MOLECULAR BIOLOGY
NEWSLETTER
Georg-August-Universität Göttingen · International Max Planck Research School
JAN 2022

Welcome message

Dear alumni, students, friends and colleagues,

In this issue of our annual Molbio Newsletter the pandemic remains a constant companion to our reports on activities, progress and achievements related to our graduate program. In a roller coaster of emotions, desires and expectations, the limited options for networking and social interactions were challenging for many of us, getting tired of yet another zoom meeting.

An internal quality review of our Molecular Biology and Neuroscience MSc/PhD programs in summer 2021 revealed that many students experience stress and thus feeling even more isolated during the pandemic. In a recent pilot project of our Molbio program we invited all PhD students to individual coaching sessions and preventive stress check-ups with an occupational psychologist, accompanied by an invitation to personal counseling sessions with the Molbio coordinator Steffen Burkhardt (see back cover of this issue for further details).

Newcomers seeting out on a hike during the orientation weeks (left). Music at the MSc graduation (right).

While all of us sincerely hope that an end of the pandemic is within reach, we would also like to review some of the positive highlights of the past year. The conversion of our three-stage admission process into a complete online procedure turned out to be a great success and we gladly welcomed a new class of wonderful MSc students, who share some of their personal experience in this newsletter. Despite all challenges, the previous MSc class could perform most lab rotation projects on site, was highly engaged in the online tutorials and seminars, and passed the MSc examinations in August with flying colors. At the end of the exam week, the students could celebrate their achievements on the first-ever Molbio MSc retreat in Goslar at the foothills of the Harz mountains. Our alumni mentoring program was also relaunched in summer 2021 and some of the mentor-mentee tandems report about their experience in this newsletter.

A dedicated group of Molbio students ensured that the long-standing tradition of our annual Horizons in Molecular Biology conference with Career Fair in September continued to be a rewarding experience with a distinguished group of internationally renowned speakers. The new batch of Molbio students had the great opportunity to follow the contributions of the online conference together, as the Horizons organizers arranged for an in-person screening event. To support networking among our newcomers, we moved our welcome and info meetings to the large Manfred-Eigen Lecture Hall and concluded our orientation weeks with a beautiful hike around Nikolausberg, followed by a delicious dinner.

Other highlights were our "double MSc graduation" in October to acknowledge the achievements not only of the current MSc graduates but also of the previous class whose graduation had to be cancelled because of the pandemic. Only a week later, our first in-house PhD retreat with an alumni career forum took place at the MPI-bpc and everyone could sense how much all of the 70 participants have been longing for scientific and social exchange. Last but not least, the pandemic could not stop our students from presenting an outstanding publication record as illustrated on the following pages. We hope you enjoy our newsletter.

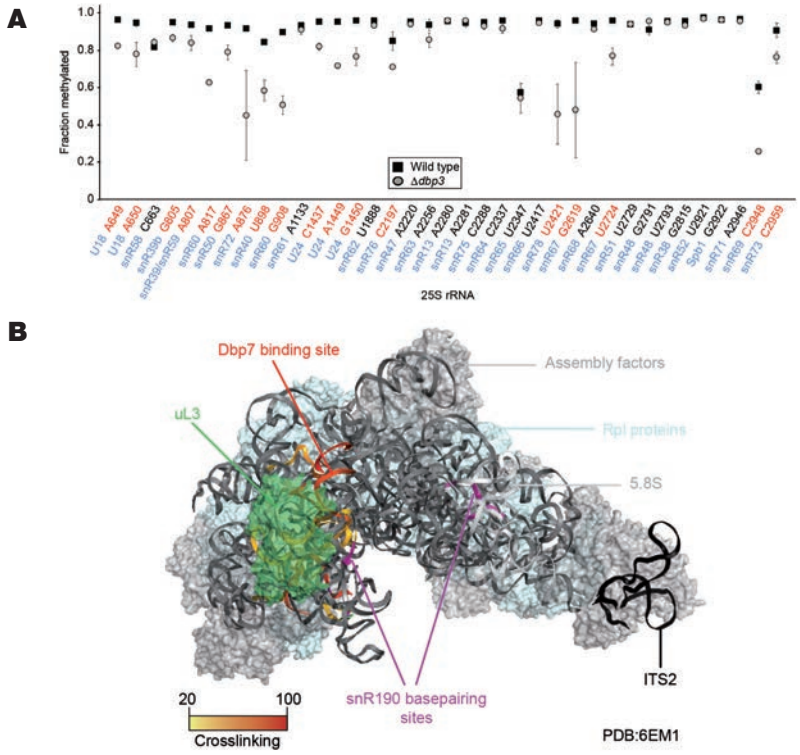
Peter Rehling, Marina Rodnina, Steffen Burkhardt

CONTENT

Unwinding activities bring functionality...

Ribosomes are highly conserved ribonucleoprotein (RNP) responsible for protein production in the cell. Their biogenesis involves correct processing, modification and properly folding of ribosomal rRNA (rRNA) concomitant with hierarchical assembly of ribosomal proteins (r-proteins). To conclude with a functional architecture, the biogenesis of ribosome employs around 200 assembly factors (AFs) providing directionality and accuracy of the process. A number of these AFs are so-called RNA helicases.

Using the energy of ATP binding and hydrolysis, RNA helicases not only unwind RNA duplex per se but consequently can remodel RNA-protein complexes. Hence, the roles of RNA helicases are vital in the biogenesis of large ribonucleoprotein (RNP) complexes such as the ribosome. During my PhD, I sought to characterize the function of two DEAD-box RNA helicases, Dbp3 and Dbp7, in the assembly of the large ribosomal sub-unit. Together with few others, these RNA helicases function during the early stages of the assembly process, a very dynamic and poorly understood time point.



Two key processes in the early stages of ribosome biogenesis are the modification and folding of the rRNAs. The modifications of rRNAs are mainly carried out by another RNPs called small nucleolar RNPs (snoRNPs). The RNA component called small nucleolar RNA (snoRNA) guides the whole complex to the target

Fig. 1: (A) Fraction of methylation of each 2'-O-methylated nucleotide along the 25S rRNA measured using RiboMeth-seq in WT and cells lacking Dbp3. (B) Identified binding site of Dbp7 modelled onto the tertiary structure of an early large pre-ribosomal particle.

PhD- and MSc-related publications 2021 (current and former students of the Molecular Biology program in bold type)

Aquino GRR, Hackert P, Krogh N, Pan KT, Jaafar M, Henras AK, Nielsen H, Urlaub H, Bohnsack KE, Bohnsack MT (2021) The RNA helicase Dbp7 promotes domain V/VI compaction and stabilization of inter-domain interactions during early 60S assembly. Nat Commun 12(1):6152

Aquino GRR, Krogh N, Hackert P, Martin R, Gallesio JD, van Nues RW, Schneider C, Watkins NJ, Nielsen H, Bohnsack KE, Bohnsack MT (2021) RNA helicase-mediated regulation of snoRNP dynamics on pre-ribosomes and rRNA 2 '-O-methylation. Nucleic Acids Res 49(7):4066-4084

Bali B, **de la Morena DL**, Mittring A, Mager T, Rankovic V, Huet AT, Moser T (2021) Utility of red-light ultrafast optogenetic stimulation of the auditory pathway. EMBO Mol Med 13(6):e13391

Barysch SV, Stankovic-Valentin N, Miedema T, **Karaca S**, Doppel J, Achour TN, Vasudeva A, Wolf L, Sticht C, Urlaub H, Melchior F (2021) Transient deSUMOylation of IRF2BP proteins controls early transcription in EGFR signaling. EMBO Rep 22(3):e49651

Belardinelli R, **Sharma H**, Peske F, Rodnina MV (2021) Perturbation of ribosomal subunit dynamics by inhibitors of tRNA translocation. RNA 27(9):981-990

... and well-being

modification site in the rRNA through base-pairing. The dissociation of this snoRNA-rRNA interaction as well as its formation has been shown to be promoted by several RNA helicases.

To understand a putative role of Dbp3 in snoRNP-mediated modification, we employ a high-throughput RNA-seq called RiboMeth-Seq to quantitatively measure the methylation of the 2'OH. We found out that several nucleotides along the 25S rRNA have sub-optimal level of methylation when Dbp3 is lacking (Panel A). In our quest to understand this observation, we found out that a subset of snoRNAs guiding this modification accumulate in the precursor ribosome (pre-ribosome) when Dbp3 is lacking. Notably, some of these snoRNAs are limiting. Furthermore, many of these snoRNAs have partially overlapping basepairing sites, and failure to release one snoRNP when Dbp3 is lacking impedes the access of the other snoRNPs, leading to decrease in methylation on the adjacent site. Altogether, our findings provide a new insight into how RNA helicases can regulate snoRNP dynamics and rRNA modification during ribosome biogenesis.

Some snoRNPs do not install modification but rather promote folding of rRNA. An example is the snR190 and we found out that its association with the pre-ribosomes is regulated by RNA helicase Dbp7. Using *in vivo* photoactivatable ribonucleoside-enhanced crosslinking and analysis of cDNA (PAR-CRAC) approach, we identified the binding site of Dbp7, which in turn support its function in the release of snR190 (Panel B). Furthermore, examination of nearby r-proteins revealed uL3 positioned close the Dbp7 binding site. Protein composition analysis via mass spectrometry of pre-ribosomes lacking Dbp7 revealed a reduction in r-protein uL3 and accumulation of Npa1 scaffolding complex shown to bind snR190. Together, these findings suggest that Dbp7 promotes the release of Npa1 complex and snoRNA190, and the binding of uL3. The r-protein uL3 stabilizes the interaction of the 3′ and 5′ end of the pre-cursor 25S rRNA promoting pre-ribosomal compaction and downstream maturation events. Interestingly, in the absence of Dbp7, early pre-ribosomes are bound for degradation.

Altogether, both works fill in some of the important gaps in our understanding of RNA helicase functions in ribosome biogenesis. Although both are non-essential, Dbp7 and Dbp3 exemplify key roles of RNA helicases in fine-tuning the assembly process to generate adequate, functional ribosomes necessary for the well-being of the cell.

Gerald Ryan Aquino completed his doctoral research in February 2021 in the group of Markus Bohnsack at the University Medical Center Göttingen. Currently he works as research associate at Evotec International GmbH.

These results were published in Aquino GRR, Hackert P, Krogh N, Pan KT, Jaafar M, Henras AK, Nielsen H, Urlaub H, Bohnsack KE, Bohnsack MT (2021) Nat Commun 12(1):6152

Bhatta A, Dienemann C, Cramer P, Hillen HS (2021) Structural basis of RNA processing by human mitochondrial RNase P. Nat Struct Mol Biol 28(9):713-723

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Cramer P, **Kokic G**, Dienemann C, **Höbartner C**, Hillen HS (2021) Coronavirus-Replikation: Mechanismus und Inhibition durch Remdesivir. Biospektrum (Heidelberg) 27(1):49-53

Cretu C, Gee P, Liu X, Agrawal A, Nguyen TV, Ghosh AK, Cook A, Jurica M, Larsen NA, Pena V (2021) Structural basis of intron selection by U2 snRNP in the presence of covalent inhibitors. Nat Commun 12(1):4491

Cruz-Zaragoza LD, Dennerlein S, Linden A, **Yousefi R**, Lavdovskaia E, Aich A, Falk RR, **Gomkale R**, Schondorf T, Bohnsack MT, Richter-Dennerlein R, Urlaub H, Rehling P (2021) An *in vitro* system to silence mitochondrial gene expression. Cell 184(23):5824-5837.e15

To make RNAs in the powerhouse

First steps in post-transcriptional processing of RNA in mitochondria

Most proteins in human cells are made in the cytosol. A few, however, are made inside mitochondria. Mitochondria's own genome codes for these proteins, as well as for all transfer RNAs (tRNAs) and ribosomal RNAs (rRNAs) required to make them. All genes in our mitochondrial genome are transcribed together as one long RNA molecule wherein rRNA and protein-coding regions are separated by tRNAs. Two precise cuts at either ends of all tRNAs within the long RNA releases individual tRNAs, rRNA and protein-encoding RNAs.

The first of these cuts – at the 5′ end of the tRNA – is made by human mitochondrial ribonuclease P (mtRNase P). While enzymes that perform tRNA 5′ cleavage are present in all forms of life, these enzymes are mostly ribozymes (RNA-based enzymes) or single-subunit protein enzymes. Only in the mitochondria of mammals, mtRNase P is a complex of three unrelated proteins which together carry out RNA cleavage and methylation. As a functionally unique complex central to mitochondrial biology, we were interested in understanding the mechanisms of mtRNase P's dual enzymatic functions and gaining an evolutionary perspective on how these different functions came together in a single complex.

