FUTURA

Journal of the Boehringer Ingelheim Fonds

Volume 41 / 1. 2026

Fighting Viruses with Viruses
How scientists are using defective viral particles against viral diseases

Projects, MD Fellowships, Results
Twelve new PhD projects, 13 MD fellowships, 16 completed theses

A BIF Fellow's Guide to Leuven
Explore lively squares, medieval landmarks, and Belgian charm

The cover illustration shows bacteriophage T4, a virus that infects *Escherichia coli*. With its icosahedral head, contractile tail, and leg-like tail fibres, T4 is an iconic model for understanding phage architecture, infection mechanisms, and virus–host interactions. As multidrug-resistant bacteria become harder to treat, bacteriophages are also attracting renewed interest as specific antibacterial agents that can kill bacteria (see project report on page 23).

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Fellows

Foundation

Publishing Information

PUBLISHED BY
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glorious mess GmbH & Co. KG
Pappelallee 78/79,
10437 Berlin, Germany
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PRINTED BY
LUC GmbH
Hansaring 118
48268 Greven, Germany

IMAGES
Boehringer Ingelheim Fonds, unless stated otherwise

COVER GRAPHIC
Carina Crenshaw, www.sugah.de

FONT
Novel, www.atlasfonts.com

COVER PHOTOS
Russell Knightley / Science Photo Library (left); sanjeri / iStock (middle); Aliaksandr / Adobe Stock (right)

PUBLICATION DATE OF CURRENT ISSUE
June 2026

Two Ways of Knowing the World

‘Those who know only their own present do not truly understand it. What we are used to is all too easily mistaken for something self-evident.’

On 11 June, we marked the 70th anniversary of the Siblings Boehringer Ingelheim Foundation for the Humanities, the oldest of the three Boehringer Ingelheim foundations, with a celebration at the Saalkirche in Ingelheim, Germany. Since its inception in 1956, the foundation has supported outstanding researchers in the humanities, mostly by subsidising printing costs for their books.

As part of the anniversary celebrations, the foundation awarded prizes to two of its fundees: the first prize of €10,000 went to Dr Elke Dubbels, professor of German at Osnabrück University, and the second prize of €6,000 to Dr Corinna Gannon, assistant curator at the Städel Museum in Frankfurt. The keynote address was delivered by historian Barbara Stollberg-Rilinger, rector of the Wissenschaftskolleg zu Berlin, an institution with a simple yet unusual mission: to give outstanding scholars a year of almost complete intellectual freedom to pursue a project of their own choosing.

You may wonder why we are discussing the humanities in this issue of *Futura*. The reason extends beyond family news from one of our sister foundations. The humanities remind us that knowledge does not exist in a vacuum. They place ideas, discoveries, and institutions in their historical and cultural context, helping us understand not only where we are, but also how we arrived here. Or, as Barbara Stollberg-Rilinger put it so succinctly: ‘Those who know only their own present do not truly understand it. What we are used to is all too easily mistaken for something self-evident.’

That is a useful warning for any researcher. The assumptions a discipline treats as obvious – about what counts as evidence, what counts as a question worth asking, what its results are ultimately for – are precisely the things historical and philosophical distance helps us to see.

Contemporary societal challenges related to natural phenomena are not solely of a technical or scientific nature. They are also questions of how societies interpret evidence, weigh consequences, and decide what to do. Scientific evidence remains indispensable, but evidence alone rarely settles public debate.

That does not diminish the value of specialisation. Quite the opposite. Progress depends on deep expertise. Yet it also depends on understanding enough of other ways of thinking to recognise the limits of one’s own. The humanities can illuminate how knowledge is interpreted and trusted – the sciences can establish it through observation, experiment, and evidence. What we are arguing for, then, is mutual understanding. Not a trading of roles, but enough fluency in the other side’s method to ask better questions of our own.

That is not a utopian aspiration. It is part of what makes scientific inquiry rigorous. In that spirit: a happy 70th to our smallest sister foundation.

Stephan Formella

Marc Wittstock

From Experiment to Exhibition: Making Art out of Used Oligo Tubes

For a creative mind, inspiration can emerge from the most ordinary materials – even from the plastic tubes used in molecular biology experiments. After completing his PhD, scientist and artist Philip Dexheimer was about to discard a large collection of oligo tubes when a suggestion from his supervisor led to a different idea: turning them into an artwork. With donations from colleagues, more than 10,000 used tubes were collected, and Philip turned them into a piece connected to the Research Institute of Molecular Pathology (IMP) in Vienna, Austria, where he spent nine years as a PhD student and a postdoc. More than 200 hours of hand-painting and assembly were required for 'Locus', which pays tribute to IMP founder Max Birnstiel, who isolated the first eukaryotic gene, the Xenopus rDNA locus. The background reproduces the exact DNA sequence using colour-coded tubes representing the four bases. The single red tube contains the 5.8S rDNA sequence first determined by Birnstiel. The final piece, sealed in epoxy resin, is now on display in the IMP foyer.

www.philippdexheimer.com

Credit: Philip Dexheimer

A **Coffee Break** for Electron Microscopy

Coffee is much more than most people's favourite hot drink: it can deodorise refrigerators, fertilise acid-loving garden plants, and even serve as a DIY exfoliating scrub. Now, researchers at Graz University of Technology (TU Graz) in Austria have added a high-tech use to that list: a shot of espresso may offer a safer way to stain biological samples for imaging. They found that espresso can serve as a viable, environmentally friendly alternative to uranyl acetate, a highly toxic and radioactive staple of biological electron microscopy.

In electron microscopy, samples must be cut into ultrathin sections and treated with a stain to enhance contrast. Without it, many microscopic structures remain difficult to see. For decades, uranyl acetate has been the gold standard, but its radioactivity makes it difficult or impossible to use in some laboratories.

The idea to test coffee as an alternative came from a surprisingly domestic observation. An ultramicrotomy specialist at the Institute of Electron Microscopy and Nanoanalysis at TU Graz noticed the dark rings left behind in dried coffee cups. If coffee could stain ceramic so effectively, why not biological tissue?

To test the idea, the researchers compared ultrathin mitochondrial sections treated under identical conditions with either uranyl acetate or standard espresso. Using specialised image analysis software, they found that espresso produced contrast values comparable to those of the traditional stain. In some cases, the coffee-based method even performed better.

The results are promising, but the team is not packing away the chemicals just yet. Further testing across a wider range of tissue types will be needed before espresso can be adopted more broadly in life-science electron microscopy. Still, for laboratories restricted by safety regulations on radioactive materials, the future of imaging may look dark, bold, and surprisingly aromatic.

Mayrhofer C, Zandonella R, Salvenmoser W, Letofsky-Papst I. Coffee – a ubiquitous substitute for uranyl acetate in staining of biological ultrathin sections for electron microscopy studies. Methods. 2025. doi:10.1016/j.ymeth.2025.08.009.

The Surprisingly **Slippery Explanation** for Slippery Ice

Every Winter Olympics, the world enters a brief but passionate love affair with curling – a hypnotic spectacle of heavy stones gliding smoothly across the ice, accompanied by frantic shouting and furious sweeping. And while the rules of curling may seem complicated to the uninitiated, the physics that make such precise motion possible are even more intricate.

For more than a century, physics textbooks have explained why ice is slippery in simple terms: pressure and friction generate a thin film of meltwater that reduces resistance. However, a new study indicates that neither pressure nor friction is required to generate a lubricating layer under many conditions. Using large-scale molecular simulations, the researchers show that sliding ice can lubricate itself even at extremely low temperatures – not through pressure-induced melting, but through disorder created by interacting molecular dipoles at the interface.

Ice forms a highly ordered crystalline lattice in which water molecules align through hydrogen bonding. Each molecule carries an electric dipole, meaning that positive and negative charges are unevenly distributed. When another material comes into contact with the ice surface, its own molecular dipoles interact with those in the crystal. Because these orientations cannot all be satisfied simultaneously at the interface, the system develops what physicists call frustrated interactions. The resulting disorder disrupts the regular lattice in the outermost molecular layers, producing an amorphous, mobile film that behaves like a viscous liquid.

This new theory also accounts for the observation that sliding gets difficult in extreme cold: the simulations show that the mobile film still forms, but its viscosity increases with plunging temperatures, offering more resistance and slowing down every slide.

Atila A, Sukhomlinov SV, Müser MH. Cold self-lubrication of sliding ice. Phys Rev Lett. 2025;135:066204.

Daddy to the Rescue: Paternal Mitochondria Restore Fertility

A tobacco plant with defective mitochondria has wrinkled, male-sterile flowers (left). The inheritance of healthy paternal mitochondria restores the flowers' full bloom.

In both plants and animals, mitochondria are almost exclusively a gift from mum, while dad's are typically shut out of inheritance. But Chinese and German researchers, among them BIF alumnus Ralph Bock, have now shown that this rule is not absolute. In tobacco plants, paternal mitochondria can make it through after all – and even restore fertility when maternal mitochondria are defective.

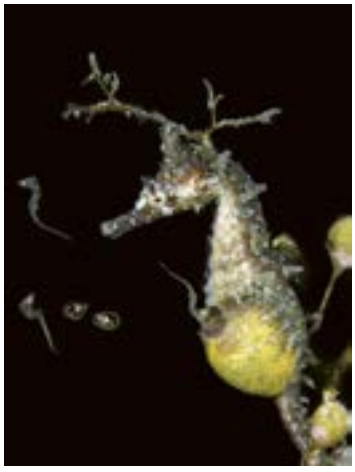
The researchers established a forward genetic screening system in *Nicotiana tabacum* using lines carrying dysfunctional mitochondrial genomes that result in slow growth, curled leaves, wrinkled flowers, and cytoplasmic male sterility. Because these plants produce functional ovaries, but sterile pollen, fertilisation with pollen from wild-type plants allowed mitochondrial inheritance patterns to be tracked.

Most offspring retained the defective maternal mitochondria, but a small fraction showed normal growth, indicating paternal transmission. Under standard conditions, paternal inheritance occurred at a frequency of around 0.18%. Transmission increased, however, to more than 7% when two factors were combined: genetic inactivation of a nuclease involved in mitochondrial DNA degradation and exposure of developing pollen to low temperature. Under these conditions, mitochondria entering sperm cells retained intact genomes.

Only a few paternal mitochondria were sufficient to rescue growth and fertility in plants carrying defective maternal organelles, demonstrating that biparental inheritance can restore mitochondrial function *in vivo*.

Gonzalez-Duran E, Liang Z, Forner J, et al. High-frequency biparental inheritance of plant mitochondria upon chilling stress and loss of a genome-degrading nuclease. Nat Plants. 2026;12:571–582.

No Womb? No Problem!



A male Korean seahorse (*Hippocampus haema*) during birth: the young are leaving the brood pouch.

Seahorses hardly do anything the ordinary way. These upright-swimming, armour-plated fish with prehensile tails already stand out among their fellow fish. So, naturally, their reproductive biology had to be just as unconventional. Seahorses belong to the fish family Syngnathidae, which includes seahorses, pipefish, and sea dragons. Here, it is the male that carries the developing young and ultimately gives birth. A team at the University of Konstanz, Germany, has now examined the cellular and molecular basis of this unusual reproductive strategy, identifying androgen-dependent tissue remodelling and atypical immune regulation that enable male pregnancy.

In syngnathid fishes, females deposit their eggs into a specialised brood pouch on the male's ventral surface, where fertilisation occurs. The embryos develop inside this pouch, receiving oxygen and nutrients from paternal tissues until live birth. The brood pouch is considered an evolutionary novelty and functionally resembles both a uterus and a placenta.

The researchers analysed gene expression in the brood pouch at single-cell resolution and compared it with that in mammalian placental tissues. During pregnancy, pouch epithelium undergoes pronounced thickening, vascularisation, and structural reorganisation, forming a placenta-like interface. However, these changes do not appear to depend on oestrogens or other classical female hormones. Instead, androgen signalling dominated the transcriptional profile, thereby generating a functional analogue of the mammalian placenta through a distinct endocrine pathway.

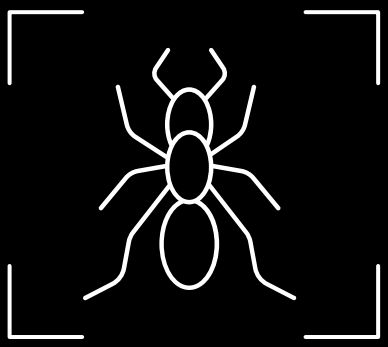
Comparative analyses across Syngnathidae support a stepwise evolutionary scenario in which external egg attachment preceded the evolution of a closed brood pouch.

Liu Y, Jiang H, Miao Y, et al. Cellular and molecular mechanisms of seahorse male pregnancy. Nat Ecol Evol. 2025;9(12):2404–2421.

Most patients receive antibody infusions on an outpatient basis, for example at a day clinic.

AROUND

2,200



ants have been digitised in three dimensions to form the core of Antscan, the world's largest online database of high-resolution 3D insect morphology. The alcohol-preserved specimens were sourced from museums and private collections worldwide. Their anatomy is so well preserved that even soft-tissue morphology could be reconstructed. Each scanned specimen is accompanied by detailed metadata, including taxonomic rank, ecological information, and geographical details.

Source: Julian Katzke et al. High-throughput phenomics of global ant biodiversity. Nature Methods, 2026.
www.antscan.info

Credits: Krebsinformationsdienst / Tobias Schwerdt (top); The noun project / BnB Studio (bottom)

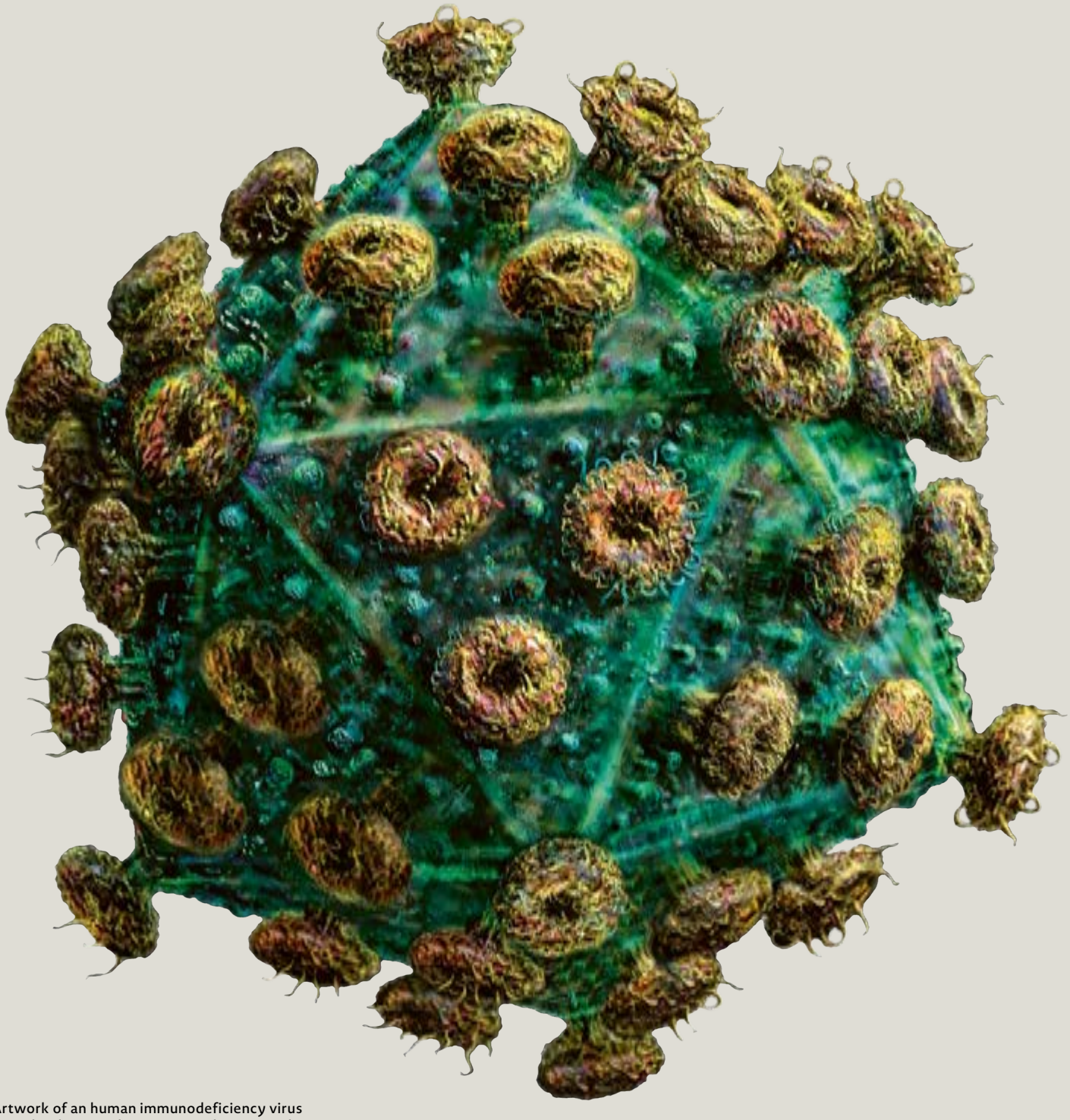
Variation is the Spice of Life – but not for Antibody Drugs

Antibody therapeutics are widely used in oncology, autoimmune disorders, and inflammatory diseases, where their activity depends on the highly specific recognition of structural motifs on target proteins. Individuals naturally differ in their genomic sequence at thousands of positions. In some proteins, a difference in a single amino acid is enough to alter the three-dimensional structure of antibody binding sites. Such changes may prevent antibody therapeutics from binding to their target in a small proportion of patients. Researchers at the University of Basel, Switzerland, report that these substitutions within antibody epitopes occur more frequently than previously appreciated.

