLE-PARTICLE CRYO-EM: A RISING STAR IN THE FIELD OF STRUCTURAL BIOLOGY
Doreen Matthies / NIH, Bethesda; Host: David Keays

24.11.16 / VBC Regular Seminar

BACTERIAL QUORUM SENSING AND ITS CONTROL
Bonnie Bassler / Princeton University; Host: Luisa Cochella

22.11.16 / Impromptu Seminar

RESOLVING FATE DECISIONS DURING DEVELOPMENT WITH SINGLE CELL TRANSCRIPTOMICS APPROACH
Igor Adameyko / Karolinska Institutet; Hosts: David Keays and Elly Tanaka

21.11.16 / IMP GL Interview Seminar

BRCA1A AND BRISC: MOLECULAR MACHINES FOR DEUBIQUITINATION
Julius Rabl / FMI, Basel; Host: Jan-Michael Peters

17.11.16 / Impromptu Seminar

DEEP PHENOTYPING ENABLED BY MICROFLUIDICS AND HIGH-THROUGHPUT QUANTITATIVE MICROSCOPY
Hang Lu / Georgia Institute of Technology; Host: Manuel Zimmer

10.11.16 / VBC Regular Seminar

HIJACKING THE UBIQUITIN LIGASE SYSTEM FOR A GOOD CAUSE
Nicolas Thomae / FMI Basel; Host: Tim Clausen

09.11.16 / Max Birnstiel Lecture

DNA SEQUENCE AND THE EPIGENOME
Sir Adrian Bird / University of Edinburgh; Host: Jan-Michael Peters

27.10.16 / VBC Regular Seminar

TRANSPOSABLE ELEMENTS, POLYDACTYL PROTEINS AND THE GENESIS OF HUMAN-SPECIFIC TRANSCRIPTION NETWORKS
Didier Trono / EPFL Lausanne; Host: Julius Brennecke

20.10.16 / VBC Regular Seminar

4D CHROMOSOME DYNAMICS: COMMONALITIES FROM E.COLI TO MAMMALIAN CELLS
Nancy Kleckner / Harvard University; Host: Ortrun Mittelsten Scheid

19.10.16 / Impromptu Seminar

MECHANISMS OF TUMOR GROWTH AND METASTASIS: FROM METABOLIC REPROGRAMING TO DORMANCY
Roger Gomis / IRB Barcelona; Host: Anna Obenauf

13.10.16 / Impromptu Seminar

STRUCTURAL STUDIES OF EUKARYOTIC TRANSCRIPTION INITIATION
Clemens Plaschka / MRC Laboratory of Molecular Biology, Cambridge; Host: Alex Stark

04.10.16 / Impromptu Seminar

BAF COMPLEX STRUCTURE AND FUNCTION IN HUMAN CANCER
Cigall Kadoch / DFCI / Harvard Medical School; Host: Johannes Zuber

29.09.16 / VBC Regular Seminar

BIOLOGY OF BEDTIME: UNDERSTANDING CIRCADIAN RHYTHMS AND SLEEP
Amita Sehgal / University of Pennsylvania; Host: VBC PhD students

22.09.16 / VBC Regular Seminar

EPIGENETIC REGULATION OF GENOMIC DNA VIA CHROMATIN STRUCTURE
Hitoshi Kurumizaka / Waseda University; Host: Peter Schlögelhofer

15.09.16 / VBC Regular Seminar

STING SIGNALING AND THE CONTROL OF INFECTIOUS DISEASE, INFLAMMATION, AND CANCER
Glen Barber / University of Miami Miller School of Medicine; Host: Thomas Decker

07.09.16 / Max Birnstiel Lecture

THE CEREBRAL CORTEX, A SUBSTRATE FOR COMPUTING IN HIGH DIMENSIONAL DYNAMIC STATE SPACE
Wolf Singer / Max Planck Institute for Brain Research; Host: Wulf Haubensak

05.09.16 / Impromptu Seminar

ALLOSTERY IN CHAPERONINS: HOW AND WHY?
Amnon Horovitz / Weizmann Institute of Science; Hosts: Tim Clausen and Madlen Stephanie

28.07.16 / VBC Postdoc Seminar

REGULATION OF FATE SPECIFICATION AND CELL BEHAVIOR IN THE CARDIOPHARYNGEAL LINEAGE OF A SIMPLE CHORDATE
Lionel Christiaen / New York University; Host: VBC Postdocs