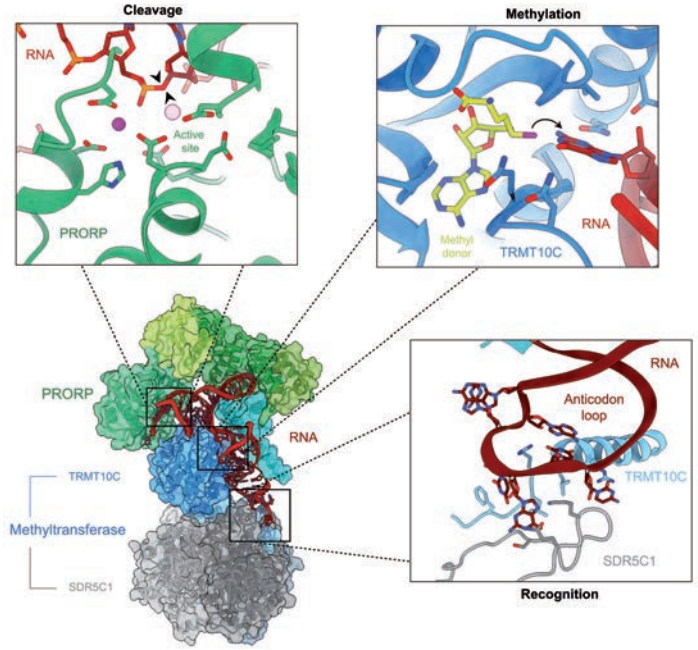

Fig. 1: Structure of human mitochondrial ribonuclease P. The atomic model of mtRNase P is shown as transparent surface, while the RNA is shown as red cartoon. Structural details of the mechanisms of tRNA recognition, cleavage and methylation are enlarged. Arrows indicate the cleavage position and methylation reaction.

To obtain molecular insights into its function, we reconstituted the human mtRNase P complex *in vitro* and determined its three-dimensional struc-

Epple R, Krüger D, Berulava T, Brehm G, **Ninov M**, Islam R, Köster S, Fischer A (2021) The coding and small non-coding hippocampal synaptic RNAome. Mol Neurobiol 58(6):2940-2051. Correction: 2954

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Grosse S, **Lu YY**, Coban I, Neumann B, Krebber H (2021) Nuclear SR-protein mediated mRNA quality control is continued in cytoplasmic nonsense-mediated decay. RNA Biol 18(10):1390-1407

Güttler T, **Aksu M**, Dickmanns A, Stegmann KM, Gregor K, Rees R, Taxer W, **Rymarenko O**, Schünemann J, Dienemann C, Gunkel P, Mussil B, Krull J, Teichmann U, Gross U, Cordes VC, Dobbelstein M, Görlich D (2021) Neutralization of SARS-CoV-2 by highly potent, hyperthermostable, and mutation-tolerant nanobodies. EMBO J 40(19):e107985

ture using cryo-electron microscopy. The structure reveals how mtRNase P complex is assembled from individual components and how the tRNA is positioned in the complex for precise cleavage and methylation. While the RNA cleaving activity resides in a single protein – called PRORP – the other two subunits, which together make the methyltransferase complex, are still required for RNA cleavage. We observed that the tRNA binds first to the methyltransferase and only then can PRORP join the complex, held in place by the methyltransferase. This explains why the two additional subunits are required.

In a surprising discovery, we observed that human mtRNase P interacts with tRNA in a manner strikingly different from all other known RNase P enzymes. Unlike most RNase P enzymes which recognize tRNAs via the conserved structure of the so-called tRNA "elbow", human mtRNase P recognizes tRNAs via conserved features in the so-called anticodon loop. The explanation for this observation most likely relates to the idiosyncrasies of mitochondrial tRNAs. The structures of elbow regions of different tRNAs are generally very similar across all forms of life and therefore, serve as "tRNA identity markers" for many enzymes, including RNase P. However, the structures of elbows of tRNAs in mammalian mitochondria are so variable that they cannot be used to reliably recognize tRNAs. Ergo, mitochondrial RNase P needs to recognize tRNAs using a different conserved "identity marker" – the anticodon loop. Since the RNA cleaving subunit by itself does not interact with the anticodon loop, it appears to have joined forces with a methyltransferase that does, to form a complex that can specifically recognize, methylate and cleave mitochondrial tRNAs. A curious case of co-evolution of mitochondrial tRNAs and RNase P!

To sum up, the structure of mtRNase P sheds some light into the evolution of a unique machinery in our mitochondria and yields insights on how this machinery works. These findings represent a piece in the unsolved puzzle that is the RNA processing in mitochondria, and hopefully, the mechanistic and evolutionary implications from this work will guide future studies aimed at solving this puzzle.

Arjun Bhatta is a doctoral researcher in the group of Hauke Hillen at the University Medical Center Göttingen.

These results were published in Bhatta A, Dienemann C, Cramer P, Hillen HS (2021) Nat Struct Mol Biol 28(9):713-723

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Click, right into the mitochondria

Monitoring mitochondrial translation with spatial resolution

If mitochondria are like a powerhouse to the cells, four protein complexes of the oxidative phosphorylation system (OXPHOS) are the engines that create the electrochemical potential, and the fifth complex is its ATP generator. The OXPHOS complexes (except one) are formed from proteins encoded in two genomes, nuclear and mitochondrial (mtDNA). Thirteen polypeptides of the OXPHOS complexes are encoded in mtDNA and synthesized on mitochondrial ribosomes. The rest of the mitochondrial proteins are nuclear-encoded, synthesized in the cytosol, and imported into the mitochondria.

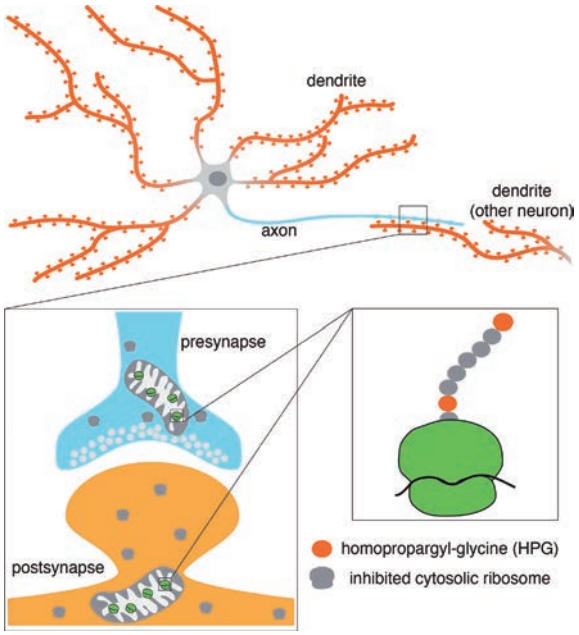

Fig. 1: An approach to tag newly-synthesized mitochondrial translation products with spatial resolution. Cytosolic ribosomes are inhibited with an antibiotic and only mitochondrial ribosomes incorporate a methionine homolog (HPG) into the protein sequences. Tagged proteins can be fluorescently labeled via a specific chemical reaction between HPG (alkyne moiety) and an azide-contained fluorophore (click chemistry). Local translation in synaptic mitochondria was shown for the first time.

The two genomes must work in harmony to maintain the correct stoichiometry of the proteins in the dual-origin OXPHOS complexes. A few regulatory mechanisms have been discovered to link mitochondrial gene expression to the cytosol. However, there is still a lot unknown about the cross-talks between cytosol and mitochondria that finetune the gene expression. Impaired mitochondrial gene expression leads to many severe diseases, mainly affecting the nervous system, heart, and skeletal muscles.

A single cell can have hundreds to thousands of mitochondria, each containing various copy numbers of the mtDNA. Therefore, heterogeneity in mitochondria is not surprising. In specialized cells like neurons or cardiomyocytes, subpopulations of mitochondria have been shown to differ in function, morphology, protein content, and regulatory pathways. Whether the level of gene expression can play a role in any of the heterogenic phenotypes is not well understood.

Kabinger F, Stiller C, Schmitzová J, Dienemann C, **Kokic G**, Hillen HS, Höbartner C, Cramer P (2021) Mechanism of molnupiravir-induced SARS-CoV-2 mutagenesis. Nat Struct Mol Biol 28(9):740-746

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Kokic G, Hillen HS, Tegunov D, Dienemann C, Seitz F, Schmitzová J, Farnung L, Siewert A, Höbartner C, Cramer P (2021) Mechanism of SARS-CoV-2 polymerase stalling by remdesivir. Nat Commun 12(1):279

Kokic G, Wagner FR, **Chernev A**, Urlaub H, Cramer P (2021) Structural basis of human transcription-DNA repair coupling. Nature 598(7880):368-372

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Conventional approaches to study mitochondrial gene expression is through labeling newly synthesized mitochondrial-encoded peptides using radioactive methionine. Such an approach, albeit very sensitive, lacks a spatial resolution to reveal single mitochondria within cells. Besides, radioisotope facilities are not commonly available.

In this project, we looked for alternative approaches to label mitochondrial-encoded proteins. We took advantage of a method called fluorescent non-canonical amino acid tagging (FUNCAT) that is based on a specific reaction so-called Click Reaction between an azide- and an alkyne moiety.

This method has been previously used to label newly synthesized proteins in the cytosol (Dieterich et al., 2010). In the adapted approach, we first inhibit cytosolic translation with an antibiotic against cytosolic ribosomes. Then, a homolog of methionine with an alkyne group, homoparapargyl-glycine (HPG), is added to the cells. Mitochondrial ribosomes incorporate the HPG into the mitochondrial-encoded proteins for a short pulse. Later, the cells are fixed and tagged proteins are labeled with an azide-contained fluorophore and can be visualized under the microscope.

We successfully applied the technique to different cell types, from commonly used cell lines to primary cells such as neurons, and induced pluripotent stem cell (iPSC)-derived cardiomyocytes. In all the cell types, particularly the highly specialized ones, we observed heterogeneity in the level of mitochondrial protein synthesis. This indicates that not all mitochondria are translationally active within a cell.

With the spatial resolution provided by this technique, we detected newly synthesized mitochondrial-encoded proteins at synaptic mitochondria. Showing active gene expression in mitochondria that are located far from the bulbous body of the neuron (soma) provides new insights into the local biogenesis and turnover of mitochondria in neurons.

This approach provides new opportunities to address the functional states of single mitochondria in diseases that are associated with impaired mitochondrial gene expression.

Roya Yousefi is currently completing her doctoral research in the group of Peter Rehling at the University Medical Center Göttingen.

These results were published in Yousefi R, Fornasiero EF, Cyganek L, Montoya J, Jakobs S, Rizzoli SO, Rehling P, Pacheu-Grau D (2021) Monitoring mitochondrial translation in living cells. EMBO Rep 22(4):e51635

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Stopping gene expression at the start

Structural insights into Integrator-mediated transcription regulation

Transcription is a highly regulated step of gene expression that allows genes to be switched on and off in response to various cues such as infection. To ensure the quickest possible response to such cues, the transcribing RNA polymerase II (Pol II) is halted immediately after transcription starts and kept ready to transcribe when the gene output is needed. This process is called promoter proximal pausing (let's call it Pausing). Pausing is unique to multicellular organisms and is orchestrated by the elongation factors DSIF and NELF. When the gene output is needed, a kinase called P-TEFb (positive transcription elongation factor b) phosphorylates DSIF, NELF and the C-terminal domain (CTD) of Pol II subunit RPB1. This leads to exchange of NELF for the elongation factors SPT6 and PAF and rapid gene expression.