The researchers analysed population-scale genomic datasets from previously published studies using computational approaches and mapped variants onto the epitopes of 87 clinically used therapeutic antibodies. Numerous naturally occurring variants were identified within antibody binding sites. Most substitutions were not associated with disease and did not impair protein function, but modelling indicated that some could weaken or abolish antibody binding. Experimental validation using four medically relevant target proteins confirmed that single amino acid changes could prevent binding of specific antibodies, whereas alternative antibodies recognising neighbouring epitopes retained activity.

Although the predicted frequency of non-responsive variants was typically below 1% in analysed populations, genotyping antibody binding sites could help explain unexplained treatment failure and improve patient selection.

Marone R, Asllanaj E, Capoferri G, et al. Single-amino acid variants in target epitopes can confer resistance to antibody-based therapies. Sci Transl Med. 2025. doi:10.1126/scitranslmed.ady4877.



Artwork of an human immunodeficiency virus particle, showing the outer membrane envelope (green) studded with surface knobs (yellow) that enable the particle to attach to host cells.

Fighting Viruses with Viruses to Treat Disease

By Mitch Leslie

Scientists are investigating different ways of using viruses to fight the viruses that make us sick. The two most promising approaches are defective viral particles and antiviral payloads delivered by viral ferries. Although the approaches differ, they share the same rationale: the parasite of my parasite is my friend.

During the late 1940s, virologist Preben von Magnus of the Statens Serum Institut in Copenhagen was performing some routine experiments on flu viruses when he noticed what he called 'a discrepancy'. He was trying to identify the best conditions for raising one strain of flu virus in chicken eggs – information that could help vaccine producers, as well as scientists who wanted to generate large amounts of the virus for study.

To grow the virus, von Magnus injected it into fertilised eggs. After allowing the pathogen to replicate for a period of time, he removed liquid from the embryos and then injected it into a new batch of eggs. He repeated the process over and over, testing whether virus production depended on factors such as incubation temperature, humidity, and even the breed of hen that laid the eggs. The discrepancy emerged when von Magnus measured the effect of diluting the virus by different amounts.

To determine how many viruses grew in the eggs he injected, von Magnus removed samples of liquid and performed two tests. One assay determined whether the samples could give mice the flu. The other measured their ability to cause blood cells to bunch up – the more viruses a sample contained, the greater the likelihood that clumping would occur. The clumping test consistently indicated that the samples contained more viruses than did the other method.

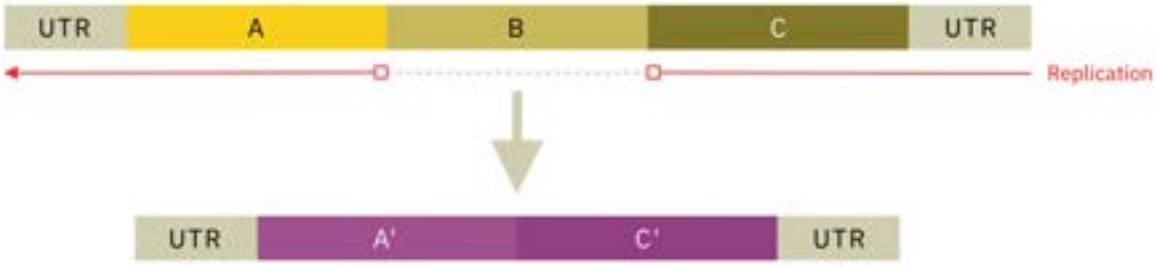
Von Magnus eventually came up with an explanation for this puzzling result, reasoning that infected cells churned out not just 'normal' viruses, but also large numbers of what he called incomplete viruses. These dud virus particles, he postulated, couldn't reproduce and infect the rodents, but were still picked up by the blood-clumping test. 'It seemed important to study the properties' of these unusual particles, he wrote. Von Magnus's follow-up research on flu revealed that incomplete viruses were common and could stymie the replication of their normal counterparts.

Researchers now refer to von Magnus's incomplete viruses as defective viral genomes (DVGs), or as defective interfering particles (DIPs) if they are packaged into a protein shell. DVGs aren't just curiosities. Scientists think they could make powerful weapons against viral diseases.

Dosing people with DVG-based drugs early enough might prevent them from coming down with an illness. Treating them once they are already infected could cut the disease short and potentially save their lives. If another pandemic begins, DVGs could serve as a stopgap, providing protection until scientists can develop vaccines.

Credit: Russell Knightley / Science Photo Library

Deletion DVGs (left) arise when the replication complex detaches and re-initiates synthesis downstream, excluding an intervening genomic region. Copyback DVGs (right) form when replication switches from the template to the nascent strand, generating complementary sequences that can base-pair to form hairpin structures.



UTR = untranslated region
Prime symbol (') denotes the copied RNA region

Modified after Williams R, Hales J, Collier W, and Gould P. Coronavirus replication: genomes, subgenomic RNAs, and defective viral genomes. Viruses. 2025;17:767.

Over the last ten years or so, scientists have made impressive progress in preclinical studies, demonstrating that DVGs can defend lab animals against a range of pathogens, including flu and Zika viruses, along with SARS-CoV-2. The next step is to apply that knowledge to create treatments for humans, says virologist Marco Vignuzzi of Singapore's Agency for Science, Technology, and Research. 'We are at the stage where in the next five years we should be able to come up with a therapy.'

Battle in the Cell

With the technology available in the 1940s and 1950s, von Magnus couldn't isolate incomplete viruses or determine why they couldn't replicate. Since that time, however, 'we've learned a lot about what they do', says virologist and immunologist Carolina Lopez of Washington University. For one thing, researchers have discovered that 'there are tons of them', she says. Numerous types of viruses produce defective genomes, including pathogens such as the Ebola, dengue, rabies, hepatitis C, polio, and chikungunya viruses.

Scientists have also discovered that DVGs can differ from normal viral genomes in several ways. Some DVGs harbour changes to individual nucleotides. In other cases, large chunks of the genome are missing. A 2022 study, for example, reported a naturally occurring version of SARS-CoV-2 that had lost 84% of its genome. Although some of these alterations are mutations that arise randomly, others regularly occur at specific sequences. These hot spots might hint at vulnerabilities to be explored for therapy.

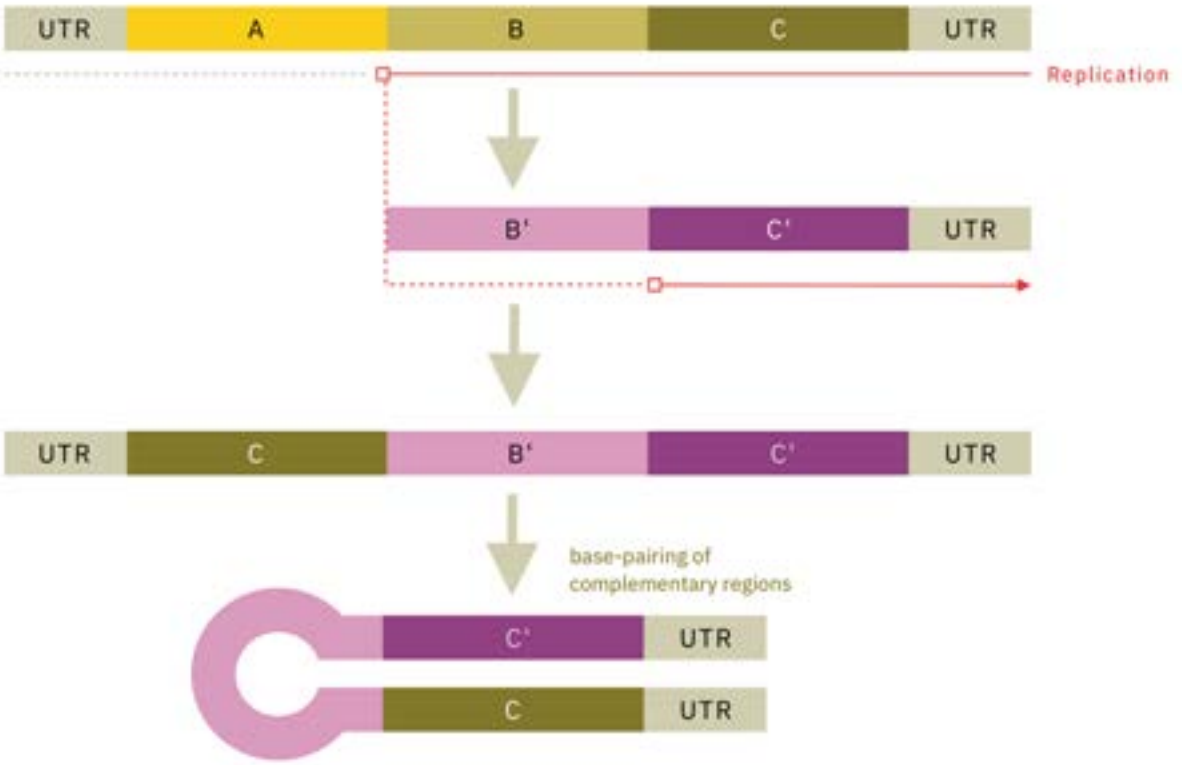
DVGs often form when RNA polymerase, the enzyme that copies viral RNA in an infected cell, loses its grip on the template, the strand it is duplicating. The enzyme may then resume copying at another place on the same template or even switch templates. So-called copy-back DVGs arise when the polymerase lets go of the template and latches onto the new strand it was making. The enzyme then starts recopying this partially duplicated piece, producing a truncated version of the genome with a hairpin structure.

DVGs differ from mutated viruses because they can't replicate on their own. They require assistance from their parent virus. When an infected cell hosts many intact viruses, its replication machinery churns out large numbers of DVGs for two reasons: DVGs are typically shorter than conventional viral genomes, so the cell can copy them more quickly. In addition, some types of DVGs, such as copy-backs and snapbacks, hog the replication machinery because their 3' ends are better promoters, leading to a higher replication rate. DVGs can also harm normal viruses by 'stealing' essential proteins. The overall effect, says virologist Raul Andino of the University of California, San Francisco, is that the defective genomes 'are poison for the real virus'.

However, the effects of DVGs on viral replication fluctuate. That's because DVGs lose their advantage as they become more prevalent in a cell. There are too few of the normal viruses that DVGs need to replicate, so the abundance of the faulty genomes declines. As a result, the number of intact viruses surges – which in turn allows DVG replication to rise again.

DVGs might foil viruses in another way. Besides interfering with replication, scientists have learned that the incomplete genomes rouse the immune system, stimulating the release of defensive proteins known as interferons and activating other protective measures. In lab animals at least, DVGs appear to induce an antiviral state, a broad-spectrum shield against viral infections.

A 2021 study by Andino and colleagues showed how powerful this effect can be. The team created polio virus DVGs and



Infographic: Stephanie Rudolph / glorious mess

then sprayed them into the noses of mice either before or after injecting the animals with the polio virus. The mice gained protection from illness if they received DVGs up to 48 hours before exposure to the virus and up to 48 hours after. In addition, Andino and his colleagues discovered that the polio DVGs shielded the animals from other respiratory viruses, including SARS-CoV-2. 'You could use this as a preventive measure', Andino says. 'There is a real utility here.'

Researchers have been refining DVGs to improve their performance in hopes of combating viruses such as HIV. The pathogen is difficult to target because 'it hides extremely well in resident tissues, in what we call viral reservoirs or sanctuaries', says biochemist Elena Herrera-Carrillo of the Instituto de Parasitología y Biomedicina López-Neyra in Granada, Spain. And, as research by Andino and other researchers has shown, DVGs tend to be effective only during a short window of time. Patients might need repeated doses to maintain protection, which would make the treatment more expensive and harder to use.

But a team led by virologist Leor Weinberger, now at the University of Miami Miller School of Medicine, USA, managed to transform defective genomes into a self-renewing treatment. Starting with a DIP they isolated from cells growing in the lab, the researchers engineered what they called therapeutic interfering particles, or TIPs, that consist of an optimised HIV genome packaged into a protective coat. The researchers' modifications allowed the TIPs to spread readily among cells and thus maintain their abundance in the body. When the scientists injected TIPs into monkeys, the particles were still detectable in the animals' blood at the end of the study 30 weeks later. The TIPs also tripled the odds of survival for monkeys infected with a relative of HIV, the researchers revealed in 2024.

In a 2025 preprint, Vignuzzi, his postdoc Fadi Alnaji, and their colleagues revealed another approach for making more effective DVGs. They started by growing flu viruses in cultured cells. Every 18 hours, they would remove some of the liquid from the cultures, which was rich in viruses and DVGs, and add it to a new culture. They repeated these transfers 72 times. 'That's a lot', Vignuzzi says. But the DVGs had time to compete and evolve. At the end of the experiment, 'we found DVGs that were even better at fighting viruses' than their counterparts that arose naturally, says Vignuzzi.

Getting Real

With advances like these, 'we are halfway' to turning DVGs into therapies, says Vignuzzi. But researchers still face practical obstacles, as well as safety concerns. Applied virologist Sascha Kupke of the Max Planck Institute for Dynamics of Complex Technical Systems in Magdeburg, Germany, and his colleagues have tackled some of the logistical issues. 'We wanted to find out whether this approach [DVGs] could be used in reality', Kupke says.

The researchers have identified a flu DVG they dubbed OP7 that is particularly potent. In experiments on cultured cells and mice, OP7 provided protection against flu viruses and other viral pathogens. As the scientists revealed in 2024, they have set up a production process in bioreactors that can generate large amounts of OP7 without requiring any infectious flu viruses, a key safety advantage for clinical application. Moreover, the cost was reasonable, says Kupke, about the same as for a conventional vaccine. 'We showed we can produce [DVGs] in an economical, feasible way', he says.