14.07.16 / VBC Postdoc Seminar

INTERPLAY BETWEEN RNA AND CHROMATIN REMODELLING FACTORS IN EMBRYONIC STEM CELLS
Thomas Fazzio / University of Massachusetts; Host: VBC Postdocs

07.07.16 / Max Birnstiel Lecture

TELOMERES AND TELOMERASE IN CANCER AND STEM CELL FAILURE
Carol Greider / Johns Hopkins School of Medicine; Host: Luisa Cochella

30.06.16 / VBC Postdoc Seminar

UNDERSTANDING TUMOR INITIATION AND PROGRESSION USING IN VIVO GENE SILENCING AND GENOME EDITING
Lukas Dow / Sandra and Edward Meyer Cancer Center; Host: Stephanie Bannister

23.06.16 / Impromptu Seminar

THE UBIQUITIN-PROTEASOME SYSTEM IN METASTASIS AND NEUROTOXICITY
Allan Weissman / National Cancer Institute; Host: Alwin Köhler

16.06.16 / VBC Regular Seminar

SELF-UNDERSTANDING OF SELF-ORGANIZATION
Ali Brivanlou / Rockefeller University; Host: Juergen Knoblich

13.06.16 / Impromptu Seminar

AFFIMERS – THE NEXT GENERATION OF MOLECULAR RECOGNITION REAGENTS
Christian Tiede / Leeds University; Host: Tim Clausen

10.06.16 / VBC Regular Seminar

MITOCHONDRIAL STRESS SIGNALING IN DISEASE, AGING AND IMMUNITY
Gerald Shadel / Yale University School of Medicine; Host: Pavel Kovarik

06.06.16 / Impromptu Seminar

DEVELOPMENT OF MAGNETICALLY GATED ACTUATORS TO STUDY NERVOUS SYSTEM FUNCTION
Mike Wheeler / University of Virginia; Host: David Keays

02.06.16 / VBC Regular Seminar

ORGANIZING LIVING MATTER: THE EMERGING ROLE OF PHASE TRANSITIONS IN CELL BIOLOGY AND DISEASE
Simon Alberti / MPI-CBG Dresden; Host: Alex Stark

12.05.16 / VBC Regular Seminar

THE TRANSCRIPTION-RELATED DNA DAMAGE RESPONSE
Jesper Svejstrup / Francis Crick Institute; Host: Oliver Bell

28.04.16 / VBC Regular Seminar

SEX-SPECIFIC STRATEGIES AND OUTCOMES OF TRANSPOSON SILENCING IN MOUSE GERM CELLS
Alex Bortvin / Carnegie Institution for Science; Host: Kikue Tachibana-Konwalski

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14.04.16 / VBC Regular Seminar

RECONSTITUTION OF CHROMOSOME REPLICATION
John Diffley / The Francis Crick Institute, Clare Hall Laboratory; Host: Rushad Pavri

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08.04.16 / Impromptu Seminar

MOLECULAR GPS – HOW CELLS NAVIGATE COMPLEX ENVIRONMENTS
Björn Hegemann / Institute of Biochemistry, ETH Zürich; Host: Andrea Pauli

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07.04.16 / VBC Regular Seminar

PHASED SIRNAS IN PLANT REPRODUCTIVE ORGANS
Blake Meyers / Danforth Center, St. Louis; Hosts: Ortrun Mittelsten Scheid, Michael Nodine, Magnus Nordborg

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06.04.16 / Max Birnstiel Lecture

CONTROLLING THE CELL CYCLE
Sir Paul Nurse / Francis Crick Institute; Host: Jan-Michael Peters

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31.03.16 / VBC Regular Seminar

MITOCHONDRIAL QUALITY CONTROL
Wade Harper / Harvard Medical School; Host: Fumiyo Ikeda

24.03.16 / VBC Postdoc Seminar

GENETIC MEDIA
Yaniv Erlich / Columbia University; Host: VBC Postdocs

17.03.16 / VBC Postdoc Seminar

CHROMATIN SINKS AND SEX-SPECIFIC AGING IN DROSOPHILA: A ROLE FOR THE Y CHROMOSOME
Doris Bachtrog / University of California, Berkeley; Host: VBC Postdocs

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09.03.16 / Max Birnstiel Lecture

PROTEIN FOLDING IN THE CELL AND THE PROTEOSTASIS NETWORK: BIOLOGICAL MECHANISM AND DISEASE IMPLICATIONS
Judith Frydman / Stanford University; Host: Ana Ramos (Clausen Lab)