What if the gene output is not needed after pausing? In such cases the 14-subunit Integrator which is found only in multicellular organisms is recruited to terminate the paused Pol II. Integrator

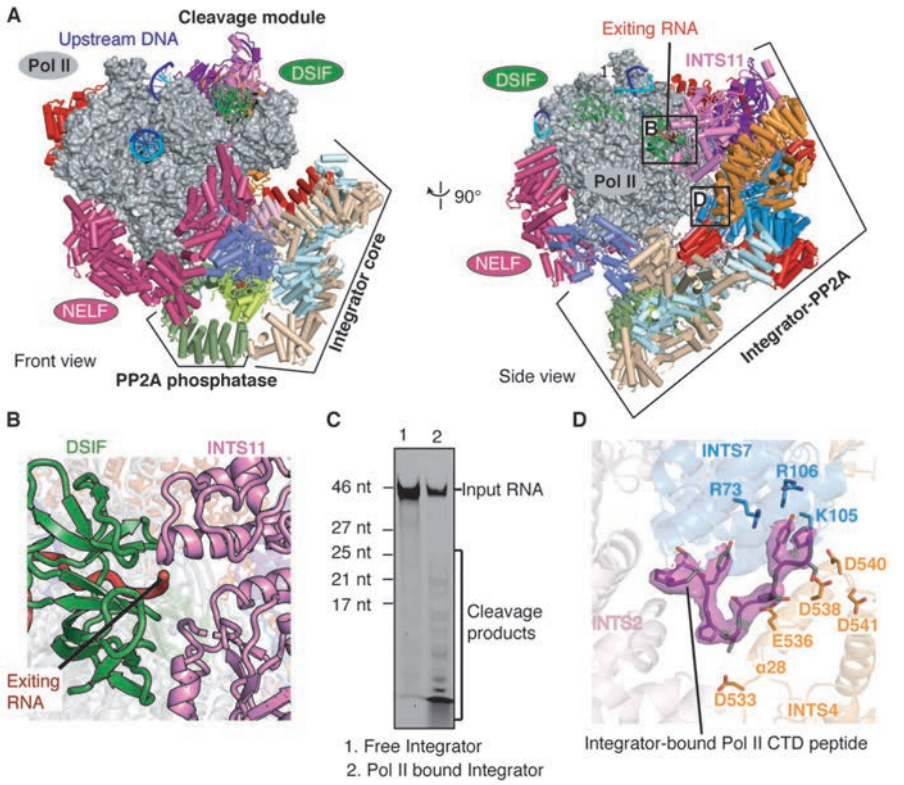

Fig. 1: Structure of Integrator-bound paused Pol II-DSIF-NELF complex and RNA cleavage. (A) Two views of the structure. Pol II as gray surface, DSIF in green and NELF in pink. Location of Integrator and PP2A are indicated by black border lines. Location of zoom-in views in B and D are shown. (B) Close-up view of INTS11, DSIF and the exiting RNA. (C) A gel showing Integrator cuts RNA only when bound to the paused complex. (D) A close-up view showing cryo-EM density of Integrator-bound Pol II CTD peptide.

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stops transcription firstly by cutting the emerging RNA using its endonuclease activity in subunit INTS11. Secondly, Integrator recruits PP2A phosphatase to counteract transcription activation by P-TEFb. Pausing and activation of transcription are well understood but the molecular mechanisms behind Integrator-mediated transcription termination are not known. This is where we came in.

To investigate how Integrator binds the paused Pol II complex to terminate transcription, we assembled a paused Pol II bound by DSIF and NELF in a test tube. We then added Integrator and PP2A to reconstitute a 34-subunit pre-termination complex (I first spent most of my PhD reconstituting the 14-subunit Integrator). We visualized the complex using cryo Electron Microscopy at a high-resolution.

The structure reveals that Integrator embraces the paused Pol II-DSIF-NELF complex by forming contacts with Pol II, DSIF and NELF. By concurrently recognizing Pol II, DSIF and NELF, Integrator distinguishes the paused Pol II complexes from other Pol II complexes and targets only paused Pol II for termination. As expected, INTS11 is perfectly positioned at the RNA exit tunnel of Pol II where it can cut the emerging RNA. We discovered INTS11 only cuts RNA when integrator binds Pol II. This prevents free Integrator from randomly cutting important RNA molecules in the cell.

Our structure also reveals how Integrator binds the Pol II CTD and positions PP2A to dephosphorylate it. PP2A is located close (~75Å) to the beginning of the CTD and can dephosphorylate most residues in the CTD thereby opposing transcription activation by P-TEFb.

Furthermore, comparing our structure to the structure of a Pol II complex released from the pause shows that Integrator cannot co-exist with SPT6 and PAF on the Pol II surface. Therefore, Integrator prevents release of paused Pol II also by physically excluding activating transcription factors.

In conclusion, pausing of Pol II is a key regulatory step in gene expression. The paused Pol II may be released into productive transcription or terminated by Integrator. Our structure provides a molecular understanding of Integrator-mediated transcription termination at the beginning of protein coding genes and sheds light on the enigmatic process of Pol II termination.

Isaac Fianu completed his doctoral thesis in summer 2020 in the lab of Patrick Cramer at the MPI for Biophysical Chemistry, where he is currently continuing his research as a postdoctoral researcher.

These results were published in Fianu I, Chen Y, Dienemann C, Dybkov D, Linden A, Urlaub H, Cramer P (2021) Structural basis of Integrator-mediated transcription regulation. Science 374(6569), 883–887

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Structural mechanism of an early translocation

Cascade of structural changes triggered by Pi release drives translocation in bacteria

Translation is the source of all proteins for all living organisms. The key element in the translation elongation cycle is a ribosome, which moves along the mRNA codon by codon synthesizing a polypeptide chain. This movement has to be fast and unidirectional. In prokaryotes it is facilitated by a GTPase - Elongation Factor G.

For 25 years it is known that GTP hydrolysis is required for translocation. But the exact mechanism of how the energy of GTP-hydrolysis drives the 2.5 MDa complex to move at the early stages of translocation was not clear.

We performed time-resolved cryo-EM aiming to visualize the structure of E. coli 70S ribosome complex with EF-G at the early stage of translocation. For the first time, we resolved a structure of 70S ribosome complex with EF-G with bound GDP-Pi in an active state, where GTP hydrolysis just happened but the release of inorganic phosphate (Pi) hasn't

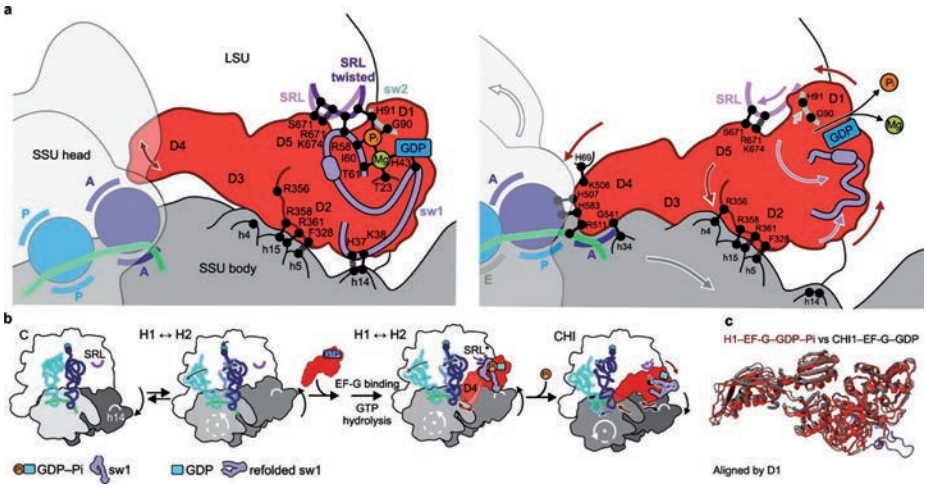

Fig. 1: (a) Scheme of the cascade of events driven by Pi-release that leads to the translocation. Domains 1 and 2 (D1 and D2) of EF-G are first stabilized in active state by the interactions with both LSU and SSU (left). Switch I acts as a bridge between the subunits while domain 4 remains motile. Then, after Pi release, in the chimeric state the switch I is refolded and the connection between the subunits is broken (right). It allows domain 4 (D4) to move into A-site of SSU body and block the backward movement of SSU head thereby providing translocation directionality. **(b)** Schematic overview of the early events of EF-G-facilitated translocation. c. Structural superposition of EF-G in active and chimeric states. EF-G acts as a rigid body and doesn't change its overall conformation.

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occurred yet and tRNAs are in a so-called hybrid state. In contrast to all other published data, we were able to see for the first time the structure of EF-G switch I and its interactions with both small and large ribosome subunits (SSU and LSU).

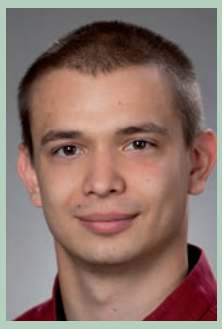
The switch I forms a bridge between the subunits thereby stabilizing the rotated state of the ribosome. C-terminal part of switch I is stabilized by interactions with GDP, coordinated Mg^{2+} ion, and Pi. Domain 4 of EF-G in active state is very dynamic and doesn't form stable interactions with the ribosome. But the most interesting observation resulted from the comparison of active state with the following chimeric state.

The structure of the chimeric state corresponds to the next structural state of the ribosome after Pi-release coupled with the translocation of SSU body along the mRNA. After Pi-release, EF-G switch I gets destabilized which leads to its refolding into an extended conformation that we were able to describe for the first time at ~5A resolution. Refolding of the switch I breaks the connection between SSU and LSU that allows SSU to rotate back which results in its sliding on mRNA. At the same moment EF-G rotates around the LSU as the rigid body. This movement places domain 4 in A-site of SSU body where it makes tight interactions with mRNA-tRNA complex.

This action is coupled with SSU head swivel which is happening due to the thermal motion. Such complex is called chimeric and it has tRNAs on P and E sites of the LSU and a/p and p/e sites respectively on SSU head and body. In this way, domain 4 works like a wedge preventing the SSU head to move back with bound tRNAs therefore making translocation unidirectional.

To sum up, the release of inorganic phosphate from the active pocket of EF-G drives the whole macromolecular complex forward to the next round of the elongation cycle.

Valentyn Petrychenko is currently completing his doctoral research in the group of Niels Fischer, Department of Structural Dynamics at the MPI for Biophysical Chemistry.



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Mapping active protein translocation during import in mitochondria

Nuclear-encoded mitochondrial proteins destined for the matrix have to be transported across two membranes. The outer membrane TOM complex and the inner membrane TIM23 complex cooperate for importing presequence-containing proteins into mitochondria. During transport, precursors are recognized by the TIM23 complex in the inner membrane for handover from the TOM complex. However, the lack of spatial and structural information on the organisation of the translocase components presents an obstacle for a molecular understanding of precursor transport across the intermembrane space.

In this work, we generated a protein with a tightly folded C-terminal domain which gets stalled during protein import and leads to formation of the TOM-TIM23 supercomplex. Subsequently, the purified supercomplex was subjected to proteomic analysis. Combining chemical cross-linking with mass spectrometry and structural modeling, we mapped the molecular environment of the intermembrane space interface of TOM-TIM23 transition zone, in the presence and absence of accumulated precursor, with amino acid resolution.

Together, our data provides an interaction map of the constituents of the active translocase that enables concerted precursor transport across two biological membranes, to understand the interplay between individual TOM and TIM23 components in a spatial context. Additionally, the TOM-TIM23 interface represents an affinity trap for presequences emerging from the TOM complex.

Ridhima Gomkale completed her doctoral research in the group of Peter Rehling at the University Medical Center Göttingen in fall 2018 where she is currently continuing as a postdoctoral researcher.

These results were published in Gomkale R, Linden A, Neumann P, Schendzielorz AB, Stoldt S, Dybkov O, Kilisch M, Schulz C, Cruz-Zaragoza LD, Schwappach B, Ficner R, Jakobs S, Urlaub H, Rehling P (2021) Nat Commun 12(1):5715

Insights on membrane fusion learned from early intermediate states

Fusion of biological membranes is essential for various biological processes such as neurotransmission or viral infection. Fusion proceeds through distinct steps including docking, merger of proximal membrane leaflets, and formation of a fusion pore. The structure of these intermediates is difficult to study due to their short lifetime. Previously, we observed a loosely and tightly docked states preceding leaflet merger using arresting point mutations in fusogenic SNARE proteins (Yavuz et al., J Biol Chem, 2018), but the nature of these fusion intermediates remained elusive. We have then utilized artificial vesicles (liposomes) in combination with interferometric scattering microscopy (iSCAT) and mathematical modelling, in order to characterize diffusional properties of vesicles arrested in different fusion stages (Witkowska et al., Biophys J, 2020).
In our work published recently in Nature Communications we determined the fine structural details of tightly docked intermediates preceding membrane hemifusion. We show that the metastable intermediate does not require but is enhanced by divalent cations and local membrane thickening at protein-free membrane patches. Molecular dynamics simulations reveal that thickening is a result of lipid rearrangements induced by dehydration of the membrane surface. Taken together, our results shed new light on the nature of membrane-membrane interactions immediately before fusion and allow for better understanding of the energy landscape and general mechanism of membrane fusion.

Agata Witkowska completed her doctoral research in the group of Reinhard Jahn at the MPI for Biophysical Chemistry in 2016. Currently, she works as postdoctoral researcher at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie (FMP) in Berlin.