Another potential obstacle is the immune system. By picking off infected cells, it could reduce the potency of TIPs or other DVG-based treatments. To assess its impact,

Some locations in viral genomes seem to be specialised for producing defective viral genomes.

theoretical immunologist Rob de Boer and his graduate student Griffin Kutler Dodd of Utrecht University, the Netherlands, built a mathematical model that tracks TIPs' effects on HIV-infected cells. They asked what would happen if the immune system killed infected cells at different rates.

If the immune response is weak, TIPs suppress HIV, the model showed. But even a modest immune counterattack makes the treatment much less effective, the pair reported earlier this year. The results don't rule out TIPs as a potential HIV therapy, says de Boer. 'The immune system is a problem here. But that doesn't mean it's not going to work.' Researchers may be able to refine the approach, identifying conditions under which it's more likely to be successful. 'We view immune responses as a challenge, not a barrier', says Kutler Dodd.

The safety of DVGs is another issue that remains unresolved. Lopez is concerned that instead of controlling viral infections, DVG-based treatments could make them worse. Her misgivings stem from an unanswered question about the faulty genomes: why do viruses produce so many of them in the first place? One possible explanation is that viruses can't help it. Their replication mechanisms have evolved for speed and naturally make numerous mistakes. If that's the case, DVGs are by-products of sloppy viral replication and serve no function.

But some locations in viral genomes seem to be specialised for producing DVGs. And it's possible, some researchers say, that DVGs benefit their parent viruses. By reducing the severity of an infection, they could help viruses persist in the body and perhaps infect more hosts. Some studies on cultured cells support this idea, Lopez notes. Vignuzzi says that showing that DVGs aid viruses in the body is extremely difficult. Still, says Lopez, the possibility is worrying enough that 'we need to be cautious'.

Your Viral Delivery Is Here

Researchers are investigating another way to recruit viruses to fight disease: using them to ferry cargoes that inhibit or eliminate other viruses. Among the virus-versus-virus approaches, this strategy stands out because potential treatments have reached clinical trials, although no drug has yet received approval from regulators.

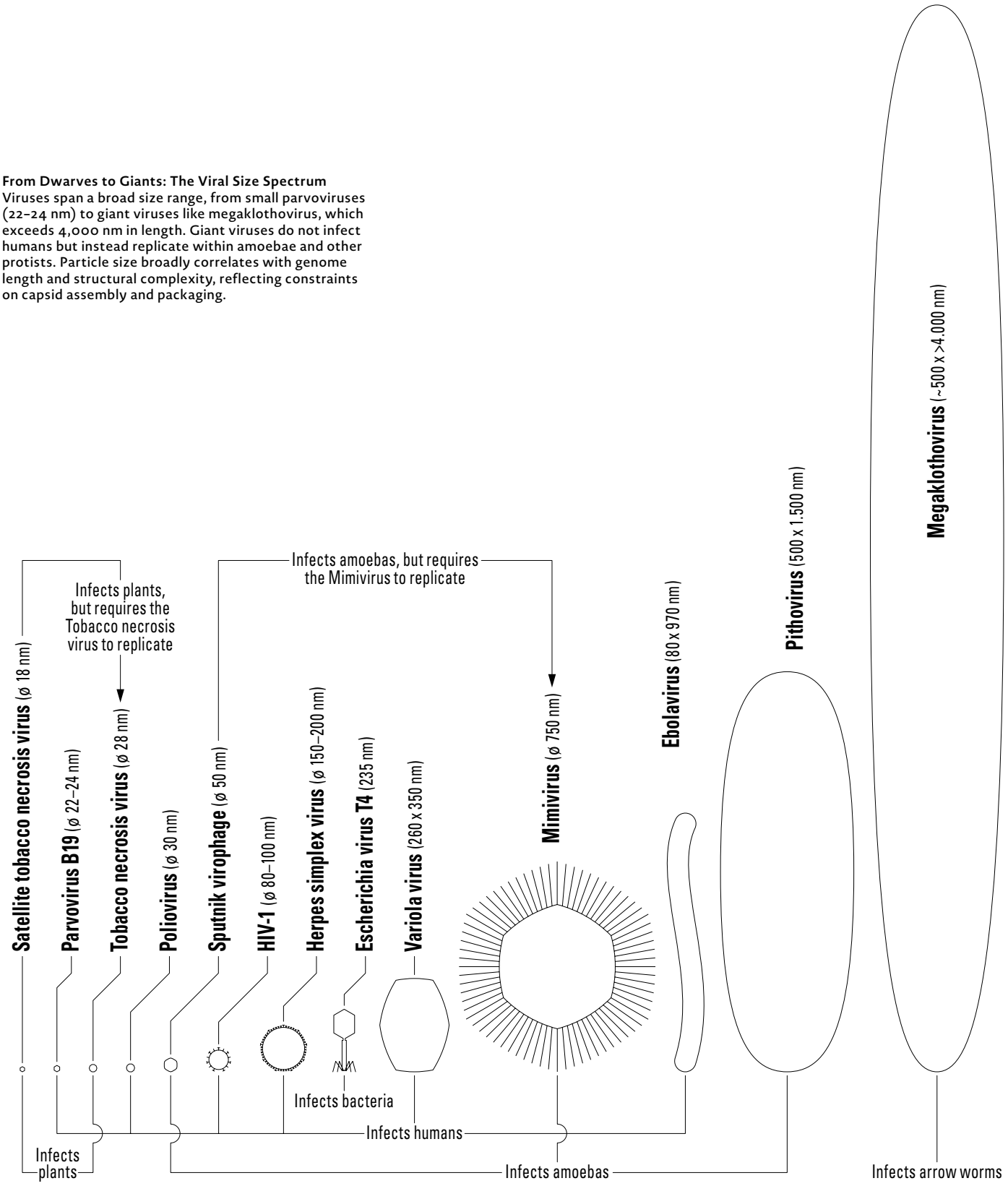
Scientists have long relied on viruses such as lentiviruses and adeno-associated viruses (AAVs) for genetic engineering because they can transport DNA to target cells and are designed in a way that they cannot replicate. LVs and AAVs are also crucial for a growing number of gene therapies for conditions such as haemophilia and Duchenne muscular dystrophy. Researchers hope that viral ferries will also help them to excise pathogens like HIV and the hepatitis B virus, which insert into patients' genomes.

Existing antiviral drug regimens let patients with HIV lead normal lives by inhibiting the virus's replication. But patients need to take the drugs continually or HIV can emerge from its hiding place in the genome and begin reproducing again. By delivering a finely tuned CRISPR tool, researchers hope to snip HIV sequences out of the genome. Natural DNA-repair mechanisms would then heal the target cell's genome.

To test this idea, researchers have loaded viral ferries with DNA that encodes an enzyme that slices DNA, often Cas9. The added DNA also encodes guide RNAs that tell the enzyme where to cut. When the delivery viruses reach their destination, the infected cell uses the DNA to make the enzyme and the guide RNAs, which can then begin doctoring the cell's genome.

The first clinical trial of this strategy, launched in 2022 by the company Excision BioTherapeutics, used an AAV to bring

From Dwarves to Giants: The Viral Size Spectrum
Viruses span a broad size range, from small parvoviruses (22–24 nm) to giant viruses like megaklothovirus, which exceeds 4,000 nm in length. Giant viruses do not infect humans but instead replicate within amoebae and other protists. Particle size broadly correlates with genome length and structural complexity, reflecting constraints on capsid assembly and packaging.



Infographic: Jörg Block

Virophages belong to a menagerie of hyperparasites, or viruses that exploit other viruses.

the DNA to HIV-infected cells. As the initial test of this approach in humans, the trial was 'a significant advancement', say researchers who weren't involved with it. And as the company revealed in 2024, the treatment appeared to be safe in the five patients who received it. However, it didn't eliminate HIV, probably because the delivery viruses didn't reach many of the cells harbouring HIV. When three of the patients stopped taking their normal antiviral medications, HIV began replicating again.

The race to improve on these results is on. Herrera-Carrillo and colleagues homed in on the guide RNAs. One possible reason that previous methods have been inefficient is that the DNA-targeting enzyme is too slow. It has to make two cuts to remove HIV's genome. But the cell's DNA-repair mechanism starts fixing the first cut before the enzyme can complete the second.

To circumvent that problem, Herrera-Carrillo and her colleagues fine-tuned guide RNAs to speed up the enzyme. Then they used a lentivirus to engineer cultured cells to produce the upgraded guide RNAs, along with a version of Cas9. By coupling two guide RNAs with similar interaction speeds, the scientists boosted the efficiency of viral removal to 97% in human embryonic kidney cells, as they revealed earlier this year.

So far, says Herrera-Carrillo, 'the data themselves are promising, but the challenges ahead are enormous'. For instance, she says, even with more efficient guide RNAs, the approach 'will not reach its full potential until we can deliver CRISPR efficiently and safely to all relevant tissues and HIV reservoir sites'.

That's why she and other researchers are also investigating non-viral delivery approaches, such as the tiny capsules known as lipid nanoparticles.

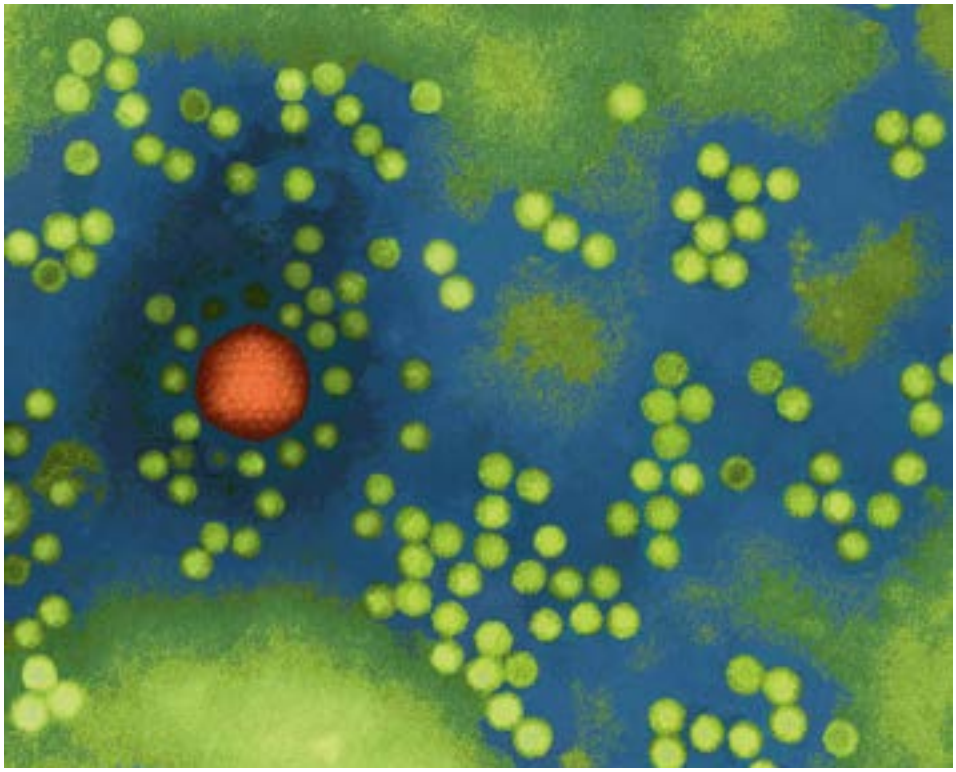
Even Viruses Get Viruses

In 2003, scientists from the Université de la Méditerranée in Marseilles, France, surprised the world by announcing that they had identified an enormous virus, which they dubbed Mimivirus, lurking inside amoebas. The behemoth is so large – around 700 nm in diameter – that it dwarfs some bacteria. Five years later, the same research group also detected tiny particles that they called virophages that appeared to be parasitising a different giant virus. In other words, giant viruses have their own viruses.

Virophages belong to a menagerie of hyperparasites, or viruses that exploit other viruses. Although these parasites come in an assortment of forms, their ecology is similar – they rely on other viruses to reproduce. One category of hyperparasites, the satellite viruses, are stripped down to the bare minimum. The satellite tobacco necrosis virus (STNV), a well-studied example of the group, is around 18 nm in diameter and sports an RNA genome that contains a mere 1,239 base pairs. In comparison, HIV's genome contains more than 9,000 base pairs, and the genomes of some giant viruses top one million base pairs. STNV's mini-genome encodes one protein, which forms the virus's protective coat.

STNV can reproduce in a plant cell only if tobacco necrosis viruses are also present. But STNV repays its helpers by hindering their replication. For example, researchers have found that tobacco necrosis viruses cause less damage to plants that have also been infected by STNV.

Compared with satellite viruses like STNV, virophages are massive. Sputnik, the first member of the group researchers discovered, is around 80 nm in diameter and boasts a genome with 18,000 base pairs. Metagenomic studies – in which researchers analyse DNA and RNA trawled from environments such as the soil, lakes, the ocean, and the guts of animals



Coloured transmission electron micrograph of particles of an adeno-associated virus (AAV, green) and a helper adenovirus (orange). Adeno-associated viruses cannot replicate independently without a helper virus, making them a safe option for delivering genetic cargo to target cells.

– suggest that virophages are widespread. However, scientists have only been able to perform lab studies on a few varieties.

Virophages and giant viruses infect single-celled eukaryotes such as amoebas and algae. Like satellite viruses, virophages need help to replicate – and they get it from the giant viruses. The mammoth viruses induce a host cell to produce a temporary organelle called a virus factory that churns out copies of giant virus DNA and proteins. But virophages co-opt the viral factory to produce their own genome and proteins.

Most virophages appear to be detrimental to giant viruses, curtailing their replication. 'The paradigm we have is that these virophages have a strong impact on the giant virus' that they interact with, says virologist Frank Aylward of Virginia Polytechnic Institute and State University, USA. But some may trigger milder effects or even coexist with giant viruses, he says.

The obvious question is whether scientists could harness virophages or other parasitic viruses to fight diseases. Nobody has established that giant viruses make people sick, says Aylward. 'We are not in any danger of getting Mimivirus infections.' However, he notes, other large viruses cause diseases in humans and domestic animals. The pox viruses, for example, are responsible for smallpox and mpox, a sometimes fatal illness that has spread worldwide in recent decades. Another type of hefty virus triggers African swine fever, an economically important disease that kills almost 100% of domestic pigs that contract it.

So far, no one has discovered virophages or similar parasites that affect the large viruses of humans or domestic animals. But in 2024, Aylward and his colleagues identified a polinton-like virus, a hyperparasite that resembles a virophage, that targets pox viruses of insects. 'So it's not such a big jump' to think that there could be comparable parasites of, say, the virus that causes mpox, Aylward says. 'Maybe there's even therapeutic potential.'

Viruses have plagued humans since the origin of our species. Although researchers have developed some powerful weapons against them, the COVID-19 pandemic illustrated how much we need better antiviral treatments. It would be sweet revenge, scientists say, if these new antiviral therapies came from viruses themselves.

TTCTL

Things That Changed The Lab

Eppendorf Tubes

The Problem:

In the early 1960s, the molecular biology revolution was just getting started. Researchers were working with smaller volumes of reagents and samples and needed correspondingly sized lab gear. The German life science company Eppendorf, which had just introduced a novel piston-driven micropipette for dispensing minute quantities of liquid, was on the case.

The Solution:

In 1962, Wilhelm Bergmann, a development engineer at Eppendorf, came up with a design for a 1.5 ml tube with a tapered tip and a hatch-like lid. Made of polypropylene, the tube was about 39 mm long and 11 mm in diameter. When model 3810, also known as the Eppi®, reached the market in 1963, it was the only small-volume, disposable tube available.