08.03.16 / Impromptu Seminar

SIGLECS: INHIBITORY RECEPTORS ON IMMUNE CELLS
Lars Nitschke / University of Erlangen; Host: Meinrad Busslinger

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02.03.16 / Mendel Lecture

A PERSONAL HISTORY OF STRUCTURAL VIROLOGY
Michael Rossmann / Purdue University; Host: Tim Clausen

25.02.16 / VBC Regular Seminar

VACCINE DESIGN FOR MALARIA AND EBOLA
Adrian Hill / University of Oxford; Host: Valneva (Andreas Meinke)

18.02.16 / VBC Regular Seminar

NEURAL MECHANISMS OF SPONTANEOUS AND LEARNED BEHAVIOR IN ZEBRAFISH
Misha Ahrens / Janelia Farm; Host: Manuel Zimmer

11.02.16 / VBC Regular Seminar

UBIQUITIN AND AUTOPHAGY NETWORKS IN HEALTH AND DISEASE
Ivan Dikic / Goethe University Frankfurt, Institute of Biochemistry; Host: Claudine Kraft

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04.02.16 / VBC Regular Seminar

CROSSTALK BETWEEN RNA PROCESSING AND CHROMATIN REMODELLING AS A MODULATOR OF GENOME INTEGRITY
Andres Aguilera / Andalusian Center for Molecular Biology and Regenerative Medicine; Host: Rushad Pavri

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05.01.16 / Impromptu Seminar

MOLECULAR MOTORS – A DIFFERENT KIND OF TRANSPORT
Winfried Teizer / Center for Nanoscale Science and Technology Texas A&M University, USA; Host: Alipasha Vaziri

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03.12.15 / VBC Postdoc Seminar

PREFRONTAL NEURONAL CIRCUITS AND MECHANISMS CONTROLLING FEAR BEHAVIOUR
Cyril Herry / INSERM; Host: VBC Postdocs

02.12.15 / Max Birnstiel Lecture

BIOGENESIS AND FUNCTION OF THE AUTOPHAGOSOME MEMBRANE
Randy Schekman / University of California at Berkeley; Host: Jan-Michael Peters

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25.11.15 / Impromptu Seminar

VCP/P97 COMPLEXES SORT OUT UBIQUITIN IN CELL CYCLE SIGNALLING, PROTEOSTASIS AND AUTOPHAGY
Hemmo Meyer / Universität Duisburg-Essen; Host: Fumiyo Ikeda

23.11.15 / Impromptu Seminar

THE ROLE OF CHROMATIN IN REPRESSION AND ACTIVATION OF THE ZYGOTIC GENOME
Nadine Vastenhouw / Max Planck Institute of Molecar Cell Biology and Genetics; Host: Andrea Pauli

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19.11.15 / VBC Regular Seminar

GENOME STABILITY AND THE CONTROL OF HOMOLOGOUS RECOMBINATION
Simon Boulton / The Francis Crick Institute; Host: Verena Jantsch-Plunger

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13.11.15 / Impromptu Seminar

REGULATION OF NEURONAL MIGRATION DURING POSTNATAL NEUROGENESIS
Richard Belvindrah / INSERM; Host: David Keays

12.11.15 / VBC Regular Seminar

PHASE SEPARATION AND TRANSPORT SELECTIVITY OF NUCLEAR PORES
Dirk Görlich / Max Planck Institute for Biophysical Chemistry; Host: Alwin Köhler

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04.11.15 / Max Birnstiel Lecture

EPIGENETIC MECHANISM DURING DEVELOPMENT: POLYCOMB AND CHROMATIN DYNAMICS
Robert Kingston / Harvard Medical School; Hosts: Meinrad Busslinger, Hiromi Tagoh

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29.10.15 / VBC Regular Seminar

THE INTERPLAY BETWEEN PROTEIN PHOSPHORYLATION AND PROTEIN UBIQUITYLATION IN REGULATING THE INNATE IMMUNE SYSTEM
Sir Philip Cohen / University of Dundee; Host: Tim Clausen

21.10.15 / Impromptu Seminar

DIRECT IN-VIVO SHRNA SCREENING FOR ACCELERATED TARGET DISCOVERY IN GASTROINTESTINAL TUMORS
Lars Zender / University of Tuebingen; Host: Johannes Zuber

15.10.15 / VBC Regular Seminar

SIGNAL AND NOISE IN PLANT STEM CELL NETWORKS
Ben Scheres / Wageningen University; Host: Michael Nodine