These results were published in Witkowska A, Heinz LP, Grubmüller H, Jahn R (2021) Nat Commun 12(1):3606

STIM1 mediates calcium-dependent epigenetic reprogramming in pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) is a dismal malignancy with a 5-year survival rate of 7-9%, one of the worst among all cancer types. PDAC patients usually present an advanced stage of the disease upon diagnosis and often develop chemotherapy resistance. With disease progression, patients are commonly administered a gemcitabine-based therapy, which is known for its clinical benefits, but also low response and concomitant high resistance rates. Still, the molecular consequences of gemcitabine resistance in tumors remain elusive.

In this study, we investigated the molecular mechanisms fine-tuned by acquired gemcitabine resistance in PDAC. We identified an amplification of a segment of chromosome 11, which included genes previously associated with gemcitabine resistance, such as Ribonucleotide Reductase Catalytic Subunit M1 (RRM1) as well as other genes, like Stromal Interaction Molecule 1 (STIM1). While the amplification of RRM1 drove gemcitabine resistance, the upregulation of STIM1 elicited a heightened Store Operated Calcium Entry (SOCE) leading to ER stress resistance and aberrant NFAT activation. Thus, STIM1 acts as a rheostat of ER stress-responsive and NFAT-driven epigenetic programs upon stress. Taken together, our study characterizes molecular mechanisms driving gemcitabine resistance in PDAC and unravels a novel mechanism employed by these tumors to overcome stress and activate alternative pathways.

Ana Kutschat completed her doctoral research under the supervision of Steven Johnsen at the University Medical Center Göttingen in 2021. Currently, she works as a postdoctoral scholar in Vienna at St. Anna Children's Cancer Reseach Institute (CCRI) and the Research Center for Molecular Medicine (CeMM).

These results were published in Kutschat AP, Hamdan FH, Wang X, Wixom AQ, Najafova Z, Gibhardt CS, Kopp W, Gaedcke J, Strobel P, Ellenrieder V, Bogeski I, Hessmann E, Johnsen SA (2021) Cancer Res 81(11):2943-2955

Structure of the human spliceosome under modulator-induced conditions

Modulation of alternative pre–mRNA splicing patterns using small molecule compounds has emerged as a promising route for cancer therapy and of other complex human diseases. Splicing modulators from the pladienolide, herboxidiene, and spliceostatin/sudemycin families target the SF3B complex of the U2 snRNP and, through a poorly understood mechanism, reduce the fidelity of intron recognition resulting in transcriptome-wide intron retention or exon skipping.
In our latest work, we combined structural biology methods (cryo-EM and X-ray crystallography) with functional assays to define the action mechanisms of known splicing modulators. The highlight of our investigation is the cryo-EM structure of an early prespliceosome arrested with a clinically relevant modulator. Besides revealing the compound's binding site in a native human complex, this novel spliceosome snapshot allowed us to derive a model for the U2 snRNP reconfiguration, stepwise formation of the extended branch helix, and accurate selection of the reactive branch site adenosine. In addition, we also discovered the surprising mechanism of SF3B's inactivation by spliceostatins/sudemycins, compounds that covalently modify a zinc finger motif belonging to the PHF5A subunit to stably bind to and lock the complex in an open, RNA-free state. By providing a structural basis for spliceosome assembly under drug-induced conditions, we think that our analyses would facilitate the design of next-generation SF3B modulators, both for therapeutic purposes and as molecular tools to probe the fundamental mechanisms of pre-mRNA splicing.

Constantin Cretu completed his doctoral research under the supervision of Vladimir Pena in 2018. Currently, he works as a postdoctoral researcher at the University Medical Center Göttingen.

These results were published in Cretu C, Gee P, Liu X, Agrawal A, Nguyen TV, Ghosh AK, Cook A, Jurica M, Larsen NA, Pena V (2021) Nat Commun 12(1):4491

New Students

Master‘s class 2021/22

Svenja Ahlmann, Germany
BSc, Georg-August-Universität Göttingen

Çağla Alagöz, Turkey
BSc, Koç University

Florian Aust, Germany
BSc, Georg-August-Universität Göttingen

Subhro Basu, India
BSc, Sri Venkateswara College, University of Delhi

Rhythm Bharti, India
BSc, Sri Venkateswara College, University of Delhi

Adil Boolani, Pakistan
BSc, Middle East Technical University, Ankara, Turkey

Mandira Choppella, India
MSc, University of Hyderabad

Joseph Neos Cruz, Philippines
BSc, University of the Philippines Diliman

Naomi Elbing, Germany
BSc, Georg-August-Universität Göttingen

Zahra Fakhraei Ghazvini, Iran
BSc, University of Tehran

André Fischer, Austria
BSc, University of Vienna, Max Perutz Laboratories

Maria Groshkova, Bulgaria
BSc, Sofia University “St. Kliment Ohridski”

Adriel Hernando, Indonesia
BSc, Bandung Institute of Technology,

Kristin Konopatzki, Germany
BSc, Ruprecht-Karls-Universität Heidelberg

Delong Li, China/Germany
BSc, Goethe-Universität Frankfurt/Main

Neringa Liutikaite, USA/Lithuania
BSc, George Washington University

Pooja Mehta, India
BSc, St. Xavier’s College (Autonomous), Mumbai

Luis Felipe Monge Mora, Costa Rica
BSc, Costa Rica Institute of Technology

Tim Prolingheuer, Germany
Master of Education, University of Bremen

Applications 2021

In 2021, 618 students from 65 countries applied.

Germany 18 / West Europe 7
East Europe 77
North America 15
Central/South America 19
North Africa 41
Central/South Africa 65
Asia, Near East 54 / Far East 324

Saruby Sharma, India
BSc, Sri Venkateswara College, University of Delhi

Ana Vučković, Serbia
BSc, University of Belgrade

Siyu Wang, P.R. China
BSc, Huazhong University of Science and Technology, University of Chinese Academy of Sciences
(Exchange program)

Sina Jasmin Wille, Germany
BSc, Georg-August-Universität Göttingen
University of Gothenburg (Erasmus)

Yi Zhu, P. R. China
BSc, Peking University

PhD projects started in 2021

Laura Ahmuda Arranz
Bioinformatic analyses of complex genomic regions in non-human primate genomes.
Lutz Walter,
Rolf Daniel,
Jörg Stülke

Jannis Anstatt
Molecular analysis of metabolically induced changes in cristae architecture.
Stefan Jakobs,
Peter Rehling,
Henning Urlaub

Carmela Rieline Cruz
Dissecting the dynamic transcriptional network during PGC development.
Ufuk Günesdogan,
Argyris Papantonis,
Shiv Singh

Nesil Esiyok
Investigating the effects of endothelial cell integration during the development of primate brain organoids.
Rüdiger Behr,
Ernst Wimmer,
Ufuk Günesdogan

Tayfun Eyyuboglu
Mechanisms of retrotranslocation in endoplasmic reticulum-associated degradation.
Alexander Stein,
Peter Rehling,
Sonja Lorenz

Nilanjan Ghosh Dastidar
Time-resolved action of aminoglycoside antibiotics by quantitative mass spectrometry.
Marina Rodnina,
Henning Urlaub,
Peter Rehling

Vaishali Goyal
Modulation of ribosomal frameshifting by shiftless protein.
Marina Rodnina,
Stefan Pöhlmann,
Markus Bohnsack

Naintara Jain
Structural analysis of the mitochondrial import translocases.
Peter Rehling,
Alex Faesen,
Kai Tittmann

Priya Kumar
Camelid-derived nanobodies to neutralize SARS-CoV-2 and future pandemic coronaviruses for therapy and post-exposure prophylaxis.
Matthias Dobbelstein,
Dirk Görlich,
Stefan Pöhlmann

Mareike Lohse
Molecular architecture of the presynaptic compartment.
Nils Brose,
Silvio Rizzoli,
André Fischer

Annabel Maisl
Self-organized patterning mechanisms in planarian regeneration.
Jochen Rink,
Ernst Wimmer,
Melina Schuh

Nadia Paglilla
Navigation of effector proteins for B cell activation requires vesicle trafficking and cytoskeleton dynamics.
Michael Engelke,
Henning Urlaub,
Lutz Walter

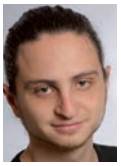
Ana Carolina Schwarzer
Role of RNA modifications in tRNA biogenesis and function.
Markus Bohnsack,
Ralf Ficner,
Claudia Höbartner

Rahul Shaha
Mechanism, regulation and structure of human pyruvate dehydrogenase complex.
Kai Tittmann,
Holger Stark,
Peter Rehling

Ryan Timothy Yu
Structural and biochemical studies of human mitochondrial RNA binding proteins.
Hauke Hillen,
Kai Tittmann,
Stefan Jakobs

Students
Graduated

The Masters of 2021



Rodrigo Alarcón
(*Marina Rodnina*)
Sub-millisecond dynamics of the bacterial translocon during membrane protein insertion.

Jannis Anstatt
(*Stefan Jakobs*)
Changes in mitochondrial ultrastructure upon alteration of metabolic substrate availability.

Artem Babych
(*Rüdiger Behr)*
Generation and 3D aggregation of human and non-human primate induced pluripotent stem cell-derived cardiac cells.

Daniel Blösel
(*Jochen Rink)*
Establishing CRISPR/Cas9-mediated genome editing in the flatworm *Schmidtea mediterranea*.

Carmela Rieline Cruz
(*Ufuk Günesdogan*)
Biochemical strategies to arrest large macromolecular complexes at different functional states.

Nesil Esiyok
(*Rüdiger Behr*)
Enhancing the structural complexity of primate brain organoids using iPSC-derived endothelial cells.

Tayfun Eyyuboglu
(*Alexander Stein*)
Investigations of yeast Der1-like family member 1 (Dfm1) ´s function in ER-associated degradation.

Vaishali Goyal
(*Matthias Dobbelstein*)
Simultaneous inhibition of the MDM2 oncoprotein and lysine demethylases.

Viktoriia Huryn
(*Johannes Söding*)
Classification of phase-separating proteins into different biological condensates with deep learning.

Naintara Jain
(*Peter Rehling*)
Molecular analysis of a ribosome-independent mitochondrial bL12m complex.

Sara Jamous
(*Argyris Papantonis*)
Investigating the molecular dynamics of senescence-Induced CTCF clustering in human lung fibroblasts.

Mareike Lohse
(*Noa Lipstein-Thoms*)
Presynaptic nanoarchitecture revealed by proximity labeling approaches.

Frederike Maaß
(*Nils Brose*)
Morphological and molecular characterization of distinct enteroendocrine cell subtypes.

Annabel Maisl
(*Jörg Stülke*)
Lipid metabolism in a minimal cell: Characterization of a putative regulator.

Carolina Monteiro
(*Sandra Goebbels)*
Age-related changes of human and mouse myelin: Ultrastructural observation and proteomic analysis.

Denys Oliinyk
(*Henning Urlaub*)
Methods for large-scale phosphoproteome analysis by data-independent acquisition mass spectrometry.

Nadia Paglilla
(*Michael Engelke*)
The Brefeldin A-inhibited guanine nucleotide-exchange protein 2 BIG2 supports the survival of B cells.

Ana Carolina Schwarzer
(*Niels Fischer*)
Mechanism of elongation factor G-mediated apramycin resistance revealed by cryo-EM.

Damla Temel
(*Alex Faesen*)
Biochemical reconstitution of the DNA damage repair effector complex Shieldin.

Chairini Thomé
(*Kate Bohnsack*)
Regulation of ribonuclease activity during cellular stress.

Akanksha Yadav
(*Johannes Söding*)
Reverse sparse logistic regression for trans eQTL discovery.

Ryan Timothy Yu
(*Patrick Cramer*)
Structural basis of TBP-TATA box recognition in a nucleosome.

The Doctors of 2021

Gerald Ryan Aquino
Molecular insights into the roles of RNA helicases during large ribosomal subunit assembly.
(Bohnsack, Ficner, Urlaub)

Rashi Goel
Targeting ion sensors to synaptic vesicles using a Nanobody against luminal Synaptotagmin 1.
(Jahn, Rizzoli, Steinem)

Katarina Harasimov
Actin promotes chromosome aggregation and accurate chromosome segregation in mammalian oocytes.
(Schuh, Bohnsack, Lenart)

Ana Kutschat
Gemcitabine resistance elicits a calcium dependent epigenetic reprogramming in pancreatic cancer.
(Johnsen, Dobbelstein, Söding)

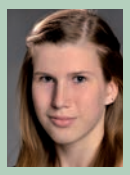
Yen-Yun Lu
Nuclear mRNA quality control factors Gbp2 and Hrb1 take part in cytoplasmic mRNA surveillance through nonsense-mediated decay.
(Krebber, Großhans, Lührmann)

Salma Sohrabi-Jahromi
Quantitative modeling of RNA-protein interactions.
(Söding, Urlaub, Habeck)

Swati Subramanian
Unravelling the role cortical myelination plays in higher brain functions.
(Nave, Rizzoli, Brose)

Cole Townsend
Structural characterization of human spliceosome activation by cryo-EM.
(Stark, Urlaub, Stein)

Zhenwei Zhang
Structural insights into early spliceosome assembly by cryo-EM.
(Stark, Urlaub, Stein)



Sofiia Reshetniak
The dynamic organization of proteins in the synaptic bouton.
(Rizzoli, Jahn, Janshoff)

200 Molbio PhD graduates!

When **Sofiia Reshetniak**'s publication in the EMBO Journal was featured as a Science Spotlight 2020 in the last Molbio newsletter, some of us may have already anticipated that this outstanding doctoral thesis will be awarded summa cum laude (see also page 21 of this newsletter). And so it happened in October 2021. A great success of which she and her PhD supervisor Silvio Rizzoli can be justly proud and for which we would like to congratulate!