The Impact:

Bergmann's brainchild was a hit. Within three years, scientists bought more than 1 million of the tubes. Eppendorf has since sold more than 1 billion of its various tube versions. They became staples in research fields such as molecular biology, biochemistry, and analytical chemistry, as well as in diagnostic and forensic labs. Scientists use them for storing and centrifuging samples, culturing cells, mixing solutions, carrying out reactions, performing PCR, and a range of other purposes.

The Advantages:

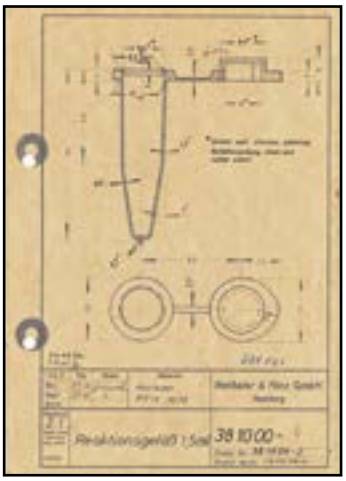
Eppendorf tubes caught on for several reasons. They are sturdy, with some of the modern models able to withstand forces of up to 30,000 × g. They are also resistant to a wide range of temperatures, from –86 °C to 100 °C, and to chemical degradation. The lid keeps the tube's contents in and contaminants out. But the lid can be flipped open with one hand, which allows users to hold the tube and pipette at the same time.

The Diversity:

The original Eppi® became the basis for an assortment of tubes that are tailored for different purposes. The models designed for PCR feature thinner walls, for example, whereas those designed for forensic analysis are guaranteed to be free of human DNA. The tubes now come in a range of volumes, from 0.1 ml to 50 ml, and Eppendorf continues to expand the portfolio to meet evolving scientific needs.

The Downside:

Although Eppendorf introduced a product line largely made from used cooking oil, most tubes are produced from fossil fuels. And they are rarely recycled in practice. Thus, they contribute to the growing problem of plastic waste.



1962 – The First Eppi®
Technical illustration of the first Eppi®, which was developed by development engineer Wilhelm Bergmann at Eppendorf Gerätebau Netheler & Hinz GmbH.

In Well-known Company
What does the Eppi® have in common with Velcro, Tupperware, or Thermos? All are what linguists call proprietary eponyms: brand names that have entered common usage as generic designations for a class of products. This lexical shift arises through frequent colloquial use and market dominance.

Credit: Wladimir Bulgar / Science Photo Library (left); Eppendorf SE (right, top); SolidMaks / iStock (right, bottom)

In the interest of our fellows, we publish only final results online, not descriptions of ongoing projects.

Accordingly, this PDF proceeds directly to the PhD Results section.

PhD Results The Boehringer Ingelheim Fonds funds excellent PhD students who are selected as much for their academic record as for their ambitious projects. Here, they present a synopsis of their findings, which aim to push the boundaries of our knowledge of the fundamental phenomena of human life.

Uncovering the timing of complex genetic events in metastatic and primary tumours

cf. BIF FUTURA 35 / 2.2020

Toby Baker
Discipline: Bioinformatician, MSci
Institute: The Francis Crick Institute, London, UK
Supervisor: Dr Peter Van Loo

Tumours develop through a series of genetic events, the timing of which is important for understanding the basic biology of the disease. Computational statistical approaches can be used to infer their relative timing based on their prevalence in tumour genomes but are less effective for the most genomically unstable tumours, such as metastases. In my PhD project, I developed two computational methods to better infer the somatic evolution of highly chromosomally unstable tumours. The first, Gain Route Identification and Timing In Cancer (GRITIC), uses a novel framework to identify and time all possible sets of events that can lead to a complex chromosomal gain state. The second method, GRITIC-single nucleotide variant (GRITIC-SNV), measures the timing of individual driver mutations and distinguishable mutational processes with much greater resolution than previous approaches.

I applied each method to a large, pan-cancer dataset of primary and metastatic tumour whole-genome sequences. Using GRITIC, I measured the rate of chromosomal gains relative to tumour whole-genome duplications and found that late genome doublings are often followed by a burst of copy number gains. I observed that tumours often arrived at their final copy number state through complex sets of events, casting doubt on the simplifying assumptions made by previous approaches. With GRITIC-SNV, I could time thousands of driver mutations, recapitulating previously known early driver mutations. I timed the occurrence of many mutational processes, finding that mutations linked to exogenous causes (such as tobacco smoke or ultraviolet light) were predominantly early, while those linked to endogenous causes (such as defective DNA mismatch repair) were predominantly late. Notably, many mutational processes with no known cause had distinctive timing behaviour across many tumours, offering a new direction for investigating their underlying mechanisms.

These two new methods enable comprehensive evolutionary analyses of the most chromosomally unstable tumours, which have previously been difficult to study. My work advances our understanding of tumour evolution and could inform future screening strategies.

PUBLICATIONS

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Dissecting the neuronal circuitry of the sleep homeostat in *Drosophila melanogaster*

cf. BIF FUTURA 36 / 2.2021

Lea Ballenberger
Discipline: Neuroscientist, MSc
Institute: Centre for Neural Circuits and Behaviour, University of Oxford, UK
Supervisor: Prof. Gero Miesenböck

Sleep is an evolutionarily conserved and essential state that has been found in all animals studied thus far. It is regulated by two interacting systems: the circadian clock and the homeostatic process. While the circadian system has been well studied, the homeostatic process (in which sleep pressure builds during wakefulness and dissipates during sleep) is not fully understood. In the fruit fly *Drosophila melanogaster*, neurons projecting to the dorsal fan-shaped body (called dFBNs) have been shown to encode sleep pressure. Activating these neurons promotes sleep, and sleep deprivation increases their excitability and activity.

To understand how dFBNs function in their neuronal network, I analysed their neuronal connections and how dFBN-connected neurons influence the regulation of sleep and are functionally connected to dFBNs. Using data from published fly connectomes, I mapped all neuronal connections of dFBNs. I found that dFBNs form connections with many different types of neurons. The largest share of postsynaptic connections was formed with hDeltaF neurons, a group of eight interneurons in the fan-shaped body that are not yet well characterised. To detect how dFBN-connected neurons are involved in the regulation of sleep, I performed a behavioural screen in which I artificially activated or inhibited the target neurons and then measured any changes in sleep. In several cases, this modulation had a clear effect on sleep; for example, activation of hDeltaF neurons showed a strong wake-promoting effect. To better understand the neurons' connection to dFBNs, I performed *in vivo* patch-clamp recordings. In this approach, I optogenetically activated the dFBNs while recording potential synaptic responses from hDeltaF neurons. This experiment revealed an excitatory as well as an inhibitory component within the same synapse. I replicated this pattern by activating the synapse using only glutamate, which suggests that the same neurotransmitter can have a dual action.

Overall, my work provides details of a central synapse that is often not detectable using two-photon imaging. Furthermore, my findings help us to understand the vast number of connections that dFBNs form and the potential circuitries that might facilitate the induction of sleep or wake.

PUBLICATIONS

The results of this project have not yet been published.

Building the master controller of growth: mechanisms of mTOR complex assembly

cf. BIF FUTURA 35 / 2.2020

Karolin Berneiser
Discipline: Biochemist, MSc
Institute: Biozentrum, University of Basel, Switzerland
Supervisor: Prof. Timm Maier

Mammalian target of rapamycin (mTOR), a member of the phosphatidylinositol 3-kinase-related kinase (PIKK) family, is the master regulator of eukaryotic cell growth. It assembles with other proteins into two distinct complexes, which act as selective kinases to modify protein substrates by phosphorylation. PIKKs have essential roles in cell growth and genomic integrity, and aberrant PIKK activity contributes to cancer and other diseases. Despite their common domain organisation, PIKKs assemble into multiprotein complexes of strikingly divergent architecture. Folding and assembly into active complexes is promoted by a conserved chaperone machinery surrounding the TELO2-TTI1-TTI2 (TTT) co-chaperone complex, but the mechanism is poorly understood.

The challenge in studying protein folding complex assembly lies in the transient and dynamic nature of molecular interactions. To map TTT recognition sites on mTOR and other PIKKs, I adapted an in-cell bioluminescence resonance energy transfer system and used it to reveal a multivalent interaction that operates mainly via the N- and C-termini. To determine the mTOR assembly states that the TTT co-chaperone recognises, I co-purified mTOR-TTT complexes from human cells and analysed them biochemically and by cryo-electron microscopy (cryo-EM). Along with proteomic studies, these approaches revealed the minimal interacting units of TTT and mTOR complexes. Furthermore, I found that TTT selectively interacts with non-activated, intermediate assembly states of the mTOR complex in a phosphorylation-dependent manner, revealing a novel link between TTT-mediated PIKK assembly and PIKK activation. To elucidate the structural basis of TTT function as part of a large chaperone machinery, I determined high-resolution cryo-EM structures of TTT alone and in complex with co-chaperones. They revealed TTT intramolecular motions that provide access to structural interfaces, which may be required for both PIKK recognition and regulation of the chaperone machinery.

My results provide insights into the dynamic and multilayered mechanism of TTT-assisted PIKK complex maturation. The in-depth structural analysis of co-chaperone complexes may aid the development of novel approaches for therapeutic intervention in cancer.

PUBLICATIONS

The results of this project have not yet been published.

Regulation of bacterial type VI secretion system during lifestyle change

cf. BIF FUTURA 37 / 1.2022

Hoi Ching (Christy) Cheung
Discipline: Microbiologist, MRes
Institute: Biozentrum, University of Basel, Switzerland
Supervisor: Prof. Marek Basler

Pathogens have evolved mechanisms to sense their surroundings and adapt their behaviour accordingly. In my PhD project, I studied *Burkholderia thailandensis*, a bacterium that typically inhabits soil and water but can transition to an intracellular lifestyle during human infection. One of its main virulence factors is type VI secretion system 5 (T6SS-5), which is important for cell-to-cell spread. The T6SS is a bacterial nano-machinery that delivers effector proteins into target cells. *B. thailandensis* has five distinct T6SSs, each serving a different function, but how their activity is regulated in response to environmental conditions was unclear.

Using live-cell confocal microscopy and infection assays on human epithelial cells, I observed the dynamics of fluorescently tagged T6SSs within individual bacteria during infection. I discovered that as the anti-eukaryotic T6SS-5 is expressed, the anti-bacterial T6SS-1 is gradually shut down. By contrast, when the bacterium is outside host cells, it activates T6SS-1 to enable bacterial competition but does not express T6SS-5. This switch is controlled by a two-component bacterial regulatory system based on the VirA sensor protein and the VirG transcriptional response regulator. I showed that overexpression of VirA and VirG *in vitro* inhibits T6SS-1 activity and induces T6SS-5 expression, while deletion of *virA* during infection restores T6SS-1 activity and blocks T6SS-5 expression. As T6SS-1 secretes toxic proteins such as lipases, T6SS-1 activity in host cells leads to mitochondrial damage and thus induces apoptotic cell death.

My work demonstrates how *B. thailandensis* carefully adjusts its attack systems in response to its surroundings, thereby optimising its survival both within host cells and in the extracellular environment. My findings could also help us understand how other intracellular bacteria use similar two-component systems to sense and adapt to their surroundings.

PUBLICATIONS

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Mechanisms of human mitochondrial RNA maturation

cf. BIF FUTURA 37 / 1.2022

Anna Franziska Finke
Discipline: Biochemist, MSc
Institute: University Medical Center Göttingen, Germany
Supervisor: Prof. Hauke S. Hillen

The function of mitochondria depends on the coordinated expression of their genome. Mitochondrial genes are transcribed as long polycistronic precursor transcripts that are processed and matured to generate functional RNAs. Transcription produces equal copy numbers of individual mRNA molecules, but their observed steady-state levels differ. This regulation is mediated partly by an RNA chaperone, leucine-rich pentatricopeptide repeat-containing (LRPPRC) / SRA stem-loop interacting RNA binding protein (SLIRP). This protein complex is also involved in mitochondrial mRNA maturation by regulating the activity of mitochondrial poly(A) RNA polymerase (mtPAP). However, how LRPPRC recognises and coordinates its large number of RNA targets and how it regulates mtPAP was largely unknown.

In my PhD project, I biochemically dissected the RNA-binding mode of LRPPRC/SLIRP and its cooperation with mtPAP using defined *in vitro* systems. Using fluorescence anisotropy, I revealed that the LRPPRC/SLIRP complex binds diverse RNAs with high affinity. By systematically analysing the RNA-binding affinities of different LRPPRC constructs, I identified domains involved in RNA recognition and showed that two of the three LRPPRC domains can independently coordinate RNA. In addition, I used cryo-electron microscopy to elucidate LRPPRC/SLIRP-RNA structures, providing molecular details of protein-RNA interactions for one domain and highlighting the modularity and flexibility of these interactions. One structure reveals the formation of a higher-order LRPPRC/SLIRP assembly with RNA, which may contribute to flexible RNA coordination. To understand how LRPPRC/SLIRP regulates mitochondrial polyadenylation, I performed *in vitro* polyadenylation assays by incubating different LRPPRC constructs with mtPAP and various RNAs. These assays identified distinct LRPPRC domains that crosstalk with mtPAP, with two domains involved in mRNA maturation, while published data indicate that the third domain is important for regulating mitochondrial translation.

My work provides a mechanistic framework for how LRPPRC integrates RNA binding with post-transcriptional regulation in mitochondria. More generally, it illustrates how modular RNA-binding proteins can coordinate multiple steps of mitochondrial gene expression.

PUBLICATIONS
The results of this project have not yet been published.

Control of entry into mitosis by Cdc25 phosphatase and Wee1 kinase

cf. BIF FUTURA 37 / 1.2022

Thomas Hammond
Discipline: Biochemist, MSci
Institute: The Francis Crick Institute, London, UK
Supervisor: Sir Paul Nurse

Mitosis involves a complex series of cellular rearrangements that lead to the equal segregation of chromosomes into two daughter cells. In eukaryotes, entry into mitosis is driven by high cyclin-dependent kinase (CDK) activity. Once activated, CDK catalyses the phosphorylation of hundreds of substrate proteins that bring about the events of mitosis. To ensure a tightly controlled transition, CDK must be activated rapidly at the correct time during the cell cycle. Our understanding of the molecular mechanisms underlying this process remained incomplete.

In my PhD project, I investigated how entry into mitosis is regulated by two conserved enzymes, Wee1 G2 checkpoint kinase (Wee1) and cell division cycle 25 (Cdc25). The kinase Wee1 adds inhibitory tyrosine phosphorylation on CDK, while the phosphatase Cdc25 removes it. The levels of Wee1 and Cdc25 have been proposed to modulate the timing of entry into mitosis in a dose-dependent manner. However, I found that varying Wee1 or Cdc25 levels in the fission yeast *Schizosaccharomyces pombe* led to only small changes in mitotic entry timing. Multisite phosphorylation by CDK has been proposed to activate Cdc25 and to inhibit Wee1, setting up feedback loops that facilitate the rapid amplification of CDK activity. I showed that mutating candidate CDK phosphorylation sites in *S. pombe* Cdc25 delayed entry into mitosis. By contrast, mutating candidate CDK phosphorylation sites in *S. pombe* Wee1 did not delay entry into mitosis. Next, I used single-cell biosensors to measure CDK activity through the cell cycle in wild-type cells and in cells where multisite phosphorylation of Cdc25 was disrupted. I found that CDK activity increased less abruptly at entry into mitosis in the cells with disrupted Cdc25 phosphorylation.

My findings suggest that Wee1 and Cdc25 levels do not strongly influence the cell cycle timing of mitosis – contrary to the previous hypothesis – and that Cdc25 phosphorylation is required for timely CDK activation. In addition to providing *in vivo* evidence for a positive feedback loop between Cdc25 and CDK, my results also call into question the role of Wee1 phosphorylation by CDK. My work thus provides new insights into the control of entry into mitosis in eukaryotic cells and challenges some existing models for Cdc25 and Wee1 regulation.