29.09.15 / Impromptu Seminar

EPIGENETIC SWITCHES AND TARGETED THERAPIES FOR B-CELL LYMPHOMAS
Ari Melnick / Weill Cornell Medical College; Host: Meinrad Busslinger

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25.09.15 / Impromptu Seminar

CORTICAL-HIPPOCAMPAL INTERACTIONS IN DECISION MAKING
Jai Yu / UCSF Sandler Center for Integrative Neurosciences; Host: David Keays

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24.09.15 / VBC Regular Seminar

THE NEURAL BASIS OF SPEED, ACCURACY AND CONFIDENCE IN A DECISION
Michael Shadlen / Columbia University; Hosts: Alipasha Vaziri, Manuel Zimmer

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21.09.15 / Impromptu Seminar

MAKING MAGNETS BY MICROBES: MOLECULAR GENETICS, CELL BIOLOGY AND FUNCTION OF BACTERIAL MAGNETOSOME BIOSYNTHESIS
Dirk Schüler / University of Bayreuth; Host: David Keays

18.09.15 / Impromptu Seminar

MOLECULAR REGULATION OF AXONAL AND DENDRITIC BRANCHES DURING DEVELOPMENT
Le Ma / Thomas Jefferson University; Host: Jan-Michael Peters

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17.09.15 / VBC Regular Seminar

FREE ENERGY AND SELF ORGANISATION
Karl Friston / Wellcome Trust Centre for Neuroimaging at UCL; Host: Alipasha Vaziri

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16.09.15 / Max Birnstiel Lecture

NEW TECHNOLOGIES FOR READING AND WRITING BIOLOGY
George Church / Harvard Medical School; Host: Johannes Zuber

04.09.15 / Impromptu Seminar

EZH2 CONTROLS CELL ADHESION AND MIGRATION VIA TALIN METHYLATION
I-hsin Su / Nanyang Technological University; Host: Meinrad Busslinger

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03.09.15 / VBC Regular Seminar

BIRTH, LIFE AND DEATH OF A PLANT EPIDERMAL STEM CELL LINEAGE
Dominique Bergmann / Stanford University; Host: Michael Nodine

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23.07.15 / VBC Regular Seminar

EMERGENCE OF COGNITION FROM ACTION
György Buzsáki / NYU Neuroscience Institut; Host: Manuel Zimmer

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17.07.15 / Impromptu Seminar

THE GENETIC BASIS OF MAJOR DEPRESSION
Jonathan Flint / Wellcome Trust Centre for Human Genetics, University of Oxford; Host: David Keays

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16.07.15 / VBC Regular Seminar

GENETIC CONFLICTS: BEYOND THE USUAL SUSPECTS
Harmit Malik / Fred Hutchinson Cancer Research Center Seattle; Host: Julius Brennecke

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09.07.15 / VBC Regular Seminar

BASIC MECHANISMS AND PHYSIO-PATHOLOGY OF THE PROTEASOME
Keiji Tanaka / Tokyo Metropolitan Institute of Medical Science; Host: Fumiyo Ikeda

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02.07.15 / VBC Regular Seminar

3D ARCHITECTURE OF THE GENOME AND CONTROL OF GENOME FUNCTIONS
Peter Fraser / The Babraham Institute; Host: Frederic Berger

25.06.15 / VBC Regular Seminar

MOLECULAR MECHANISMS OF MICROTUBULE TIP TRACKING AND CENTRIOLE FORMATION
Michel Steinmetz / Paul Scherrer Institute; Host: Tim Clausen

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23.06.15 / Impromptu Seminar

3D STRUCTURE OF ACETYLCHOLINESTERASE: HOW ARE ANTI-ALZHEIMER DRUGS, NERVE AGENTS AND AUTISM RELATED?
Joel Sussman / Weizmann Institute; Host: Marcin Suskiewicz (Clausen Lab)

17.06.15 / Max Birnstiel Lecture

INFLAMMATION, HOMEOSTASIS AND DISEASE
Ruslan Medzhitov / Yale University; Host: Meinrad Busslinger

11.06.15 / VBC Regular Seminar

DIFFERENT CELLS COUNT DIFFERENTLY: CENTROSOME NUMBER REGULATION IN DEVELOPMENT AND DISEASE
Monica Bettencourt Dias / Instituto Gulbenkian de Ciencia; Host: Alex Dammermann

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10.06.15 / Impromptu Seminar