Source: iStock

What Sofiia didn't know when she defended her thesis is that this defense also has an additional special meaning for us, as Sofiia is the **two hundredth PhD graduate** of our Molecular Biology Program. A good occasion to thank all our students who had put their trust in us when they had entered our program. And our PhD alumni, 203 by now, distributed over 23 countries, are doing well regardless of the various career paths they have chosen after their graduation. A reason to celebrate!

Supercharging T cell immunity to treat cancer

My path from basic science to working on a cure for cancer

Of all the subjects we learned during our Molecular Biology curriculum the class I liked the least was immunology. By far. Immunology felt like you were trying to grasp the complexity of the entire universe all at once. Multiple signaling cascades within a cell were intersecting and interacting in a way that made it impossible to neatly write down what was happening. And then you had all these different cell types that regulated and influenced each other via those same signaling cascades. Every attempt to describe what was happening made my head spin.

During my PhD at the Raz lab at the MPI I studied how cells migrate within developing embryos from their origin to their final destination in the organism to serve their function. The problems were complex, but not immunology-type complex. We were able to discover some of the mechanisms behind the guidance of these cells, which happenstance, also applied to the regulation of migration of immune and cancer cells. I reconsidered my aversion to immunology and joined the Krummel lab at the University of California San Francisco in 2010, where I was studying how immune cells migrate to where they need to be in order to mount a successful immune response, and why does this process fail in diseases such as cancer?

The struggle was real. Oncology and immunology are huge fields with lots of talented people trying to make a difference. The competition is fierce and not always friendly or fair, and your success depends on a constellation of mentorship, institutional support, perseverance, and of course, luck. Five long years later, I was exhausted but I knew I wanted to continue to work in the field, just not in an academic career. With the help and

Bijan Boldajiour

training of the Postdoctoral Office at UCSF I was able to put together a good resume and prepare for job interviews.

Luck was on my side: I joined a new research group at Pfizer in 2015 that was developing engineered T cells for the treatment of cancer, bringing in my experience in cancer immunology and animal models. The technology was fairly new and was having incredible success at treating childhood and adult leukemias: In essence, you take T cells from the blood of cancer patients, genetically engineer them to express receptors that recognize cancer cells, expand them to large numbers and infuse them back into patients. The patients in these clinical trials had failed every other treatment and yet would experience remarkable recoveries and become cancer-free within weeks after this new treatment.

I spent three years at Pfizer as a bench scientist, where we had to overcome many technical and biological hurdles – I can't count the number of times we had to explain to senior management that things were not working because 'we are building the plane as we are trying to take off'. Over time, I was also responsible for leading teams and supervising other scientists. The switch from researcher to manager was difficult as these skills are not taught in academia. With the help of coaching programs and a supportive supervisor I grew into that role. In 2019, these skills allowed me to transition to a new role at Kite Pharma, which had recently been acquired by the large pharmaceutical Gilead. I

Bijan Boldajipour completed his doctoral research in the group of Erez Raz at the MPI for Biophysical Chemistry. He graduated from the Molecular Biology Program in 2009. From 2010 he continued his research as a postdoctoral fellow at the University of California, San Francisco before he joined Pfizer as a scientist in 2015. In 2018 he moved to Kite Pharma as Director Technology Development. Since 2019, Bijan works as Senior Director at Lyell Immunopharma in South San Francisco.

Supercharging T cell immunity to treat cancer (continued)

was asked to guide scientists in their transition from working in a small and often chaotic startup company to a more structured large pharmaceutical company. The stories of these often-young scientists of how they built a company from scratch, their excitement about bringing a drug into the clinic, and the eventual reward when Kite was acquired were exhilarating.

A few months into my time at Kite Pharma I was approached by former Pfizer colleagues that had joined a mysterious new startup called Lyell Immunopharma that was led by the former founders of Juno, another startup in the field that had also been sold to a large pharmaceutical company. The scientific masterminds behind this new company had no smaller goal than making T cells so powerful they could attack and cure solid tumors, something that so far had not been possible. The ideas were bold, the strategy was audacious, and the management was charismatic. Our companies' guiding principles are science, respect, courage and collaboration. I was sold and left Kite after 9 months to join a startup that did not even yet have labs.

Lyell moved into new custom-built headquarters in South San Francisco in October 2021

The NASDAQ stock exchange in New York City celebrating Lyell's first day of a publicly traded company in June 2021

The three years since have been anything but boring. Being able to develop the strategies of the company and then build the labs in San Francisco and Seattle to our ideas was truly inspiring. We hired incredibly talented and collaborative people that believed in our mission. We even persuaded an entire academic group from the National Institutes of Health to join us; today we have more than 200 employees in three locations. Not everything we planned worked out and we changed strategies a few times, which was never easy. We had to say goodbye to colleagues that had become friends a few times, and of the original scientists that started with me only two are still with the company.

It has been a long journey, and I look back on tumultuous times but I do not regret moving on from academic research. One of the projects I worked on at Pfizer is showing successes in treating patients with multiple myeloma; Lyell's first project is going to be tested in breast and lung cancer patients this year. Being able to work products that may someday help people that are fighting for their life is nothing I ever imagined I would be able to do. A lot of things didn't work out but working with colleagues that are working towards a common goal and where we try to be good colleagues to each other make the setbacks seem smaller and less frustrating. And we never give up hope to be able to say at some point, that drug – we did that.

From academia to industry

My journey at Boehringer Ingelheim

Upon finishing my PhD at the Max Planck Institute for Biophysical Chemistry I have joined Boehringer Ingelheim as a Management Trainee in Biopharmaceuticals and moved to Biberach in the south of Germany. The idea of my trainee program is to facilitate smooth transition of young natural scientists from research into business & management.

Left: Natalia after kissing the Gänseliesel. Right: Exploring Biberach – view of the city from the observation platform. Photo taken on my first weekend in Biberach

But first things first – what motivated me to join a trainee program? Back in 2019 I knew that I wanted to switch to industry but the big question I had was what kind of position I want and in which area I would like to work. And this is when I stumbled upon various trainee programs, which help answering exactly this question by providing insights into various areas of the company.

Now, how does my trainee program work? The main part of the program are 6 to 9 month rotations in different departments of the company. Typically, one rotation is spent abroad but because of the corona pandemic it was not possible for me. Nevertheless, I got to work with colleagues from all over the world in online meetings and conferences. During rotations I learned about the function & tasks of each department, their overall contribution, and interfaces to other areas.

Each department has routine tasks and project work. Routine tasks are for instances manufacturing of drugs – it happens continuously using an established procedure in defined facilities with dedicated teams. On the other hand, projects are temporary and have a clear goal – for example, optimization of a process or introduction of new equipment, and once this goal has been reached, the project is completed. As a trainee I was mainly involved in the project work assuming a role of a project manager. I was leading teams of experts, often from different areas of the company, and coordinating their tasks towards reaching our project's goal(s).

Another big chunk of my work was working together with our leadership team – presenting & discussing projects, negotiating timelines and budget and so on. In addition, I was also working as a team member and occasionally did routine tasks, such as writing reports or reviewing documents.

A few words about my transition from academia to industry. Soft skills (time management, independent working, critical thinking) along with international experience gained during the graduate school have made the switch pretty smooth and let me adapt to the new role very quickly. Alongside with rotations, I had many opportunities for professional and personal development. I could attend multiple trainings in project & change management, communication but also finance & controlling to improve my business understanding of our processes. In addition, I worked closely with an experienced

Natalia Korniy completed her doctoral research in the group of Marina Rodnina at the Max Planck Institute for Biophysical Chemistry in spring 2019, followed by a few months as postdoctoral research asssociate. In November 2019 she joined Boehringer Ingelheim as Management Trainee Biopharma. Since December 2021, Natalia works at Boehringer Ingelheim as Senior Global Quality Manager.

From academia to industry - my journey at Boehringer Ingelheim (continued)

mentor who gave me guidance and career advice and had an open ear for my questions and concerns. Finally, there is also a very active trainee community bringing together trainees from different programs and countries. Last year we organized the Biopharma Academy 2020 event to let students & PhD students learn about biopharmaceuticals in general and within Boehringer Ingelheim in particular, and a few MolBios were on board as well.

In summary, through working in different areas of the company, trying out different roles and being exposed to various projects, I gained a solid understanding of how a bio(pharma) company operates and built a great network. This let me find my own niche within the company and helped me make a well-informed decision about the next carrier step.

So what comes next? In December 2021 I successfully finished my trainee program and started a new job as a Senior Global Quality Manager @ Boehringer Ingelheim. In my new role, I will be responsible for global digitalization in GMP labs, which test the quality of our products before they could be released to patients. I am very excited and looking forward to my new task!

Honors and Awards

Faculty Members (current and former)

Bertram Brenig received the thirteenth Illumina Agricultural Greater Good Award 2021.

Patrick Cramer was awarded the Louis-Jeantet Prize for Medicine, the Hector Science Award and the Gregor Aminoff Award of the Royal Swedish Academy of Sciences.

Ivo Feußner has been included in the 2021 list of „Highly Cited Researchers“, referring to the most cited scientists in their field worldwide.

Stefan Hell became Honorary Fellow of the International Union of Physiological Sciences.

Herbert Jäckle became international honorary member of the American Academy of Arts and Science and member of the Chinese Academy of Sciences (CAS).

Erwin Neher became Honorary Fellow of the International Union of Physiological Sciences

Marina Rodnina was awarded the Albrecht Kossel Prize of the German Chemical Society.

Students (current and former)

Tayfun Eyyuboglu was awarded a PhD fellowship by Boehringer Ingelheim Fonds.

Maximilian Fünfgeld achieved the third place at the DMEA Newcomer 2021 Award.

Bettina Görner was awarded Capital's Junge Elite 2021 „Germany's Top 40 under 40“.

Rohan Kapoor was awarded a doctoral fellowship from the German Academic Scholarship Foundation (Studienstiftung des deutschen Volkes).

Tabrez Siddiqui received the 2021 Young Investigator Award from the Canadian Association for Neuroscience (CAN).

Claudia Schmidt was honored with the Otto Hahn Medal of the Max Planck Society.

Summa cum laude distinctions for their doctoral theses and defense in 2021 were awarded to **Katarina Harasimov**, **Ana Kutschat**, **Sofiia Reshetniak** and **Salma Sohrabi-Jahromi**.

In addition, summa cum laude was awarded for the PhD defenses of **Rashi Goel**, **Cole Townsend** and **Zhenwei Zhang**.

Congratulations!

Episode IV: A new hope

Writing this piece is not only a great opportunity to share the exciting transition in my life with our wonderful community but also to take a retrospect of the past year, having just celebrated the 1st anniversary of the Saka Lab.

First let me take a few steps back. I graduated from the Molbio program at the end of 2013, after studying the nano-to-micro scale organization of membrane proteins with high-resolution microscopy as a PhD student in Rizzoli Lab. I then stayed in Göttingen for another two years finishing up papers and tackling exciting follow-up projects.

The first Saka Lab Retreat in our 2G+ isolation bubble in the Black Forest.https://www.embl.org/groups/saka/

First maskless gathering of the year. The lab enjoying some Turkish food and saying farewell to the first summer intern.

In retrospect, it may have been a better idea to move on to a new postdoc position faster (as the academic clock starts ticking). But, after the PhD, I got to experience this sweet feeling of being in the comfort zone with an empowering grasp of my research, which happens rarely in science, and it did take me a while to let it go. I also used this time to figure out which of my own limits to push next, to travel for postdoc interviews in the US, and prepare my fellowship applications, which helped me to stack 4 years of external funding for my next position.