PUBLICATIONS
The results of this project have not yet been published.

DDX3X and DDX3Y dosage imbalance drives sex bias in Burkitt lymphoma

cf. BIF FUTURA 37 / 1.2022

Kaiyue Helian
Discipline: Haematologist, MSc
Institute: Cambridge Stem Cell Institute, University of Cambridge, UK
Supervisor: Dr Daniel Hodson

Non-Hodgkin lymphoma, a cancer of the lymphatic system, is the fifth commonest malignancy worldwide. The most aggressive subtype is Burkitt lymphoma (BL), which arises from a stage of B-cell maturation known as the germinal centre. Deletion or loss-of-function mutations of the RNA helicase DEAD-box helicase 3X (DDX3X) are frequently found in BL and in other forms of aggressive lymphoma driven by the MYC oncogene. The Hodson group had shown that male lymphoma cells with DDX3X mutation gain ectopic expression of, and become dependent on, its almost identical paralogue, DDX3Y. The aim of my PhD project was to explore this concept of switched paralogue dependency by comparing the molecular functions of DDX3X and DDX3Y in B-cell development and MYC-driven lymphomagenesis.

The epitope tagging of the endogenous loci of DDX3X and DDX3Y in lymphoma cell lines permitted efficient side-by-side immunoprecipitation, which enabled me to identify protein and RNA interactomes. I found that the paralogues have largely redundant functions, including regulating ribosome biogenesis and translation initiation. My results suggested, however, that subtle differences may exist, most notably the possibility that DDX3X and DDX3Y bind differently to the components of the eukaryotic initiation factor complex. In parallel, I used conditional mouse models to show that deletion of *Ddx3x*, but not *Ddx3y*, led to impaired germinal centre function, cell proliferation, and accelerated MYC-induced lymphomagenesis. These phenotypes are most likely to be linked by the decrease in total DDX3 dosage in male mice with *Ddx3x* deletion, since DDX3Y was expressed much less than DDX3X. The total DDX3 dosage was less in female mice with heterozygous mutations of *Ddx3x* than in wild-type mice, but still high enough to maintain normal functionality. My results show that the total DDX3 dosage is tightly controlled during lymphomagenesis, with a sweet spot of 'low but not no' DDX3 expression that is permissive for tumour formation. The ability to achieve this sweet spot in males but not females may explain why the incidence of BL is three times higher in men than in women.

My work provides new insights into sex-specific mechanisms of cancer and highlights DDX3Y dependency as a potential therapeutic vulnerability in male lymphomas.

PUBLICATIONS

The results of this project have not yet been published.

Uncovering neural architectures for robust and flexible motor control in *Drosophila*

cf. BIF FUTURA 37 / 1.2022

Femke Hurtak
Discipline: Physicist, MSc
Institute: Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland
Supervisor: Prof. Pavan Ramdya

To advance knowledge and develop interventions for motor disorders, it is crucial to understand the neural architectures responsible for robust and flexible motor control. In my PhD project, I used the *Drosophila melanogaster* nervous system to investigate neural circuitry organisation. I focused on the descending neurons (DNs), which are essential for movement coordination. These cells form a highly interconnected, structured processing layer between the brain and the ventral nerve cord (VNC), the invertebrate equivalent of a spinal cord.

I demonstrated that command-like DNs, previously thought to trigger behaviours independently, actively recruit networks of other DNs. Using connectome analysis and functional recordings, I revealed that this recruitment is necessary for complex behaviours like forward walking. I showed that the DN networks are organised into behaviour-specific clusters interconnected by predominantly inhibitory synapses, thereby supporting action selection via mutual inhibition. I also showed that inhibition is a core element of VNC network organisation. Descending signal integration in the VNC revealed a modular and relatively shallow circuitry in which motor neurons are often one interneuron away from DN inputs. I hypothesised that this shallowness facilitates efficient translation of descending commands into motor patterns, while local VNC dynamics handle temporal patterning. To understand how movements are coordinated when a DN is activated, I analysed all neurons that are directly downstream of the DNs that trigger backwards walking. The results of this circuit analysis suggested a model where targeted pre-motor inhibition helps select and coordinate muscle groups for specific movements.

My results reveal that modularity in the *Drosophila* motor system ensures behavioural robustness and distributed control. By updating the framework for understanding how biological neural networks generate diverse, adaptive behaviours, my work may aid the design of more distributed artificial control systems.

PUBLICATIONS

Braun J*, Hurtak F*, Wang-Chen S, Ramdya P. Descending networks transform command signals into population motor control. Nature. 2024;630:686-94.

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* Shared authorship

How brain cells use their long branches to interpret what we see

cf. BIF FUTURA 38 / 1.2023

Anyi Liu
Discipline: Systems Neuroscientist, MSc
Institute: University College London, UK
Supervisor: Prof. Matteo Carandini

Understanding how a single neuron integrates and processes the immense inputs it receives remains a central challenge in systems neuroscience. In neurons of the visual brain, the apical dendrite is anatomically positioned to collect diverse inputs, yet its precise functional contribution in the living brain is unclear and has been subject to conflicting reports.

In my PhD project, I aimed to address this gap in knowledge by combining apical dendrite cutting with functional imaging in awake adult mice. Through this causal manipulation, I compared the visual responses within the cell before and after cutting. In a complementary approach, I used glutamatergic input mapping to measure the spatial origin of excitatory apical inputs. I found that removing the distal part of the apical dendrite (the apical tuft) did not alter basic visual tuning: orientation and direction selectivity were largely preserved. Instead, loss of the apical tuft caused a selective reduction in the amplitude of the response to the strongest stimuli. This effect was stimulus-dependent: neurons that preferred large visual stimuli reduced their responses significantly after cutting, whereas neurons tuned to small stimuli were largely unaffected. Input mapping provided a mechanistic explanation for this finding. Neurons preferring large stimuli had broader and more spatially distributed areas of apical input, consistent with apical dendrites conveying distal visual information not captured by the soma. In contrast, neurons preferring small stimuli received more compact apical inputs and thus showed minimal pruning effects. Together, my results support a model in which apical dendrites do not set the basic visual tuning of the neuron but instead boost somatic responses when they carry non-redundant, spatially extended information. Such a model would be consistent with so-called coincident-detection theories of apical function in brain slices.

Overall, my work provides direct causal evidence for a context-dependent modulatory role of apical dendrites in visual processing. More broadly, it establishes an experimental framework that can be extended to behavioural and learning paradigms to test how apical pathways contribute to higher-order cortical computations.

PUBLICATIONS

The results of this project have not yet been published.

Molecular mechanisms of intracellular pathogen transport by dynein motors

cf. BIF FUTURA 36 / 2.2020

Giulia Manigrasso
Discipline: Molecular Biologist, MSc
Institute: MRC Laboratory of Molecular Biology (LMB), Cambridge, UK
Supervisor: Dr Andrew P. Carter

Cytoplasmic dynein is a microtubule-based motor that powers the long-distance transport of organelles, vesicles, and other cytoplasmic contents from the cell periphery towards the centre. While dynein typically moves cellular cargoes, it can also be hijacked by pathogens that rely on intracellular transport for parts of their replicative cycle. For example, the intracellular bacterium *Orientia tsutsugamushi* exploits dynein and microtubules to reach its subcellular niche at the perinucleus, and herpes simplex virus type 1 (HSV-1) undergoes dynein-dependent movement from the axonal tip of sensory neurons to the nucleus. The ability of these pathogens to co-opt dynein motors is well documented, but the molecular mechanisms underlying this process are not.

In my PhD project, I investigated the molecular mechanisms of dynein recruitment by incoming *O. tsutsugamushi* bacteria. Using a combination of biochemical and cell biological approaches, I identified an interaction between the bacterial surface cell antigen C (ScaC) and bicaudal D cargo adaptor 1 (BICD1) and 2 (BICD2), two proteins with known roles in connecting dynein to its cargoes. Using single-molecule *in vitro* motility assays, I showed that ScaC activates BICD1 and BICD2, thereby promoting the assembly of motile dynein-cargo complexes. Finally, in collaboration with Jeanne Salje's group (University of Cambridge, UK), I showed that the ScaC-BICD interaction is essential for perinuclear translocation of *O. tsutsugamushi* in infected cells. In parallel, I optimised a pipeline to study HSV-1 motility in iNeurons cultured in microfluidic chambers. After refining infection protocols to visualise nuclear capsid translocation by immunofluorescence, I began exploring high-efficiency knockdown strategies in iNeurons to aid future work in the Carter lab.

My work defines a molecular pathway for bacterial transport and provides a foundation for further studies on how perinuclear movement affects the *O. tsutsugamushi* life cycle.

PUBLICATIONS

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Real-time assembly of the regulatory *msl*-2 mRNP complex

cf. BIF FUTURA 36 / 2.2021

Marco Payr
Discipline: Biochemist, MSc
Institute: European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
Supervisors: Prof. Janosch Hennig, Dr Olivier Duss

Translation is a crucial process in cells, and its regulation is essential for proper gene expression and cellular viability. However, the kinetics of mRNA ribonucleoprotein (mRNP) assembly on untranslated regions and the relationship of complex assembly to translational regulatory activity are still not well understood. In my PhD project, I investigated how different mechanisms of mRNP complex assembly synergistically achieve tight translational repression. To this end, I employed multicolour single-molecule fluorescence microscopy to track the assembly of multi-subunit mRNP complexes in real time.

I used sex-lethal (Sxl)-mediated translational repression of male-specific lethal 2 (*msl*-2) during female Drosophila dosage compensation as a model system. Using single-molecule imaging, I showed that Sxl targets its binding sites via facilitated diffusion and double binding to multiple sites on *msl*-2, which prolongs RNA-bound dwell times. My results also revealed that the recruitment rate of another RNA-binding protein, upstream of N-ras (Unr), is accelerated 500-fold by RNA-bound Sxl. This was unexpected, as it has been shown that Unr does not interact with Sxl in the absence of *msl*-2. The contribution of a heterogeneous nuclear ribonucleoprotein, Hrp48, to the translational repression of *msl*-2 has been reported, but its connection to Sxl and Unr had not been established. Using single-molecule imaging and reporter gene assays, I showed that Hrp48 indirectly stabilises RNA-bound Sxl/Unr via ATP-independent RNA remodelling.

By studying complex assembly in real time, I have provided a framework for understanding how multiple RNA-binding proteins dynamically cooperate with RNA to achieve tight translational repression. My results provide insights not only into the mechanisms of translational regulation but also into the complex processes involved in mRNP assembly and how its kinetics govern translational repression. This knowledge contributes to a better understanding of how differential gene expression is linked to the dynamic interactions between proteins and RNA in various biological contexts, such as disease modelling.

PUBLICATIONS

Payr M, Meyer J, Geissen EM, Hennig J, Duss O. Real-time tracking of mRNP complex assembly reveals various mechanisms that synergistically enhance translation repression. Cell Rep. 2025;44(11):116492.

Target recognition drives PIWI* complex assembly for transposon silencing

cf. BIF FUTURA 36 / 2.2021

Júlia Portell i de Montserrat
Discipline: Biochemist, MSc
Institute: Institute of Molecular Biotechnology (IMBA) and Institute of Molecular Pathology (IMP), Vienna, Austria
Supervisors: Dr Julius Brennecke, Dr Clemens Plaschka

Transposable elements are selfish genetic elements that threaten genome integrity, but defence mechanisms have evolved to restrict their activity. The PIWI-interacting RNA (piRNA) pathway, which acts mainly in animal gonads, uses PIWI-clade Argonaute proteins and their associated piRNAs, a class of small RNAs that guide PIWI proteins to complementary transposon transcripts for silencing. Nuclear PIWIs (e.g. *Drosophila* Piwi) silence targets co-transcriptionally by promoting heterochromatin formation, while cytoplasmic PIWIs (e.g. *Drosophila* Aubergine and Ago3) cleave transposon RNAs, initiating the so-called ping-pong amplification cycle for piRNA biogenesis. Although many factors required for heterochromatin formation and ping-pong amplification have been identified, how target recognition by PIWI-piRNA complexes is coupled to the recruitment of downstream effectors was unclear.

In my PhD project, I found that recognition of complementary target RNAs induces the assembly of higher-order PIWI-centred complexes, which I termed PIWI*. These assemblies – which consist of target-engaged PIWI, the Maelstrom protein, and a member of the gametocyte-specific factor (GTSF) protein family – act as effector-recruiting hubs. Using genetics, biochemistry, and structure-guided modelling, I showed that nuclear Piwi* assembles upon target recognition and recruits the nuclear RNA export factor 2 (Nxf2) of the silencing factor interacting nuclear export variant (SFiNX) complex as a direct second-layer interactor, thereby linking target recognition to co-transcriptional silencing. I showed that in the cytoplasm, analogous Aubergine* and Ago3* complexes form with GTSF paralogues and Maelstrom. Aubergine* then recruits spindle-E, an RNA helicase essential for ping-pong.

PIWI* formation is conserved across metazoans, underscoring its ancient role in genome defence. My work closes the long-standing gap between sequence-specific recognition and the execution of silencing.

PUBLICATIONS

Yu C, Manolova T, Tirian L, Handler D, Hohmann U, Nemčko F, Portell-Montserrat J et al. RNA decay via the nuclear exosome is essential for Piwi-mediated transposon silencing. BioRxiv [Preprint]. 2025. doi: 10.64898/2025.12.16.694471.

Portell-Montserrat J, Tirian L, Yu C, Silvestri G, Hohmann U, Handler D, et al. Target RNA recognition drives PIWI* complex assembly for transposon silencing. Mol Cell. 2025;85(17):3288-305.e6.

Cell-stereotyped DNA repair outcomes are widespread during genome editing

cf. BIF FUTURA 36 / 2.2021

Moritz Schlapansky
Discipline: Genome Biologist, MSc
Institute: Institute of Molecular Health Sciences, ETH Zurich, Switzerland
Supervisor: Prof. Jacob Corn

Advances in genome editing have brought us closer to curing previously incurable genetic diseases. However, because editing relies on cell-specific DNA repair pathways, outcomes vary across cell types. Understanding how cellular context shapes editing outcomes is crucial for genome engineering in both the lab and the clinic.

In my PhD project, I developed scOUT-seq (single-cell outcomes using transcript sequencing) to map molecular editing outcomes and gene expression profiles at allelic and single-nucleotide resolution. I showed that outcome profiles are consistent between conventional bulk DNA sequencing and scOUT-seq. I then used scOUT-seq to map outcomes across cell types in human haematopoietic stem and progenitor cells, upper airway organoids, and complex tissues of living mice such as liver and brain. These data revealed cell type-specific patterns that are masked in bulk measurements. My analyses showed that editing outcomes vary greatly yet reproducibly between cell types within the same tissue: some types preferentially generated insertions, others favoured deletions, and several displayed a strong enrichment of inversions and translocations. Homology-directed repair was frequent in megakaryocytes and erythroid precursors but rare in stem cell populations. While stem cells exhibited a bias towards small deletions, liver progenitor cells showed a shift towards microhomology-mediated repair. In the brain, distinct neuronal classes shared stereotypical editing patterns. Using differential gene expression analysis and interpretable machine learning models, I uncovered the genes associated with each outcome. This information can be used as a starting point for functionally dissecting the pathways that orchestrate genome editing.

My findings show that genome editing is strongly shaped by cell identity and that bulk profiles reflect mixtures of diverse cell types rather than single populations. By providing large-scale, cell-resolved maps of editing outcomes, my work improves the predictability of genome editing in heterogeneous tissues and supports the development of more precise and effective research and therapeutic strategies.

PUBLICATIONS

Schlapansky MF, Schröder MS, Santinha AJ, Rothgangl T, Ioannidi EI, Cullot G, et al. Cell-stereotyped DNA repair outcomes are widespread during genome editing. BioRxiv [Preprint]. 2025. doi: 10.1101/2025.10.23.684114.