ROLE OF TET, DNMT3A, AND COHESIN MUTATIONS IN AML PATHOGENESIS
Ross Levine / Memorial Sloan Kettering Cancer Center; Host: Johannes Zuber

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05.06.15 / Impromptu Seminar

A HIGHLY COMPARATIVE TIME-SERIES ANALYSIS ENGINE
Ben Fulcher / Monash University; Host: Andrew Straw

03.06.15 / VBC Regular Seminar

AUXIN: A VERSATILE REGULATOR OF PLANT GROWTH AND DEVELOPMENT
Mark Estelle / University of California San Diego; Host: Wolfgang Busch

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27.05.15 / Impromptu Seminar

SENSE AND SENSIBILITY – VISUAL DESIGN PRINCIPLES FOR SCIENTIFIC DATA
Martin Krzywinski / Canada's Michael Smith Genome Sciences Centre; Host: VBC PhD Students

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21.05.15 / VBC Postdoc Seminar

GASTROINTESTINAL, LIVER AND PANCREAS STEM/PROGENITOR CELLS AND 3D-ORGANOID CULTURES
Meritxell Huch / Gurdon Institute, University of Cambridge; Host: VBC Postdocs

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06.05.15 / Max Birnstiel Lecture

NEURONAL AND THEORETICAL FOUNDATIONS OF CONSCIOUSNESS
Christof Koch / Allen Institute for Brain Science; Hosts: Wulf Haubensak, Alipasha Vaziri, Manuel Zimmer

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30.04.15 / VBC Regular Seminar

SINGLE MOLECULE IMAGING OF DNA RECOMBINATION
Eric Greene / Columbia University; Hosts: Luisa Cochella, Julius Brennecke

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16.04.15 / VBC Regular Seminar

ORGAN COMMUNICATION IN DROSOPHILA
Norbert Perrimon / Harvard Medical School, HHMI; Host: VBC PhD Students

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09.04.15 / VBC Regular Seminar

SPECIFICITY IN THE UBIQUITIN SYSTEM
David Komander / MRC Laboratory of Molecular Biology; Hosts: Alwin Koehler, Tim Skern

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31.03.15 / Impromptu Seminar

DECISION-MAKING IN ANIMAL GROUPS
Gonzalo Polavieja / Champalimaud Institute; Host: Andrew Straw

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19.03.15 / VBC Regular Seminar

TEMPORAL AND SPATIAL REGULATION OF MITOSIS AND CYTOKINESIS BY PROTEIN PHOSPHATASE 2A
Francis Barr / Department of Biochemistry, University of Oxford; Host: Egon Ogris

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17.03.15 / Impromptu Seminar

TO MODEL THE CONNECTOME, OR NOT: A CASE STUDY IN C. ELEGANS
Shawn Lockery / University of Oregon; Host: Manuel Zimmer

10.03.15 / Impromptu Seminar

CRYO EM STRUCTURE OF THE CONTRACTILE VIPA/B NANOMACHINE IN TYPE VI EFFECTOR SECRETION
Petra Wendler / Gene Center Munich; Host: Tim Clausen

17.02.15 / Impromptu Seminar

UNTANGLING COMPLEX NEURONAL DYNAMICS BY CROSS-EMBEDDING
Taro Toyoizumi / RIKEN Brain Science Institute; Host: Manuel Zimmer

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12.02.15 / VBC Regular Seminar

CELL FITNESS FINGERPRINTS AND CELL SELECTION IN AGEING, NEUROBIOLOGY AND CANCER
Eduardo Moreno / University of Bern; Host: Alex Stark

10.02.15 / Impromptu Seminar

EVOLVING LIMB REGENERATION, A STORY OF CONSERVATION AND INNOVATION
Elly Tanaka / Center for Regenerative Therapies, Dresden; Host: Jan-Michael Peters

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05.02.15 / VBC Regular Seminar

DNA DAMAGE RESPONSES IN DEVELOPMENT, AGING, AND DISEASE: INSIGHTS FROM C. ELEGANS
Björn Schumacher / University of Cologne; Host: Verena Jantsch

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03.02.15 / Impromptu Seminar

NEURAL CIRCUIT CONTROLLING MATING BEHAVIOURS IN THE FEMALE FRUIT FLY
Carolina Rezaval / University of Oxford; Host: Luisa Cochella

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29.01.15 / VBC Postdoc Seminar

ENVIRONMENTAL SENSING BY IMMUNE CELLS
Jose Henrique Veiga Fernandes / IMM; Host: VBC Postdocs