During my PhD, I realized how new tools broaden our scientific horizons and open the way to answer scientific questions more effectively. Combined with the joy I get out of solving problems, I have grown a passion for developing tools and methods. This led me to take a postdoc position in Wyss Institute for Biologically Inspired Engineering at Harvard University, which offered a very interdisciplinary research environment focusing on repurposing natural materials and processes for highly translational applications. Here, I not only learned about DNA nanotechnology, but also got exposed to an innovation-oriented mindset. While I was working on adapting DNA-based tools for addressing the limitations of fluorescence microscopy in Peng Yin's group, I also seized some additional opportunities to get training and hands-on experience in many additional aspects of translational science, including IP law, biotech entrepreneurship, technology transfer and science commercialization. I also actively worked in the Volunteer Consulting Club and helped new biotech startups with their strategic planning.

These experiences helped me shape the career path I wanted to follow. I have seen that running a new lab and creating a start-up had some striking similarities, but one allowed keeping a more active engagement with science. I decided that having my own research group in an academic environment that supports innovative and collaborative science while keeping strong ties to applications outside of academia would be the most suitable route. Hence I started to look for opportunities where I can realize this vision. I narrowed my search to cities that I can imagine living an enjoyable life and institutions where there is a dynamic and international community. I ended up having a few interviews in the U.S. and two interviews at EMBL.

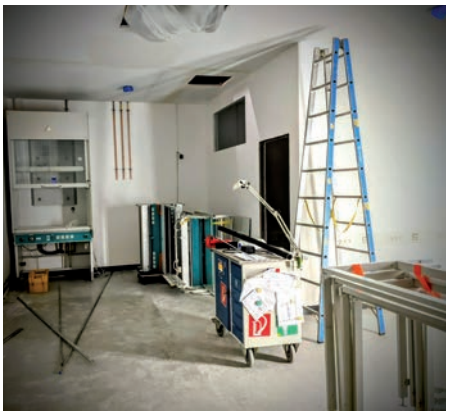
Episode IV: A new hope (continued)

A new chapter

After interacting with many groups in Heidelberg, EMBL's collaborative outlook on research and its strong international structure and well-established support system felt like a great fit to me, and I started my independent research group at EMBL Heidelberg Genome Biology Unit in December 2020. On the side, I am also continuing to work with a couple of my previous colleagues to spin out a biotech company in Boston.

My research group focuses on developing and applying new labeling tools and methods, such as DNA-based barcoding for spatial omics and multi-modal/multiplexed imaging, to investigate the spatial and molecular organization of cells across scales. We aim to utilize these approaches to uncover the role of organizational heterogeneity in intricate conditions like cancers, neurodegeneration and aging, and provide new insights into cellular homeostasis, disease formation, and drug response.

One of the major challenges for young groups is having access to motivated and talented team members. In that regard, starting my group at EMBL has been an amazing privilege. I started recruiting for my group as soon as I accepted the offer myself, and I am currently looking for the 4th PhD student to join the team. In 2022, we will be reaching 10 people (all hired via remote interviews), with multiple shared post-doctoral candidates that bring in new perspectives and dynamism to the group. This also means that my on-the-bench presence is disappearing much faster than I anticipated, and managing my time as a PI, maintaining group coherence, and creating new funding streams are becoming major priorities. The additional responsibilities I had taken as a postdoc to manage multiple projects and collaborations, write grants and train junior lab members, are now serving me well to adapt to this fast transition. However, regardless of how much one prepares for this role, the amount of power and responsibility that is handed off to academics from day 1 of being a PI is really massive. Being the sole person to make many critical decisions on a daily basis is definitely an active challenge for me. But I started to appreciate the empowerment and freedom that comes with it. I also very much enjoy the mentorship aspect and how rewarding it is to touch the lives of fresh scientists' and be a part of their journeys.



Starting the lab from scratch.

On the personal side, going through 2 intercontinental moves in 5 years (especially this last one being in the middle of a pandemic) has been particularly difficult. This requirement to always be on the move and reset our lives every few years does become a little less exciting over time and takes some adaptation. Moving from Boston (an eventful city that really grew on me) to Heidelberg (a small town I did not know much about beyond its picturesque castle) was one of the toughest parts of the decision for me. Literally landing to Germany right before the winter lock-down did certainly not make it any better. What has been really helpful to get settled here was to find a cohort of fellow group leaders in the same "life-reset" boat. Forming a sense of community and belonging are not things to be taken for granted and together with my partner Koray, a fellow Molbio alumnus, we are trying to find to a new balance.

My group leader position here is a 5+4 year arrangement, and although 9 years sound like a long time, I am already well aware of its finiteness. Though the thought of going through another reset point down the line is scary, it is also somewhat refreshing to know that I'd be able to pause and re-evaluate my path with a renewed perspective before making the next move.

Sinem Saka completed her doctoral thesis in European Neuroscience Institute under the supervision of Silvio Rizzoli. She graduated from the Molecular Biology Program in October 2013. After a bridging post-doc at the European Research Council in Brussels, Sinem continued her research at the Wyss Institute for Biologically Inspired Engineering at Harvard University, as a postdoctoral research fellow supported by EMBO and HFSP Fellowships. In December 2020, she joined European Molecular Biology Laboratory (EMBL) Heidelberg Genome Biology Unit as a Research Group Leader, and currently has a joint appointment at the Cell Biology and Biophysics Unit.

Pregnancy and research: Mission possible

By the time I'm writing this, I've already become a mother and it wouldn't come as a surprise to anyone that I consider my daughter the biggest blessing in my life. I've always wanted to start a family, but I never expected this would happen during one of the most mentally and physically challenging times in the career of a scientist – the PhD studies. I've wondered so many times what would happen, how things would develop after having a kid, and is it possible to pursue a scientific career and be a mother at the same time. There are many women, who are both successful scientists and mothers, and who I've always admired for their motivation to keep chasing their scientific goals, as well as for their courage to do this while starting a family.

A few days after getting to know I was pregnant, I went to my supervisor's office, excited to share the big news, but also nervous and insecure what his reaction would be and how things would be from now on. It turned out there was nothing to worry about and I was happily surprised when he started congratulating me with a big smile on his face. There were many things we had to discuss and arrange with regards to my lab work, especially because I was not allowed to perform a big part of the methods. Consequently, in order for me to be able to keep on working on my scientific project, he hired another person to help me with the tasks I couldn't do on my own, which allowed me to make further progress on my project. Without such an assistant my work would have been very difficult and delayed in time. I was also able to work from home on the days I wasn't feeling well, and I also had the flexibility to plan my experiments and my whole schedule the way I wanted. This flexibility is something one should really have during such a time, and it's something I really appreciate. In addition to my supervisor, all other lab members were of great support to me from the very beginning of this journey, which I'm extremely grateful for. Moreover, I also received great support from the MolBio program, which, once again, made me realize that this is indeed one of the best graduate programs in Germany! One of the most valuable kinds of support came from the IMPRS family support program that provided a big part of the finances needed to hire a technical assistant to help me with my lab work. Furthermore, through the MolBio program, I got in touch with a person who helped me understand how things work in Germany, what kind of documents would be required and which institutions I should contact in order to receive the financial help every mother in Germany is eligible for. Taken together, working on a research project while creating a new life is not as impossible as it might seem at first, as long as you surround yourself with people who could offer their support. There are many people who made my life easier during this challenging time and to whom I'd like to thank wholeheartedly!

As much as I wish there were only flowers and happy moments, I couldn't deny there were many difficulties and obstacles on the way. One of the biggest challenges was to arrange my work in a way that allows me to perform as many tasks as possible on my own. We all know many biological and chemical substances are hazardous, but it takes something more to really appreciate that. Learning that there is a fragile life developing inside you really makes you recall all the safety measures you need to follow when working in a scientific lab. I've always been an extremely careful person when it comes to lab safety, but this definitely took things to another level! Something that makes my skin crawl even today is the fact that before getting to know I was expecting a child, I had been working with various cell division inhibitors in the first few weeks of my pregnancy, which is the most crucial phase for the developing embryo. If such compounds are considered hazardous to the adult organism, imagine what they could do to the embryo, which has just began to divide and grow!

Vella Nikolova started her doctoral research under the supervision of Matthias Dobbelstein in the Department of Molecular Oncology at the University Medical Center Göttingen in May 2020. Since October 2021 she is on maternity leave.

Pregnancy and research: Mission possible (continued)

In addition to all the safety precautions I had to take, there were also new physical limitations that I had to find a way to cope with. To say the least, I couldn't lift heavy objects anymore, so I always had to ask someone to help me carry some things around. I also used to work full-day without eating and taking any breaks, simply because I didn't feel any hunger and fatigue, but this was not possible anymore. Furthermore, there's no denying that the Coronavirus pandemic made the overall situation more challenging and insecure for me. At that time, it was not recommended for pregnant women to get vaccinated, so I had to be extremely careful and really take care of myself and my health.

On a final note, a long time ago pregnancy and research sounded to me as two self-excluding concepts, but after spending almost my whole pregnancy in the lab, I learned that I was wrong. The living proof that one could get the best of both worlds is my daughter, who is peacefully sleeping in the other room. I owe a lot to my supervisor, to all lab members, to the MolBio coordinators and to many other people who supported me throughout this unforgettable journey and who made it possible for me to keep on doing lab work while growing a new life. I'm looking forward for the day when I'll be able to explain to my daughter that I was a scientist working in a research lab during a pandemic and what all the challenges I faced were. Becoming a mother and having to raise a child is a great source of motivation to give your very best in all aspects of life. Just like any other mother, I want to be a role model for my child, so I now feel even more motivated to pursue my scientific career. I'm thrilled what the future has prepared for me and I believe the best is yet to come!

Our Molbio student representatives

MSc student representatives

Congratulations to our newly elected MSc student representatives **Joseph Neos Cruz** (upper photo) and **Neringa Liutikaite** (lower photo). Your dedicated engagement during the orientation weeks and the first months of the new academic year helped all newcomers to have a smooth and lively start.

Many thanks to our former MSc student representatives **Josefa Torres** (upper photo) and **Lucia Winkler** (lower photo). Your valuable contributions were very helpful to navigate your MSc class through a challenging year during the corona pandemic and also made our first Master's retreat in Goslar at the end of the examination week a great success.

PhD student representatives

Congratulations to our newly elected PhD student representatives **Debojit Saha** (upper photo) and **Atmika Paul** (lower photo). You were elected in September 2021, at a time at which the local COVID-19 infection rates were close to zero and we were able to resume larger Molbio events such as our MSc graduation or PhD retreat. In the meantime, the pandemic picks up speed again and we are thankful for your support in these challenging times.

Many thanks to our former PhD student representatives **Katarina (Ina) Harasimov** (upper photo) and **Gaurika Garg** (lower photo). You invested a lot of time and effort to make the conversion of our three-stage admission process to a complete online procedure a great success. As PhD representatives of our program, you also participated in the organizatin of our internal accreditation (quality review) in summer 2021. We appreciated your reliable and dedicated support very much.

Career and a baby in the midst of a pandemic

As I started writing this article, all the wonderful memories of the beautiful town "Göttingen" came alive. I joined the IMPRS Molecular Biology Program about 10 years ago. I was homesick but the scientific exposure I received was inspirational and kept me going. Besides, the void which was created being far from home was soon filled by people I met in Göttingen, and that is how I also met my husband, Kundan. He joined the Molbio program one year before me and guided and supported me throughout. After completing my Ph.D. in 2016, Kundan and I got married and soon he moved to the UK to grab the new opportunity as a Post Doc at Ludwig Cancer Research at the University of Oxford, and I followed him.

Kundan and Heena in front of Bridge of Sighs, Hertford College, exploring Oxford in the first year

Oxford is known as the "City of Spires" because of its beautiful skyline of Gothic towers and steeples most of which belong to the oldest colleges and buildings in the University. The town is full of students but also very popular among families because of some of the best schools. Fortunately, Oxford is also a hub for many emerging biotechnology start-ups as they get seed funding from Oxford Science Innovation which is an early-stage venture capital firm for research-based spin-outs from the University.

In 2017, I applied and got into one of these start-up companies called Evox Therapeutics. Since then, I have been an integral part of its exponential growth both in terms of science and people. I experienced the struggles of a new start-up and got a sneak peek into how they evolved to become lead biotech companies. In Evox, we engineer exosomes - naturally occurring vesicles - to deliver protein or nucleic acid-based therapeutics to treat diseases with unmet needs. My job was permanent, and I was very happy and satisfied with my new role as a scientist.

The only thing which is constant in this world is indeed a "change". As we got settled in our new life in Oxford, we started thinking about extending our family. Kundan was born ready to be a father. For me, I felt secure with the job and very soon realized that this is the right time for us. During my pregnancy, the company was very supportive and the maternity policy, although not as good as Germany's, was decent compared to many other companies in the UK.