How inhibitory neurons in the human brain are built during development

cf. BIF FUTURA 39 / 1.2024

Clara Siebert
Discipline: Developmental Biologist, MSc
Institute: Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, University of California San Francisco, CA, USA
Supervisor: Prof. Arnold Kriegstein

In humans, most interneurons are generated in the ganglionic eminences (GEs), three short-lived structures in the developing nervous system. The medial ganglionic eminence (MGE) has a unique structure in primates that is thought to support the immense production of interneurons: nests of immature neurons expressing doublecortin (DCX), a neuronal migration protein, are surrounded by progenitor cells. However, the cellular diversity and organisation of human GE progenitors are poorly understood.

In my PhD project I defined progenitor identities, division behaviours, and spatial organisation in human GEs. By live imaging all three GEs, I revealed the presence of outer radial glia-like progenitors, a cell type usually found in the cerebral cortex and thought to be a key driver of tissue expansion during development. Based on my discovery that these cells also account for a large fraction of divisions in the GEs, I proposed that they help expand the GEs during the second trimester. Using spatial transcriptomics, which visualises RNA expression directly in tissue sections, I identified a spatially distinct niche in the MGE that produces interneurons expressing cellular retinoic acid binding protein 1 (CRABP1). I found that this niche extends pathways that immature neurons move along, called migratory streams, towards the cortex and striatum. Using electron microscopy, I also resolved the cellular architecture of the human MGE and identified a differentiation gradient from radial glia to intermediate progenitors to DCX+ nests. I propose that this organisation supports interneuron production through a multistep amplification. To test a mechanism of DCX+ nest formation, I generated MGE organoids from human pluripotent stem cells and showed that loss of the cell adhesion molecule protocadherin-19 disrupts DCX+ nest formation.

My findings reveal outer radial glia-like progenitors as key contributors to human GE expansion and define the cellular organisation of a primate-specific interneuron niche in the MGE. They also establish protocadherin-mediated cell sorting as a mechanism shaping interneuron production in the developing human forebrain.

PUBLICATIONS

Siebert CV, Song M, Moriano JA, Li Z, Silla AC, Walker M, et al. Progenitor diversity and architecture of the human ganglionic eminences shaping the basal ganglia. BioRxiv [Preprint]. 2026. doi: 10.64898/2025.12.31.697063.

An engineered nuclease for nucleosome-resolution chromosome conformation capture

cf. BIF FUTURA 34 / 1.2019

Jan Soroczynski
Discipline: Biochemist, MBiochem
Institute: The Rockefeller University, New York, NY, USA
Supervisor: Prof. Viviana Risca

Genome folding in the nucleus brings distant regulatory elements into contact with the genes they control. These contacts can be mapped using chromosome conformation capture (3C), which fragments and ligates cross-linked chromatin. High-throughput 3C (Hi-C) uses restriction enzymes, which limits its resolution to kilobases. Micrococcal nuclease (MNase)-based 3C (Micro-C) achieves nucleosome resolution, but MNase is biased towards AT nucleotide pairs, can over-digest, and requires end repair and extensive titration.

To improve on these enzymes, I repurposed caspase-activated DNase (CAD) so it could be activated orthogonally and controllably by tobacco etch virus (TEV) protease, which is widely used in protein engineering. CAD, which cuts DNA between nucleosomes during apoptosis, cleaves with low sequence bias and no exonuclease activity, producing ligation-ready ends that make end repair unnecessary. Based on this engineered nuclease, I developed the 3C method CAD-C, which I used to map contacts in three human cell lines at nucleosome resolution. CAD-C does not need titration and is more sensitive than Hi-C and Micro-C at detecting contacts at active promoters and enhancers. Efficient ligation often yielded multi-nucleosome chains that preserved the order of ligated fragments, with each fragment retaining a nucleosome footprint. Sequencing these chains produced CADwalks: per-molecule records of the identity and order of nucleosome contacts. CADwalks showed that some nucleosomes shuttle to distant loci while neighbours stay local, and that shuttling nucleosomes are enriched at active regulatory sites.

CAD-C provides a simpler, more sensitive route to obtaining nucleosome-scale contact maps and a new single-molecule view of chromatin folding.

PUBLICATIONS

Soroczynski J, Anderson Westcott L*, Zuo W*, Ou A, Canaj H, Hickling J, et al. CAD-C: An engineered nuclease enables repair-free *in situ* proximity ligation and nucleosome-resolution chromosome walks in human cells. BioRxiv [Preprint]. 2025. doi: 10.64898/2025.12.22.695891.

Soroczynski J, Anderson LJ, Yeung JL, Rendleman JM, Oren DA, Konishi HA, Risca VI. OpenTn5: Open-source resource for robust and scalable Tn5 transposase purification and characterization. BioRxiv [Preprint]. 2024. doi: 10.1101/2024.07.11.602973

Soroczynski J, Risca VI. Technological advances in probing 4D genome organization. Curr Opin Cell Biol. 2023;84:102211.

CDK-substrate interactions and the temporal order of the cell cycle

cf. BIF FUTURA 38 / 1.2023

Sarah Willich
Discipline: Cell Biologist, BSc
Institute: The Francis Crick Institute, London, UK
Supervisor: Sir Paul Nurse

During cell division, eukaryotic cells must ensure that their DNA is replicated before being divided into two daughter cells. Cyclin-dependent kinases (CDKs) initiate major cell-cycle events through the phosphorylation of their substrates. The fission yeast *Schizosaccharomyces pombe* can drive its cell cycle through the increasing activity of a single cyclin-CDK complex. S-phase (early) substrates are phosphorylated at low CDK activity, while mitotic (late) substrates require high CDK activity to be phosphorylated. How this difference in substrate sensitivity to CDK activity, and thereby the temporal order of the cell cycle, is established remains to be determined.

My PhD project was designed to test the hypothesis that early substrates interact more readily than late substrates with cyclin-CDK, which allows them to be phosphorylated at low CDK activity. However, I found that early and late substrates were phosphorylated with comparable kinetics by cyclin-CDK in a protein lysate made from *S. pombe* cells. In addition, my protein modelling using AlphaFold2-Multimer predicted that early and late substrates would interact with cyclin-CDK. However, *in vivo*, in living cells, early substrates are known to be phosphorylated faster than late substrates. This led me to hypothesise that something about the cellular environment contributes to CDK substrate sensitivity. Therefore, I investigated whether subcellular localisation could be a key determinant of CDK substrate phosphorylation kinetics. By comparing the *in vitro* and *in vivo* phosphorylation kinetics of CDK substrates, I found that substrates in the nucleus, where CDK is enriched, were phosphorylated faster than cytoplasmic substrates. This led me to conclude that it is the subcellular localisation of CDK and its substrates, rather than intrinsic substrate properties, that shape CDK substrate sensitivity to CDK activity.

It remains to be established how localisation within the nucleus ensures that DNA replication substrates are phosphorylated before mitotic substrates. CDK is known to interact with a component of origins of replication, so future studies should investigate whether disrupting this interaction interferes with the phosphorylation of early substrates.

PUBLICATIONS

The results of this project have not yet been published.

MD FELLOWS 2025 With its MD fellowships, the Boehringer Ingelheim Fonds helps outstanding medical students to pursue an ambitious experimental project in basic biomedical research. Candidates study in Germany and change institution and city for at least ten months to work in an internationally renowned laboratory.

In 2025, 13 fellows were granted an MD fellowship.

Investigating neural regulations of radio-resistance in diffuse midline glioma

Johann Bühse
Duration: 02/25–01/26
Project at: Harvard Medical School, Dana-Farber Cancer Institute, Boston, MA, USA
Supervisor: Prof. Mariella Filbin
Home University: Charité – Universitäts-medizin Berlin

A pallial proxy for the electron leak hypothesis of sleep? An analysis

Jakob Häuser
Duration: 11/25–09/26
Project at: University of Oxford, Centre for Neural Circuits and Behaviour, UK
Supervisor: Prof. Gero Miesenböck
Home University: Heidelberg University

Structural basis of human sweet taste

Johanna Heckmann
Duration: 09/25–06/26
Project at: Yale University School of Medicine, Pharmacology Department, New Haven, CT, USA
Supervisor: Prof. Joel A. Butterwick
Home University: University of Würzburg

Investigating the impact of hepatocyte polyploidy in MASH

Marc Höll
Duration: 10/25–08/26
Project at: ETH Zurich, Institute of Molecular Health Sciences, Switzerland
Supervisor: Prof. Markus Stoffel
Home University: Münster University Hospital

Dissecting the somatic imprint of germline genomic instability in neuroblastoma

Emily Jorswieck
Duration: 02/26–01/27
Project at: Harvard Medical School, Dana-Farber Cancer Institute, Boston, MA, USA
Supervisor: Prof. Riaz Gillani
Home University: Heidelberg University Hospital

Oligodendrocyte precursor cell-dependent remodelling of neural circuits in glioma

Kim Kilian
Duration: 08/25–07/26
Project at: Stanford University, Howard Hughes Medical Institute, Department of Neurology and Neurological Science, CA, USA
Supervisor: Prof. Michelle Monje
Home University: University of Hamburg

Neural mechanisms of inflammation-induced sleep: dissecting the IL-1β-mediated sleep response

Vincent Marquardt
Duration: 09/25–08/26
Project at: Arc Institute, Palo Alto, CA, USA
Supervisor: Prof. Christoph A. Thaiss
Home University: University of Marburg

Molecular characterisation of XRN1-resistant subgenomic RNAs in Usutu virus and their role in replication & pathogenesis

Helen Muhr
Duration: 11/25–10/26
Project at: Columbia University Irving Medical Center, Department of Biochemistry and Molecular Biophysics, New York, NY, USA
Supervisor: Prof. Anna-Lena Steckelberg
Home University: Düsseldorf University Hospital

Pro-inflammatory IFNγ^{+}FoxP3^{+}Tregs as drivers of autoimmune disease

Philipp Müller
Duration: 05/26–04/27
Project at: Harvard Medical School, Massachusetts General Hospital, Center for Immunology and Inflammatory Diseases, Charlestown, MA, USA
Supervisor: Prof. Thorsten R. Mempel
Home University: University Hospital of Munich (LMU)

Detailed characterisation of FASP genes affecting entrainment in circadian regulation and phase

Annegrit Rohlmann
Duration: 03/26–12/26
Project at: University of California, San Francisco, Department of Neurology, CA, USA
Supervisors: Prof. Louis Ptáček and Prof. Ying-Hui Fu
Home University: University of Münster

Brain-immune crosstalk in myocardial infarction

Laurine Sprehe
Duration: 05/25–05/26
Project at: Harvard Medical School, Massachusetts General Hospital, Corrigan Minehan Heart Center, Boston, MA, USA
Supervisor: Prof. Wolfram Poller
Home University: Heidelberg University Hospital

In vivo imaging of macrophage polarisation during immunotherapy with CDNP-R848 in experimental glioma models

Luca Waffenschmidt
Duration: 07/25–06/26
Project at: Harvard Medical School, Massachusetts General Hospital, Institute for Systems Biology, Boston, MA, USA
Supervisor: Prof. John Chen
Home University: Heidelberg University

Investigating age-related changes in body-brain communication

Elena Wuppinger
Duration: 10/25–09/26
Project at: Arc Institute, Palo Alto, CA, USA
Supervisor: Prof. Christoph A. Thaiss
Home University: University Hospital of Munich (LMU)

Foundation The Boehringer Ingelheim Fonds (BIF) is a public foundation – an independent, non-profit organisation for the exclusive and direct promotion of basic research in biomedicine. The foundation pays particular attention to fostering junior scientists. From the start, it has provided its fellowship holders with more than just monthly bank transfers: seminars, events, and personal support have nurtured the development of a worldwide network of current and former fellows.

The BIF alumni seminar 'Rare and Spare' from 20–22 February

What Is the Best That Can Happen? This.

'What stayed with me most was the feeling of being part of something bigger, a genuinely open and inspiring community.' From our point of view, creating this feeling is the best that can happen at our seminars. It describes exactly what we strive for, motivating us to give you more of the same.

So, what led to this feedback? On Friday, 20 February, a crowd of 150 alumni, BIF staff, and speakers converged at Collegium Glashütten, 45 minutes north of Frankfurt am Main, Germany, for our European alumni seminar. Its topic was 'Rare and Spare', inspired by – but not restricted to – rare diseases.

We started on Friday night with a talk by Martin Lercher from Heinrich Heine University Düsseldorf, Germany, about the concept of night and day science and how it can help one to have that rare good idea. The concept goes back to Nobel Prize winner François Jacob, who distinguished between the rigorous collection of data and testing of hypotheses and theories during 'day science' and the unfettered open-mindedness of 'night science', in which everything is possible, everything can be thought, and everything discussed. This can free creativity.

After the talk, the get-together, as usual, was marked by animated discussions, meeting old friends, and making new ones.

The next morning started off with an impressive talk by Anna Wedell from the Karolinska Institute, Stockholm, Sweden, who talked about screening newborns via whole-genome sequencing for rare diseases. Together with fellow researchers and clinicians, she has established a network that offers rapid diagnostics. A diagnosis can lead either to treatment with existing drugs or regimens or spur further research. This has already led to personalised treatments, sometimes even within days. It is a low-cost approach that can save lives and money by preventing severe health issues.

Next up was Sally Hofmeister, coordinator of the Advisory Board of the World Duchenne Organization, one of the oldest patient organisations. Her youngest son died of Duchenne in his thirties. She gave a passionate account of why it is so important to include the voices of patients and their families in rare disease research.

Before lunch, Julian März from the University of Zurich, Switzerland, posed the thorny question of how to allocate the rare resource of money in the healthcare system, which led to a lively discussion.

After lunch, there were two parallel tracks. Martin Lercher led several exercises to get into a night science frame of mind. Among other things, he asked the participants to find a possible connection between their work, no matter how far apart they seemed to be. At least one collaboration is already planned as a result of this workshop.

The other track was a new networking format called story circles. We asked our alumni to come together in groups of four to six and exchange stories according to a prompt. The feedback showed that, indeed, it was seen as a relaxed format that allowed for deeper and more intimate exchange than formats such as speed dating.

Greek mythology and the latest neurological research melded into an exciting story in the talk by Hannah Monyer from Heidelberg University Hospital, Germany. She talked about her research on how rare cells in the brain, so-called director cells, orchestrate and influence spatial memory formation.

As the last speaker on Saturday, Eckhard Wolf from LMU Munich, Germany, showed how pigs can be genetically altered so that their organs, especially hearts, can be used for transplantation in humans, a much-needed addition to rare donor organs. He gave a timeline for their routine use that is measured in years, not decades.

After dinner, two groups of about 25 people, led by our managing directors, took a walk through the surrounding woods, lit only by burning torches. Even though most of the snow from Friday had melted, it was a much-appreciated opportunity to stretch their legs and get some fresh air.

On Sunday morning, Swedish journalist Maria Eriksson talked about her experiences of living for one year in the sharing economy, renting out not just her spare bedroom, but also – or at least trying to – her toilet. Her main message was that sharing takes and generates trust between people. Her closing question was: 'What is the best that can happen?'

Well, we at BIF think it does not get better than the atmosphere at our alumni seminars. We hope that, for all who were there, this applies too.

Participants:
150 alumni, speakers, and BIF staff

Content:
6 talks, 1 workshop, 1 networking event, 2 torch walks, 1 exhibition on rare diseases, 6 fantastic meals, and many, many discussions among old and new friends.

From Theory to Practice:
The programme was a mix of more applied and more theoretical approaches to the topic, meant to offer something to everyone.

Networking Works:
About 70 participants came together in 12 story circles to test our new networking format. The feedback showed that we should keep it.