22.01.15 / VBC Regular Seminar

TIMING IS EVERYTHING IN ECOLOGY
Ian Baldwin / MPI for Chemical Ecology; Hosts: Ortrun Mittelsten Scheid, Magnus Nordborg

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15.01.15 / VBC Regular Seminar

REGULATION OF RECEPTOR-KINASE MEDIATED INNATE IMMUNITY
Cyril Zipfel / The Sainsbury Laboratory; Host: Armin Djamei

14.01.15 / Max Birnstiel Lecture

TARGETING IMMUNE CHECKPOINTS IN CANCER THERAPY: NEW INSIGHTS AND OPPORTUNITIES
James Allison / University of Texas, MD Anderson Cancer Center; Host: Meinrad Busslinger

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09.01.15 / Impromptu Seminar

EVOLUTIONARY TRANSITIONS PROVIDE INSIGHTS INTO RNAI AND CENTROMERE BIOLOGY
Ines Anna Drinnenberg / Fred Hutchinson Cancer Research; Host: Stefan Westermann

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08.01.15 / VBC Regular Seminar

ARCHITECTURE AND DYNAMICS OF GENOME – NUCLEAR LAMINA INTERACTIONS
Bas Van Steensel / Netherlands Cancer Institute; Host: VBC PhD Students

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IMP'S AWARDS AND HONOURS

Graduated cylinder.

Awarding excellence

Securing funding for scientific research is a highly competitive process, and winning prestigious grants is the result of an exceptionally high standard of research. Similarly, scientific awards are given to the very best researchers to celebrate their excellent work and its contribution to our understanding of biology.

In 2015 and 2016, many IMP Group Leaders, post-docs and PhD students were recognized with prestigious grants to pursue their research and scientific awards to celebrate it.

"I am very happy about this grant and the opportunities it opens up for my young lab", said Anna Obenauf. "It will allow us to continue long-established collaborations with complete scientific freedom, building on the excellent infrastructure of the IMP."

"This award is a great honour and encouragement to further expand our research in the field of functional cancer genetics", said Johannes Zuber. He points out that new genetic tools offer fascinating opportunities for finding and probing therapeutic targets such as BRD4: "We are currently witnessing a true revolution in functional genetics, which will enable us to search for better cancer therapies in entirely new ways."

2016

MARTINA MINNICH
Karl Landsteiner Prize (November 2016)

FLORIAN WEISSMANN
VBC PhD Award (November 2016)

FLORIAN GRÖSSL
Mattias Lauwers Award (November 2016)

ANNA OBENAUF
WWTF Grant, project call "Precision Medicine" (September 2016)

THOMAS WIESNER
Silver award, LEO Pharma Research Foundation (August 2016)

JAN-MICHAEL PETERS
ERC Advanced Grant (March 2016)

TIM CLAUSEN
ERC Advanced Grant (March 2016)

RENPING QIAO COUDEVYLLE
Hertha Firnberg Grant (March 2016)

URSULA SCHÖBERL
Hertha Firnberg Grant (March 2016)

JOHANNES ZUBER
Deutscher Krebspreis / German Cancer Prize (February 2016)

2015

HARRY KAPLAN
Mattias Lauwers Award (November 2015)

ANNA OBENAUF
ASciNA Award (November 2015)

DAVID KEAYS
Otto-Loewi-Award (September 2015)

ALEXANDER STARK
Elected Full Member, European Molecular Biology Organization (EMBO), Heidelberg (May 2015)

DAVID KEAYS
Elected Member, "Young Academy" (Junge Kurie), Austrian Academy of Sciences (April 2015)

ALIPASHA VAZIRI / MANUEL ZIMMER
WWTF Grant Life Sciences Call "Imaging" (March 2015)

ANDREA PAULI
HFSP Career Development Award (March 2015)

ALEXANDER STARK
ERC Consolidator Grant (February 2015)

Disseminating knowledge

Scientific research contributes to our understanding of the world by building on existing knowledge. This process involves disseminating new findings through peer-reviewed publication. When research is reviewed, considered robust and reproducible, and published in a journal, it is then available to researchers around the world to examine, analyse and use for their own work, ultimately citing the original publication in their papers.

Researchers at the IMP publish frequently in high-impact journals, which are very competitive and have high standards for acceptance. By publishing in internationally recognized peer-reviewed journals, IMP's researchers ensure their work has the biggest possible impact on future studies, contributing to our understanding of biology.

Tubes with fly food.

BUSSLINGER

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