In 2019, Kushagr (Kush, guess who insisted the name start with "K") came into our lives and I went to one year of maternity break. Unfortunately, in the UK fathers are only allowed to take 10 days off but with the help of our families, we came to new arrangements and started enjoying our lives with Kush. I was aware that all my projects went to

Heena Sharma was a PhD student in the group of Marina Rodnina at the MPI for Biophysical Chemistry and graduated on November 2016. In August 2017 she joined Evox Therapeutics Ltd in Oxford, U.K. as a scientist where she works as a group leader since 2022.

Kundan Sharma was a PhD student in the group of Henning Urlaub at the MPI for Biophysical Chemistry and graduated in April 2015. In 2017 he started as postdoctoral researcher at Ludiwg Cancer Research in Oxford. In summer 2019 he moved to OMass Therapeutics where he is currently working as a senior scientist.

Heena and Kundan got married in 2016. Their son Kushagr was born in 2019.

Career and a baby in the midst of a pandemic (continued)

other people and, honestly, it did bother me but at the same time I was not ready to give away my special and very precious time with Kush, I was legally allowed to take one year off, and I took full advantage of it. During the same time, Kundan also moved away from academia and joined a biotech company called OMass Therapeutics, a drug discovery start-up using Mass Spec at its core to investigate protein-ligand interactions.

Celebrating Kush's second birthday in 2021

I joined back in May 2020 when COVID-19 was at its peak. Nurseries were closed and the work from home culture was encouraged. We juggled between lab work, teams' calls, and taking care of Kush, who needed a lot of attention. After a year break, I was looking forward to resuming my career as normal, but the pandemic was not helping and there was no family support because of the travel ban.

During my maternity break, I joined basic online courses on project management, and instead of starting a new lab work immediately after my re-joining, I helped our new program manager director get on board with science and started managing exploratory projects. This helped me to get back to work slowly and catch up with ongoing scientific activities.

Soon, nurseries opened, and Kush started his new journey but poor him also got exposed to hundreds of other viruses. He fell sick every two weeks, sometimes fever but sometimes only cough. We never sent Kush to nursery with fever, and we still don't, but during the pandemic, we could not send him until we get a negative Covid test report even if he was fine the next day. This meant to take time out for almost a week again and again.

We both work in small fast-paced companies, we had commitments, planned experiments, and deadlines to meet. It was extremely stressful, but we both sat down and discussed how we could best manage the situation. We worked in shifts and shared the space and responsibilities. Luckily, my line manager is a very nice lady with two kids. She completely understood my situation and gave me full flexibility on my working hours. We continued to work in odd hours as we wanted to deliver, and we passed the phase victoriously and both got promoted at the end of the year.

Kundan and I work at the same site, which has made our commute a bit easier. Somehow the restriction that we need to leave at 5:00 p.m to pick Kush from nursery has made us more efficient and organized. Whether the job is 9-5? Well, it depends on the day. Many times, we both resume work after Kush goes to bed or early morning before he wakes up. Kush spends most of his time during the week in nursery, but on weekends we enjoy our family time together. Away from India, where Kush has so many cousins and extended family, we feel nursery plays an important part in developing his social life.

I will start as a Group leader this year, and I am ready for new challenges. I believe the work-life balance is not a 9-5 job, but it is the satisfaction which we get in our work and family lives.

The clear path *versus* the right path

The PhD journey is filled with excitement, disappointments, hopes and uncertainty. During this roller coaster of up and downs, it is sometimes hard to find time and energy to think about what´s next. This can be even more overwhelming if, by the time you are reaching your final year, you have realized that academic research is not the right path for you. The alumni mentoring program is a great platform to connect with somebody that has been through the same.

Why did you decide to become a mentor/mentee?
Valentina: I decided to become a mentee to get inspired and to get an insight into the daily life of a scientist in industry. I love doing science, but industry was never an option since my academic advisors often referred to it in a negative way, or simply did not know much about it. This slowly changed when I started participating in career fairs and connecting to professionals from industry. I realized that the only way to truly understand a career path is to form a meaningful connection with somebody that is working in the field. This is how I got paired with Marta, who is working as Head of Structural Biology at ZoBio, and I couldn´t have been happier!
Marta: Throughout my PhD I was completely embedded in the academic world: my supervisors and advisors were academics, most of my friends were PhD students and post-docs. When I started thinking about my next step, I missed having recurring contact with someone from the "outside world", someone who could tell me first-hand what it is like to work outside academia. When I heard about the mentorship program I thought "hey, now I'm one of those people who work in industry…", but I was worried about the time commitment. However, when Steffen brought to my attention Valentina's "perfect match" application I simply could not resist!

Are you happy with the outcome of the mentoring program?
Valentina: Marta was such a great mentor! She helped me not only with my career, but also to tackle my last year of PhD. Conflicts, publications, thesis writing and pandemic… She was always available whenever I had a question. Moreover, we had a great time together in Leiden and I am so grateful to her for showing me around her lab and organizing a tour of the neighbouring building. She also introduced me to the best Italian restaurant I have ever tried abroad – thank you Marta!
Marta: I really enjoyed the experience! Valentina was very enthusiastic and had several (sometimes difficult!) questions that also "forced" me to think about how to deal with certain topics. I always had the feeling Valentina appreciated my input and suggestions. It felt really great to be able to help someone!

What would you recommend for future mentees/mentors?
Valentina: I recommend the book "The salmon leap for PhDs" to get some initial idea on your career path. Don´t be afraid to ask anything that comes to your mind, but also be respectful and ask your mentor if it´s ok to talk about certain topics. Be proactive and take initiative.
Marta: I really enjoyed the open atmosphere we had during our sessions and would recommend it to all the future mentees and mentors! I think key ingredients in building this atmosphere are mentees asking any questions they may have, without fear of sounding naïve, and mentors taking those questions seriously and giving thoughtful feedback, putting yourself in your mentees' shoes. As an added benefit, you may learn something about yourself. Also important was to leave some room for "unexpected topics" – we did have a plan early on (thanks to Valentina!), but we often detoured into new events. And last but not least: do chat regularly. It helps building the relationship throughout and beyond the program!

Valentina Manzini is a final-year doctoral student under the supervision of Matthias Dobbelstein at the University Medical Center Göttingen. Valentina will defend her PhD thesis in spring 2022.

Marta Gião Carneiro completed her doctoral research in November 2015 under the supervision of Christian Griesinger at the MPI for Biophysical Chemistry. In February 2016, she joined ZoBio BV in Leiden, The Netherlands, as a postdoctoral scientist applying NMR-based structural biology to support fragment-based drug discovery programs. Since 2019, Marta has been Head of Structural Biology at ZoBio.

Our experience in the mentoring program

Today we would like to tell you about our experience as a mentoring tandem in the 2021 cohort of the alumni mentoring program – we, that is Gaurika, now in her final year of PhD thesis in the Molbio program, and Annette, an alumna of the Molbio program and currently a project leader with McKinsey.

Gaurika already knew that consulting might be an interesting career path for her because she enjoyed tackling problems, finding solutions and working in a team. She had also already actively taken steps to gain valuable experience and to start building her consulting toolkit by gaining experience working for a pro-bono consulting company that helps the issue of sustainability. However, Gaurika wanted to better define and narrow down her options and develop a clear path forward. She also wanted to learn more about the application and interview process and life as a consultant in general.

Annette graduated from the Molbio program in 2011 and then pursued two postdocs, one at the Salk Institute in La Jolla, USA, and the second at the Hubrecht Institute in Utrecht, the Netherlands. She then joined McKinsey as a business consultant in 2016, focusing on healthcare and pharma topics in her client work. She first joined the Düsseldorf office and is currently living in Munich. While wanting to share her experience regarding moving from science to consulting, Annette also wanted to use the mentoring relationship to reflect on her own career path and future plans.

Due to Covid, we could not meet in person (yet) but instead talked via Zoom every 4-5 weeks. While we kept our virtual meetings pretty informal and personal, we also always tried to come up with concrete deliverables/ next steps. For example, we developed a list of potentially interesting consulting companies, prioritized the options and then Gaurika could use the time until the next meeting to contact the recruiters or do more research on open questions (for example German language requirement).

Gaurika then also did some research to identify interesting recruiting events to learn more about the different companies and grow her network. We together shortlisted our choice of event events, for which Gaurika drafted the cover letters and CV, on which Annette then gave feedback.

Gaurika got accepted to attend an exciting event at a company in fall and enjoyed it very much. She is now planning to apply for consulting positions at multiplce firms after submitting her PhD thesis. We are of course continuing to plan the next steps together and Annette will further support her in the application and interview process.

Talking honestly about career choices and the pros and cons of life as a consultant versus academia or industry but also comparing the advantages of different opportunities within consulting have proven helpful for both as a tandem. The program allowed Gaurika to get honest feedback, valuable insights, and a great mentor. It also allowed Annette to take a step back, to appreciate and share what she has learned and experienced but also to develop her own plan on things to change. In the end, sharing different perspectives, learning from each other and knowing there is someone who listens objectively and doesn't judge is an experience we both benefitted from.

Gaurika Garg is a final-year doctoral student under the supervision of Patrick Cramer at the MPI for Biophysical Chemistry.

Annette Denker completed her doctoral research in November 2011 under the supervision of Silvio Rizzoli at the European Neuroscience Institute Göttingen. After postdoctoral research at the Salk Institute for Biological Research, San Diego, USA and the Hubrecht Institute, Utrecht, Netherlands she joined Mc Kinsey & Company, where she currently works as Engagement Manager.

An opportunity to explore diverse career options

Oleh
After getting matched with Alice, I was quite surprised to learn that she joined the Molbio program just a year before me. Yet I have never met Alice before the Mentoring Program, because her career took her in a direction very different from that of most of the Molbios I knew. And this neatly illustrates the hallmark of the Mentorship Program – it allows the mentees to get mentorship from the alumni that explored a very diverse variety of career options.

The entire experience was greatly facilitated by the structured approach of the Mentoring Program. The introductory workshop provided useful insights about the possible frameworks for mentorship experience satisfying for all the parties involved. It was of course great to see the familiar faces of Molbios and Neuros at the introductory sessions and later – at the mentee meetups. The latter were great for sharing the experience about the mentorship, job search, and simply friendly banter. They were also a part of a very welcome slow return to in-person social life that was sorely missed in the preceding month of the pandemic.

The mentoring itself made me feel much more informed about the career path I am interested in. While I had opportunities to learn about this during the career or networking events, it is undeniably more effective to have at-length conversations about these matters. I got to better understand the aspects of transitioning from academia I did not give much thought to before and to hear a first-hand detailed account of what I would be signing up for. Alice was incredibly helpful with giving advice on the preparation for applying for jobs, recommending useful resources, and providing insight on what is important when applying, especially coming from academia.

Overall, at the end of the Mentoring Program I find myself far more confident about my next career steps. I can only wholeheartedly recommend the GGNB students to participate and am looking forward to hopefully returning in a few years as a mentor.

Alice
When I was approached to participate in the mentoring program, I thought back to the many considerations and open questions I had when choosing the right path for myself. Thus, it was quickly clear to me that I want to contribute my share to support a mentee in this crucial phase.

Due to Oleh's openness and interest in my experience both in consulting and industry, we covered a variety of aspects regarding the numerous differences between academia and industry. While I hope that our exchange was insightful for Oleh to make up his mind, also I appreciated the chance to reflect through Oleh's well thought-through questions.

Over the course of our conversations, we narrowed the focus more down towards the application for consulting jobs, discussing best practices and pitfalls regarding CV, covers letter and case interviews.

I truly hope my guidance will help Oleh on his path and wish him only the best!

Oleh Rymarenko completed his doctoral research in the group of Dirk Görlich at the Max Planck Institute for Biophysical Chemistry in June 2020, where he is still working as a postdoctoral research associate.

Alice Buchner graduated from the Molecular Biology MSc Program in 2015 before she moved directly into consultancy with Bain & Company. Currently, Alice works as Senior Manager Strategic Projects at Gilead Sciences in Munich.

Keep calm and have a mentoring session on zoom

Why I chose the mentoring program

In the final year of my PhD, I was facing a big question: What to do after my PhD? The usual dilemma occurred to me: Should I stay in academia, or should I go to industry? These are the kind of questions that can be potentially answered by you, but better with the right guidance from a carefully chosen mentor. Who could be an ideal mentor for me? Somebody who completed the PhD in the same scientific group as me, pursued a career in the Mass Spectrometry and gained research experience preferably in both academia and industry. Luckily, Kundan matched my selection criteria and when I read his profile, I was excited to have him as my mentor. Fortunately for me, he was very enthusiastic about the idea of guiding a fellow MolBio from the same lab as him and he was immediately on board.