Food for Thought:
At BIF, we make sure to feed our fellows and alumni well. At Glashütten, this is a very easy task as the kitchen staff deliver high-quality food every time.

Rare Diseases, Seen Through Art:
In collaboration with the German network for chronic rare diseases, ACHSE, we exhibited artworks by patients suffering from a variety of rare diseases.

Credits: Kirsten Achenbach, Anna Sichler (both BIF)

Papers in the Spotlight

In 'Papers in the Spotlight', we present papers from current fellows and recent BIF alumni. The selection criteria are based not only on scientific merit but also on the general interest of the topic. If you would like to see your paper discussed here, send an e-mail to kirsten.achenbach@bifonds.de.

Building synthetic human chromosomes

We can already build synthetic bacterial and yeast chromosomes. Now, Simona Grazioli, supervised by Jason Chin at the LMB in Cambridge, UK, has found a way to do the same with human chromosomes. While bacterial chromosomes are usually simple loops, the 23 pairs of human chromosomes are linear, much larger, and possess a complex organisation.

Being able to engineer human chromosomes will help us understand how they function, treat disease, and programme therapeutic cells to perform only a very specific set of functions. Simona and her colleagues developed a way to extract a human chromosome from its cell, insert it into an embryonic stem cell of a mouse, where it can be manipulated without risk, and then put it back into a human cell. With the same approach, a wholly artificial human chromosome could be built.

Why take the mouse cell route? Moving human chromosomes eliminates the danger of any unwitting consequences to other chromosomes in the human cell. The second reason is that they are not essential in the mouse cell. They can be modified by inserting artificial sections. In most cases, this worked without compromising the mouse cell's ability to copy its own and the human chromosomes during cell division.

The method may sound simple, but there were some main hurdles to clear. The first was moving a human chromosome both in and out of cells without breaking it. Another hurdle was to remove one of the two original chromosomes from the human cell once the altered chromosome was inserted. The team's procedure achieved both with high fidelity.

The team moved chromosomes 4, 20, and 21 back and forth, and they only gained a small number of mutations along the way. The team also showed that they could safely transfer three further chromosomes and manipulate them in the mouse cell, and they replaced a 10 kb section with an artificial one. In an unexpected twist, the authors found that in the mouse cell, the telomere cap of the human chromosome lengthened to what is usual for mice. But the cap quickly returned to the human norm once it was back home.

While it will be a decade or more before we could theoretically develop a fully synthetic human genome, we now have a way to take a human chromosome out of a cell, dissect it, redesign it, and put it back.

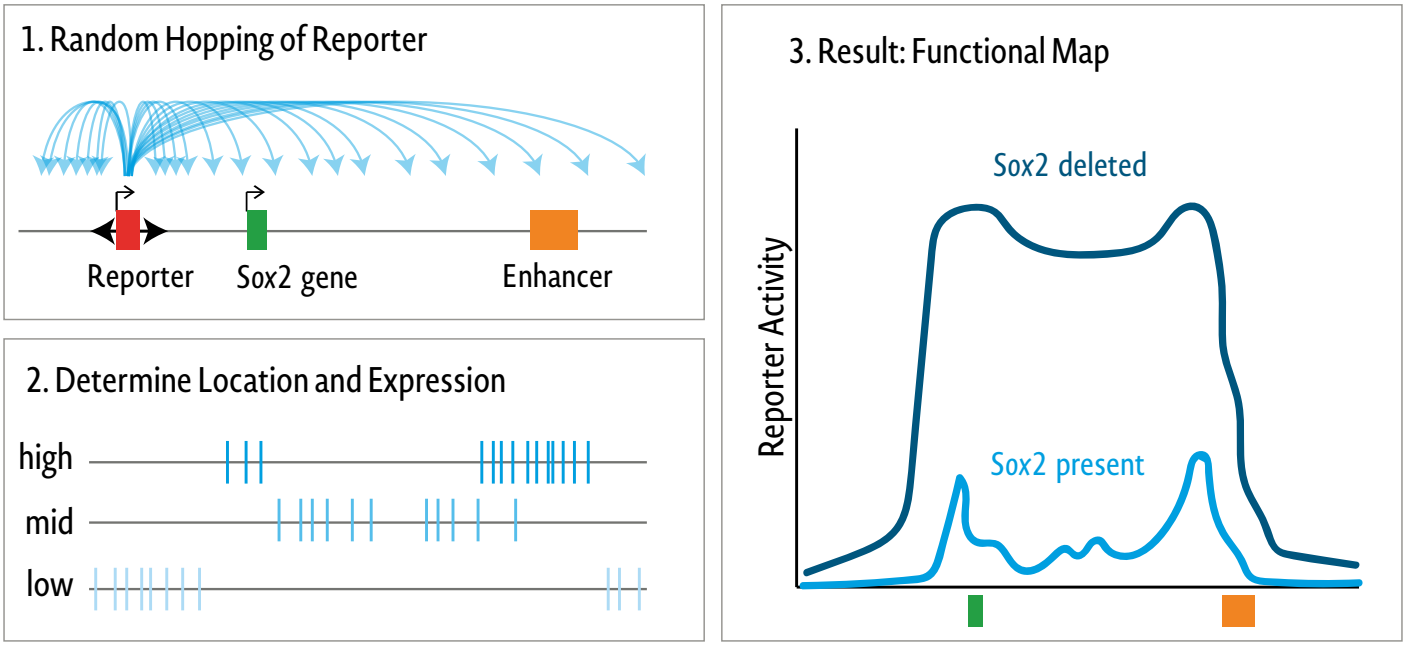
REFERENCE

Petris G*, Grazioli S*, van Bijsterveldt L*, et al. High-fidelity human chromosome transfer and elimination. Science. 2025;390:1038–1043. doi:10.1126/science.adv9797.

*Shared authorship

Simona Grazioli, fellow 04/21–03/24

Credit: Juan Moyano / Stocksy



Sox2 reporters were hopped to thousands of places around the Sox2 locus to map the activity of the Sox2 promoter. This showed that the Sox2 gene confines the reach of its enhancer. After deleting Sox2, the reporter increases its activity and reach. Green: location of the Sox2 gene; orange: location of the enhancer. Illustration modified after Eder M, Moene CJK, Dauban L, et al., 2025.

The common ground of real estate and genes: location

For retail real estate, only three things count: location, location, location. The same is true for genes. Enhancers – DNA elements that activate genes via their promoters – can act over long distances. But how their position within the folded genome relative to their target affects gene activity has remained unclear.

Christine Moene and her colleagues in the lab of Bas van Steensel, at The Netherlands Cancer Institute, Amsterdam, devised a method to systematically move DNA elements, in their case a promoter, to thousands of locations. By measuring how strongly the promoter was activated by the enhancer, the group proved that the key is physical contact probability in 3D space, not linear distance. In a surprise finding, they also showed that the coding sequence of a gene can strengthen its ability to engage an enhancer.

The group studied the *Sox2* locus, a highly folded DNA domain with only one gene, regulated by a cluster of enhancers, the SCR. First, they coupled the promoter of *Sox2* with a reporter. Then they jumped this construct around using the Sleeping Beauty (SB) transposon. In different cells, it inserted at about 6,500 different locations across a ~2 Mb region spanning the *Sox2* topologically associating domain (TAD) and surrounding regions. By sorting the resulting cells based on their reporter expression level, they created a high-resolution map of where the enhancer can activate transcription.

The resulting curve showed two peaks: close to *Sox2* and in the centre of the SCR. The curve also closely followed independent data for contact probability within the TAD. This proved that it is not just linear distance along the DNA strand that predicts activation. Promoters that hopped outside the TAD showed a sharp drop in activity, confirming that TADs function as regulatory domains, not just structural ones.

Due to rare deletions during transposon insertion, some cells lost the endogenous *Sox2* gene. In these cells, reporter activity rose dramatically, up to 50-fold. By probing this further, for example by adding not just the promoter but the whole gene to the reporter, the authors found that the endogenous *Sox2* gene and the reporter compete for activation by the enhancer. They also found that the gene's coding sequence helps *Sox2* to compete more effectively, possibly by stabilising contact with the enhancer.

In summary, the authors give us a new method, which can be adapted to relocate many different DNA elements. They proved its worth by showing that for genes, optimal location is about 3D contact. More importantly, they show that different genes seem to compete for enhancers just as much as businesses do for customers.

REFERENCE

Eder M*, Moene CJI*, Dauban L, et al. Functional maps of a genomic locus reveal confinement of an enhancer by its target gene. Science. 2025;389:eads6552.
*Shared authorship

Christine J. I. Moene, fellow 06/22–05/24

Infographic: Carina Crenshaw

How to find molecular glues by design, not chance

Imagine you could tell cells to just trash disease-causing proteins. We know several drugs that do just that; they are called molecular glues. They enable E3 ligases to attach ubiquitin, the cellular tag for 'trash, please degrade', to proteins. So far, all such glues have been found by pure chance. But now, Miquel Muñoz i Ordoño from the group of Georg Winter at the Austrian AITHYRA Institute* has given us an efficient way of altering known ligands for problematic proteins and testing them by the thousand for their glue potential.

Just like some real glues rough up a surface for better adhesion, ligands that work as molecular glues change the surface of the protein to which they bind. This allows other molecules, for example E3 ligases, to attach to the altered surface and mark these proteins for destruction. Molecular glues are therefore a special type of chemical inducer of proximity (CIP), which allows us to tackle drug targets that we could not reach before because nothing would stick to them.

Molecular glues lack the easily accessible design principles of classical CIPs, making them hard to find, but their favourable therapeutic properties make them worth it. Miquel and his colleagues noted that many known glues differed only slightly from other ligands for the same protein. They wondered: is this the clue to finding glues? They developed a method to structurally alter known ligands and test them for glue-like activity directly in living cells by combining high-throughput chemistry with a functional screen.

For proof of concept, they chose a ligand of eleven-nineteen leukaemia (ENL), which plays a central role in certain forms of acute leukaemia. Via a 'click chemistry'-based approach, they built a library of altered ligands. Next, they built a reporter that told them whether ENL was being degraded by the cell's recycling machinery in the presence of an altered ligand.

Among the thousands of compounds they tested in human cell lines, there was one that clearly dampened ENL-dependent cell growth by primarily affecting ENL and genetic programmes controlled by ENL. Their new glue first binds ENL, and this shapes the interaction surface in such a way that it now recruits a cellular ubiquitin ligase, which marks ENL for degradation. This characteristic mode of action is what makes molecular glues so specific.

With this method, we can now systematically search for glues instead of just hoping to stumble upon them, and may be able to offer new therapies for hard-to-treat diseases.

Finding the right molecular glue has so far been a game of chance, but now we have a promising method for designing it.

* Funded by BIF's sister foundation, the Boehringer Ingelheim Stiftung.

REFERENCE

Shaum JB, Muñoz i Ordoño M, Steen EA, et al. High-throughput ligand diversification to discover chemical inducers of proximity. Nat Chem Biol. 2026. doi:10.1038/s41589-025-02137-2.

Miquel Muñoz i Ordoño, fellow 05/22–04/24

Seventy Years of Support for the Humanities

BIF's Sister Foundations

The Siblings Boehringer Ingelheim Foundation for the Humanities supports outstanding scientists through printing subsidies, mostly for doctoral theses. In the humanities, books are one of the most important tools, as they allow researchers to explore complex ideas in great depth.

From left to right: board member Benedikt Stuchtey, Christoph Boehringer, keynote speaker Barbara Stollberg-Rilinger, the awardees Corinna Gannon and Elke Dubbels, and board members Uta Degner, Christiane Schildknecht, and Ulrich Rehm.

On the occasion of its 70th anniversary, we proudly celebrated the Siblings Boehringer Ingelheim Foundation for the Humanities, the oldest of the three Boehringer Ingelheim foundations. The festivities took place on 11 June at the Saalkirche in Ingelheim, Germany.

On this day, the foundation awarded prizes for outstanding work to two scientists from among its fundees. The first prize, worth 10,000 euros, went to Elke Dubbels, professor of German at Osnabrück University. Corinna Gannon, assistant curator at the Städel Museum in Frankfurt, received the second prize, worth 6,000 euros.

After the awardees were lauded and applauded, Barbara Stollberg-Rilinger, rector of the Wissenschaftskolleg zu Berlin and a renowned historian, spoke about the value of research in the humanities. She laid out why they, just like the natural sciences, should not solely be driven by the dictate of usefulness. Their most valuable contribution is not in presenting solutions after a problem arises. It starts earlier: they strengthen critical thinking and the power of discernment by questioning assumptions and viewpoints. Thus, they open our minds to different possibilities. As an example, she examined how today's democracies developed. Their rise was not as inevitable as it seems today. This helps us better understand which forces and processes shape political systems, which is valuable knowledge to have.

Although **Elke Dubbels** studies a time long before the advent of social media, her work focuses on a surprisingly current phenomenon: rumours as factors of political power. She examines dramatic texts from the 17th to the early 19th century that demonstrate just how crucial 'what was said' was – even in times when the population had no formal say. The focus is on rulers struggling to maintain their public standing. The plays make it clear that a form of 'public opinion' already existed before the term was coined in the late 18th century. Yet the dramas do not merely serve as a mirror of political communication. They analyse, exaggerate, and interpret events – and transform power struggles into narrative forms such as tragedy or comedy. This reveals that political interpretation has always also been a matter of staging.

Magical objects have fascinated people for centuries, while also offering insights into cultural and media history. **Corinna Gannon** explores where their supposed power comes from and who can harness it, focusing on the little-studied category of talismans. She shows that their influence derives not only from their appearance, but also from their material, manufacture, and cultural context. Around 1600, ideas from early science and natural philosophy made the notion of powerful objects seem plausible. Gannon's research on the famous Kunstkammer of Emperor Rudolf II reveals these beliefs were less about 'hocus-pocus' than about historical ways of understanding the world. It can also help us better understand the present: even though hardly anyone believes in magic today, we still attribute power to objects and images.

Credits: Frank Daum (top); Wallstein (Gerüchte); De Gruyter (Artefakte)

Profiles

Zoltán Nusser
Institute: Hungarian Academy of Sciences, Budapest, Hungary
Fellowship: Postdoctoral research award 2000–2006

Professor Attila Losonczy
Institute: University of Texas, Dallas, TX, USA
Fellowship: 2002–2003

Zoltán Nusser and **Attila Losonczy,** a former PhD student in Zoltán's lab, have been awarded an ERC Synergy Grant together with Ivo Spiegel from the Weizmann Institute in Israel. The team wants to analyse the different molecular compositions, gene expression patterns, and changes in activity during learning. This will enable them to find out what types of long-term synaptic plasticity processes occur when a spatial memory is formed in the hippocampus and which molecules are involved in different cell populations. The ERC Synergy Grants are open to teams of two to four leading researchers working together to solve ambitious research problems and come with funding of – in this case – €12 million for six years. The 2025 call attracted 712 proposals, of which 66 projects were funded, putting the success rate well below 10%. As Prof. Maria Leptin, President of the European Research Council, said: 'The competition was fierce, with many outstanding proposals left unfunded.' The call was also more international, with 40% of funded proposals including at least one PI outside the EU or its associated countries. Women account for 25% of the principal investigators.

Katharina Sonnen
Institute: Hubrecht Institute, Utrecht, The Netherlands
Fellowship: 2008–2010

Katharina Sonnen has been awarded an ERC Consolidator Grant for her project 'Oscillating Signals: Somitogenesis – Information transmission by noisy oscillators'. She will use the €2.1 million to decode the principles underlying how cells use oscillating chemical signals to transmit biological information in the noisy environment of cells and tissues. She will study both embryonic and adult tissues of mice and humans.

Professor Leif Ludwig
Institute: Berlin Institute of Health, Berlin, Germany
Fellowship: 2011–2012

Leif Ludwig has been awarded a Heisenberg professorship in Stem Cell Dynamics and Mitochondrial Genomics. He started in February at his institution, the Berlin Health Institute at the Charité. The professorship is funded by the German Research Foundation (DFG). He uses the mitochondrial genome for high-throughput studies on blood and bone marrow cells to map and track blood stem cells. He also studies mitochondrial mutations and the mechanisms by which they lead to different cellular and metabolic phenotypes. His research is expected to lead to new therapies, especially as he combines basic research and application-oriented studies.

Professor Volker Haucke
Institute: Leibniz Institute for Molecular Pharmacology (FMP), Berlin, Germany
Fellowship: 1994–1997

Volker Haucke, Director at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) and professor of molecular pharmacology at Freie Universität Berlin, has been awarded his second Reinhart Koselleck Grant by the Deutsche Forschungsgemeinschaft (DFG). He will receive €5 million in total over five years for his interdisciplinary research on how presynapses – the transmitting junctions of nerve cells – assemble from small transport packages in the axon during development and how they change in the mature brain.

Michael Sieweke
Institute: Center for Regenerative Therapies Dresden (CRTD), Germany
Fellowship: 1991–1992

The European Innovation Council (EIC) is funding the StemPhage project with €2.5 million. It is led by BIF alumnus **Michael Sieweke** together with two further researchers, Anke Fuchs and Angela Jacob. They want to develop a novel immune cell therapy based on modified macrophages for solid tumours and prepare it for clinical application. StemPhage is one of only three projects funded by the EIC in Germany and among 40 selected from 611 applications across Europe.

Professor Stefanie Dimmeler
Institute: University of Frankfurt, Germany
Fellowship: 1991–1992

Stefanie Dimmeler, spokesperson for the Cardio-Pulmonary Institute (CPI) Cluster of Excellence and principal investigator at the German Centre for Cardiovascular Research (DZHK), has received the Science Award of the Hector Foundation, worth €200,000, for developing new approaches to repairing damaged hearts. She will also be admitted to the circle of Hector Fellows. Together with her team, Stefanie Dimmeler has shown how the inner lining of blood vessels is regulated by non-coding RNAs and how vascular protection and healing processes can be strengthened.

Credits (from top to bottom): Zoltan Nusser; UTSW; Hubrecht Institute; Leif Ludwig; David Aussenhofer; CRTD; Marco Schilling / Hector Stiftung

Professor Ivan Đikić
Institute: University Hospital Frankfurt, Germany
Fellowship: Postdoctoral Award 1997

Ivan Đikić has been selected as the recipient of the Theodor Bücher Medal for his outstanding achievements in biochemistry and molecular biology by the Federation of European Biochemical Societies (FEBS). He will be presented with the medal at the 50th FEBS Congress in Maastricht, the Netherlands, in July 2026, where he will deliver the FEBS Theodor Bücher Lecture on 'Guardians of cellular homeostasis: the ubiquitin–autophagy axis'.

Professor Antonella Dost
Institute: University of Copenhagen, Denmark
Fellowship: 2016–2019

Antonella Dost has joined reNEW Copenhagen, the Novo Nordisk Foundation Center for Stem Cell Medicine, as an associate professor. With her lab, she will develop human lung organoid models to advance our understanding of lung regeneration and chronic lung diseases, including chronic obstructive pulmonary disease (COPD). COPD is the fourth leading cause of death worldwide and may affect up to 600 million people by 2050. Her goal is to translate research into novel therapies that repair damaged lung tissue and restore lung regeneration.

Professor Patrick Maschmeyer
Institute: University of Copenhagen, Denmark
Fellowship: 2018–2020

Patrick Maschmeyer is newly appointed professor for AI-based predictive immune analytics at the Danish Institute for Systemic Inflammation Research, which closely collaborates with the German University Hospital Schleswig-Holstein to investigate cellular and molecular mechanisms of dysregulated immune responses in chronic inflammatory diseases. Previously, he was a postdoc in Berlin in the group of BIF MD fellow Leif Ludwig.

Professor Leo Kiss
Institute: University of Duisburg-Essen, Germany
Fellowship: 2007–2010

In April, **Leo Kiss** became a junior professor of cellular biochemistry at the University of Duisburg-Essen. Together with his group, he wants to decode the information stored in ubiquitin chains using a cellular biochemistry approach, by combining the biochemical synthesis of ubiquitinated proteins with their intracellular delivery and monitoring. This will enable them to define the intracellular roles of ubiquitin chains, identify ubiquitin chain interaction partners, and understand the underlying molecular mechanisms.

Professor Edward Lemke
Institute: Institute for Molecular Biology, University of Mainz, Germany
Fellowship: 2003–2005

Edward Lemke has been elected as a member of the ERC Consolidator Grants Panel 2025 for the Biotechnology and Biosystems Engineering section. Panel members play a vital role in the ERC's evaluation of grant proposals. They are top scientists and scholars from all over the world who help the ERC select the best project proposals. They have specialist as well as generalist competence and should not act as representatives of a single discipline or a particular line of research.

Prof. Alexaner Meissner
Institute: Max Planck Institute for Molecular Genetics, Berlin, Germany
Fellowship: 2003–2005

Alexander Meissner has been honoured by the International Society for Stem Cell Research (ISSCR) with the 2026 ISSCR Momentum Award for exceptional work in developmental and stem cell epigenetics. He will receive the award during ISSCR 2026 in Montréal, Canada, from 8–11 July 2026. Over the past 20 years, Alexander has studied how cell identity is established, maintained, and reprogrammed. Through his pioneering genomic and epigenomic studies, he defined key mechanistic steps underlying somatic cell reprogramming and pluripotency, helping to establish the conceptual and technical foundations of induced pluripotent stem cell research.

Evgenij Fiškin
Organisation: Stipple Bio, Cambrigde, MA, USA
Fellowship: 2011–2013

In 2021, BIF alumnus **Evgenij Fiškin** co-founded Stipple Bio, which recently emerged from stealth after raising a $100M Series A round. Stipple Bio is dedicated to advancing precision oncology therapies that target tumour-specific epitopes. These are defined as sections of antigens bound by an antibody's paratope, existing only on the surface of tumour cells, allowing for highly selective targeting. Evgenij conceptualised and built the so-called Pointillist platform to identify tumour-specific epitopes. Together with his team, Evgenij discovered and developed the company's lead asset, STP-100. This antibody-drug conjugate is scheduled to enter the clinic in early 2027.

Credits (from top to bottom): BCII / Uwe Dettmar; University of Copenhagen; Patrick Maschmeyer; Leo Kiss; Thomas Harmann; David Aussenhofer, Evgenij Fiškin

A BIF Fellow's Guide to ...

Leuven

Travelling is fun – especially with insider tips from locals! In each FUTURA, the BIF invites one or more fellows to show you around their city. In this edition, your guide is Loran Heymans.

Facts and Figures

Country: Belgium
Population: approx. 105,000
Area: 56.6 km²
Students: more than 60,000
Famous for: a vibrant university life, historical architecture, and being the home of Stella Artois beer
Website: www.visitleuven.be

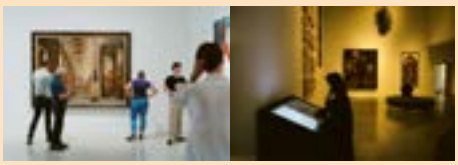
Best Sights

Arenberg Castle: A beautiful 16th-century Renaissance château set in a quiet park on KU Leuven's science campus.

Botanical Garden (Kruidtuin): Escape the city in this relaxing garden with a variety of plants and multiple greenhouses.
Leuven Town Hall and Saint Peter's Church: Two iconic architectural buildings crown the Grote Markt square of Leuven.
University Library and Tower: This stunning library and historical landmark is my personal favourite.

Activities

Groot Begijnhof: This UNESCO World Heritage Site offers a peaceful atmosphere and a glimpse into the historical life of the beguines.
Abdij van Park: One of the best-preserved abbey sites in Europe.



M – Museum Leuven: A contemporary art museum with a diverse collection of modern art and temporary exhibitions.
Brewery Stella Artois: Visit this historic brewery to learn about the brewing process and be introduced to Leuven's famous beer, Stella Artois.

Where to Stay

Begijnhof Hotel: Close to the famous Groot Begijnhof.

Martin's Klooster: A 16th-century former convent turned into a beautiful hotel right in the historic centre.
Pentahotel: A stylish, modern hotel in the gastronomic heart of Leuven.

Restaurants

Raffat: A Pakistani restaurant that is favoured by most of our neuroscience department.
Sud Sud Bistro: Food-sharing and drinks with a Mediterranean twist.
Pepas: You can't visit Belgium without trying a 'frituur', and Pepas does an amazing job of making it vegan.

Domus: Traditional Belgian dishes paired with Domus's own-brewed beer.

Nightlife

De Blauwe Kater: Enjoy a variety of beers while listening to unique jazz or blues concerts on Mondays.
Malz: Craft beer bar with a selection of 500+ beers, ciders, meads, and (natural) wines.
Oude Markt: The 'Old Market Square' is considered the longest bar in Europe.
Optimist: Bar and restaurant in a historical building that hosts multiple events.

Loran Heymans is 25 years old and comes from Belgium. Her supervisor is Professor Karl Farrow, PhD, from the Flanders Institute for Biotechnology in Leuven.

New Funding Scheme CoMove for Dual-career Scientists

Credit: Victor Torres / Stocksy

It is often said that great minds think alike. No wonder, then, that there are many couples in which both partners have promising scientific careers. But as science often involves international mobility, dual careers can be hard to achieve without one partner compromising their career prospects. It is difficult to find a location that has adequate positions and/or funding for both partners. Often, one of them must make a sacrifice.

To avoid losing such scientific talent, the Boehringer Ingelheim Stiftung, BIF's sister foundation, started a new funding programme in November 2025. It supports exceptional scientists who wish to relocate to a region in Germany or Austria where their partner has accepted, or is negotiating, an academic position such as a professorship. The programme's aim is to enable the accompanying partner to establish a new research group or relocate an existing one.

CoMove offers flexible funding to develop an internationally competitive research programme at a host institution that is prepared to offer a long-term appointment and institutional support. The funding encompasses up to €1.5 million for up to five years and may be used towards scientific personnel, consumables, and project-related equipment, as well as travel and publications.

Applications can be submitted at any time. The three-tiered selection process, which involves external peer review and an interview via videoconference, is expected to take 4–5 months.

To be eligible, researchers must have international experience and visibility, and must propose an original and creative research programme on fundamental questions in the biological, medical, or chemical sciences that will significantly advance their field. They also have to have been offered a position as established researchers, which provides them with access to lab and office space as well as administrative support for the duration of the CoMove funding.

More information can be found at boehringer-ingelheim-stiftung.de

Upcoming Events

10–11 July
Meeting of BIF's Board of Trustees
The trustees decide on the allocation of fellowships, review the proposals for the International Titisee Conferences, and handle all matters of fundamental importance for the foundation.

29 Aug–4 Sep
Progress Seminar
Progress seminar for current PhD fellows working in Europe in scenic Hirschegg (Kleinwalsertal), Austria. On the agenda: project presentations by all participants, discussion of career topics, and guided hiking tours in the surrounding Alps. Further details will be sent with the invitation.

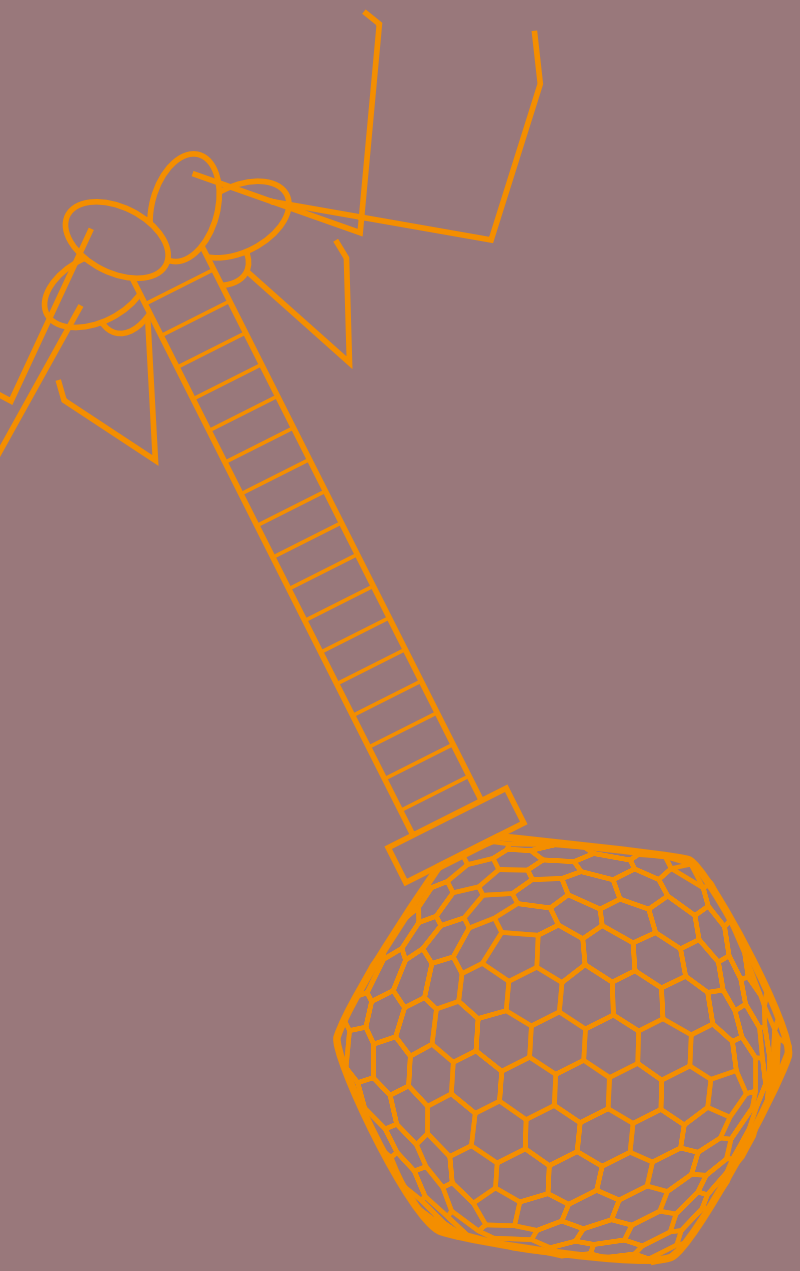
19–23 Oct
133rd International Titisee Conference, Titisee, Germany
The 133rd ITC, titled 'When and why do antibiotics fail', will be chaired by Nathalie Q. Balaban, Jerusalem, Israel, and Deborah T. Hung, Cambridge, MA, USA, and span the broad interdisciplinary aspects of antibiotic failure, from health policy and infectious diseases to microbial physiology, metabolism, evolutionary biology, systems biology, and biophysics.
ITC participation is by invitation only.

13–14 Nov
Meeting of BIF's Board of Trustees
The trustees decide on the allocation of fellowships, review the proposals for the International Titisee Conferences, and handle all matters of fundamental importance for the foundation.

20–25 Nov
Communication Training, Lautrach, Germany
Communication seminar for PhD and MD fellowship holders working in Europe. The meeting will take place in Lautrach, Germany. Participants will have the opportunity to work on their writing and presentation skills with various coaches, as well as to learn more about designing graphs and figures. Further details will be sent with the invitation.

11 Dec
BIF Christmas Party
Organised by current BIF fellows, we invite you to our office in Mainz to celebrate the end of the year with us. There will be food, drinks, and music. All BIF fellows and alumni are welcome. We also offer a few sleeping places in the office.

Need an update on upcoming events?
Check our website at www.bifonds.de



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ISSN 0179-6372