How has it helped?

Soon we started having our regular monthly meetings via zoom and it felt that we were going to be a good match on every level. Even though some of our meetings were spontaneous, I was well-prepared before each meeting, already listing the topics and questions worth discussing at that point. Having an agenda gave a structure to our meetings, but we did not follow it blindly. Sometimes the discussion drifted into unexpected directions and Kundan helped me focus on the right topics. Indeed, guiding someone involves asking the right questions and he did that well.

The main topic of our meetings was whether to leave academia and make the jump to industry, and if yes, when was there a right time to do it? Kundan was just the right person to consult since he had gained research experience in both academia and industry. I learned that in academia there is a high degree of scientific freedom, but it entails an uncertainty in the long run as you are often not tenured. In addition, there is a pressure for publications to maintain your competitiveness and attract your own research funding. On the other hand, in industry you can enjoy stability with less uncertainties about the future. However, the degree of scientific freedom decreases as every biotech company is goal-oriented and for a starting scientist position it can be more repetitive and less exciting.

Another important factor that contributed to my decision-making was that a short post-doctoral experience can be very advantageous as you can broaden your technical skills and increase your chances of getting hired for a senior scientific position by a company. Given all the information I have been exposed to, I decided to maintain my flexibility and high degree of freedom that I very much enjoy in academia for the time being by pursuing a post-doc. My priorities might change with time and a move to industry is very likely in the future.

An additional important revelation that emerged from our conversations was how people see me in the research-based job market. As a biologist in a mass spectrometry group, I might be perceived either as someone who does not fit to hard-core biology labs or as someone who is not an expert on the technical aspects of MS. However, I could be an asset for those biology labs that have an extensive collaboration with Mass Spec facilities. I have now realized how people could perceive me and what they would expect from my CV.

What now?

I have narrowed down my options and identified the next steps for my scientific career. In the next two remaining months, we will focus on refining my CV and practicing some mock interviews. Even though the alumni mentoring program officially ends in March, my connection with Kundan will continue outside the context of the program. I was very happy when he encouraged me to contact him if I need any advice from him in the future. In my opinion being honest and open-minded with your mentor will help you get the most out of the alumni mentoring program.

Sofia Ainatzi is a third-year PhD student under the supervision of Henning Urlaub at the MPI for Biophysical Chemistry.

Kundan Sharma was also a Molbio PhD student in Henning Urlaub's group until his graduation in 2015. After postdocs in Göttingen and Oxford he is now a senior scientist at OMass Therapeutics.

Dreams coming true

What riding horses tells me about life

Which memory did you choose?
The first time I rode the broom.

Harry Potter and the Prisoner of Azkaban

I am writing this on 3 January 2022. I feel blissfully happy. I just had my first riding lesson this year, after a two-week break and two weeks is an awfully long time when you are used to riding 3-4 times a week. Am I an addict? Probably. But I give up. Or rather – I give in! After waiting a quarter of a century, I finally gave in to my lifelong dream of riding a horse and my life has never been better. Despite the pandemic, despite losing my job and building a new career in the meantime, once I let horses back into my life, things started working wonderfully for me.

Is this an obsession? A madness? A passion? All the above? Maybe. Ever since I can remember, my biggest dream was to ride a horse. That dream came true one day in winter when I went to a park in Moscow, not far from where I lived back then, and spent all my pocket money on my first ever ride through the forest. I still remember the horse's name – Agat. They asked me if I knew how to ride and I lied, I said yes. I was so scared they wouldn't let me join. I was 15 then and I still remember that first ride, with snow everywhere, no idea how to hold the reins or balance when galloping. I did not fall that day, beginner's luck.

Since then, I have used every opportunity to ride, and my favorite thing has been riding outside – there is nothing like a hearty gallop through open fields. That was back in my twenties, before I went to university and had to put my passion on hold. That hold lasted a quarter of a century. I knew it was there, waiting for me, but there was always something that interfered – no time, no money, not for me, – all the petty excuses that block our dreams. My dream was becoming more and more unreal, and I did not know how to approach it anymore. Until one day in summer 2019.

With Balckan, my half board lovely Henson horse I am fortunate to ride once a week

It was easier than I thought. I went to one of the riding clubs nearby and signed up for lessons. A colleague at work recommended The Equestrian Center at the Orsay University, and it felt like the right place to go. I barely spoke French and had forgotten everything I knew about horses, including how to ride them. I started again from zero, signing up for a beginner's class and it felt great to be a student again practicing my favorite sport.

I am often told that riding a horse should not be a big deal, it is the animal that does all the work while the rider just sits there. Yes, it might look that way, but this is far from being the case. When I finally got back in the saddle, I had to face the hard truth: I needed to learn everything again from scratch. It was not like riding a bike, it did not come back to me easily. I had to build up the muscles again and find the right balance. It was neither glamorous nor

First win in a team of two (80 cm, Club 2)

fun, it was very painful. I was no longer the age I was when I stopped riding. I had no idea all those muscles even existed, let alone were needed for riding. My instructor told me that there were 364 muscles in total for riding. But the most important thing for me was that my passion was still alive, I loved being back in the saddle and was prepared to do all it might take to learn how to ride properly.

"Drop your stirrups! Now, trot!" How? It's all bumpy and jumpy – how am I supposed to stay in that saddle? Riding the so-called sitting trot without stirrups is a much loathed, painful but essential

Dreams coming true (continued)

First competition (70 cm, Club 3)

exercise for anyone who wants to master riding skills. During this exercise, we let our bodies discover the posture that works best to maintain the balance. A good balance is essential not only for effortless riding but also for communication with the horse. A skilled rider conveys most commands to the horse by shifting his or her body axis. These commands are usually invisible to the outside observer who may wonder how the horse knows what to do.

My favorite discipline is show jumping. There is a basic rule to it: never look down at the obstacle. Although being aware of its position and estimating the number of strides and speed is important, it is essential to focus on a point behind the obstacle. One of the interesting discoveries I made when jumping over the barriers is that the horse can sense my hesitation. The best jumps turned out to be those I was confident of achieving, while having a plan for what was coming next – a turn, a stop, another jump. It feels like magic – an invisible force that carries me over a barrier that may look impossible to master at first glance. Sometimes I use this principle in difficult life situations. I make a plan and set my sights beyond the challenge as though it was already over. Never look down!

"Arrêt!" (French for "Stop!"). Someone is on the ground. I had often seen other girls fall. This happens when a horse gets spooked or too excited or when an obstacle jump goes wrong. That won't happen to me, I thought – until I was thrown off myself one day. And then again. And again. As classes became more advanced and I was allowed to mount stronger, less docile horses, occasional falls are inevitable. Fear crept in. That was not pleasant. It was totally new to me, since I had never felt such fear before. Excitement before jumping an obstacle – yes. But never fear. A primal, spline-tingling fear that made my body rigid. The horses sense it, and my job is to use that fear productively.

It has been a little over two years and about 200 riding hours since I have been back in the saddle. A life-changing experience, which has made me feel stronger in so many ways. Riding horses is a multidimensional process. We must learn how to communicate and cooperate with different animals, each with its own character and whims. We need to be patient and persistent. If something has not worked today, it will work tomorrow, or the day after, just keep on trying. We learn how to overcome our own fears and insecurities and tap into inner reserves of strength and energy. In my case, I learned some French as well, an added bonus. Last summer I was fortunate enough to take part in competitions, still internally because of the world health situation. This year, I look forward to my first ever external competition. A new challenge to embrace!

Elena Kardash completed her doctoral research in 2008 in the group of Erez Raz at the MPI for Biophysical Chemistry. After positions as postdoctoral researcher at various institutes (ZMBE, Münster, Milano University, University of Geneva, CNRS at Gif sur Yvette), Elena started as freelance scientific editor for Cactus Communications in summer 2021.

Life in the new normal

In contrast to the 2019/2020 batch – which was still able to experience the first part of the program without any COVID related issues – and the 2020/2021 batch – which truly got the full pandemic reality – we can be seen as the hybrid batch, experiencing several ups and downs and a society that to some extent got used to live with this pandemic.

Accordingly, our very first activity as proud Molbio newcomers, the annual conference "Horizons in Molecular Biology", was a hybrid one. Like in 2020, the conference itself was organized online, but due to the engagement of our program coordinators, Steffen and Kerstin, most of us were able to follow the contributions together in a big lecture hall. This meant that despite the hygiene and distance regulations, we still had the chance to meet in person and get to know each other.

With those first acquaintances, we were looking forward to our orientation week, which besides organisational issues, also offered activities like the guided city tour, where even people who already knew Göttingen learned a lot about the city. We also learned a lot in the intensive German courses, even if German revealed itself as a quite difficult language. Nevertheless, we had fun undertaking the offline, intensive German course and later practicing the basics with our German peers! The grand finale of the orientation weeks was our hike to the Hotel Beckmann, where a beautiful sunset, delicious food and brilliant company rewarded us for our efforts.

Orientation weeks: Hike around Nikolausberg with panorama dinner

Soccer game Molbio *versus* Neuro

Hanging out with the Molbio seniors at Schillerwiesen

Soon after the successful start, we had found our new normal for the pandemic. Because we were all vaccinated (some of us even 4 times!), we were lucky to have most classes in person at the Ludwig Prandtl Hall. Like many of the lecturers commented, we were happy to finally meet and have lectures in person. Although socially distanced, we were able to interact more closely and form friendships in the small-group methods courses. The methods courses also taught us about so many different topics and provided us with a glimpse into the diverse labs participating in our program. Even seemingly mundane experiences like occupying more than half the bus up the hill to our lectures in the mornings and scheduling or running to our weekly covid PCR tests helped us build community.

But of course, we were not studying ALL the time. In fact, we were able to attend a number of events, which provided us opportunities to interact with people outside the program. The soccer game we organized with our Neuro batchmates brought out the competitive spirit in each of us. Even though the Neuros won by a landslide (we vowed to defeat them next time!), we were still grateful that the event brought us closer together. We also had the chance to hang out with our seniors at the Schillerwiesen Park, where they shared their experiences in the program and imparted some helpful tips to our batch over some pizza and beer.

Although the COVID situation was not getting any better, we didn't let that ruin our holiday spirits. We organized a holiday baking event – ensuring that

Life in the new normal (continued)

everyone attending was fully vaccinated and tested negative – where we made different kinds of cookies that could easily fill up our stomachs ten times over. Lastly, who can forget the time when we rushed to the Christmas Market after our methods course? It's moments like this, when you're holding a hot mug of Glühwein while being surrounded by people you consider as your second family away from home, that makes each one of us thankful and gives us an optimistic outlook that maybe things will get better after all.

In times as unsteady as today, the multifaceted support of the program is more valuable than ever. Steffen and Kerstin have supported us at each step – from arranging arrival transport during unexpected Deutsche Bahn strikes, to keeping us updated about the minutest changes in schedules and regulations. We, the Molbios, have also always been there for each other, be it locating missing student ID cards, helping find things in the city, or caring for unwell classmates.

Looking back in time, being a part of this program has struck a different chord in each of our hearts: for some it has strengthened the inner spirit with newfound independence, while for some it dissolved past worries of "fitting in" into a diverse class. We are grateful that this year's hybrid program enabled us to bond with each other and form new friendships. Although the uncertain clouds of COVID never seem to leave room for clear skies, we still look forward to the dawn of a new year filled with opportunities to learn and grow in a global, extended family!

Svenja Ahlmann, Joseph Neos Cruz,
Neringa Liutikaite, Saruby Sharma

Celebrating Maria's birthday at Kiessee

Baking christmas cookies

Göttingen Christmas Market

Group photo before the Christmas break

The light through the tunnel

Featuring the first ever Molbio MSc retreat in Goslar

Five months after I started my master's degree, I finally arrived to Göttingen! One of the biggest fears going on my mind then was how I will develop friendships with my colleagues when I arrived in the middle of a pandemic. During the first few months, Germany had a nationwide lockdown. Moreover, we could not plan any culture nights as the ones that were possible before the pandemic for bonding between the students. Thinking that I would have had to do a lot of effort to initiate conversations with people from different backgrounds, I am really glad that I was wrong about that. One by one, my batch mates invited me out, while checking the regulations every day. We tried to tackle our year of lectures, tutorials and lab rotations while getting to know each other in some very innovative ways such as small meetings in front of lakes, in the forest, or any open area one could think of.

The Molbio MSc class of 2020/21 at the MSc retreat in Goslar

Through the darkness of the pandemic, our friendships glowed like candles that kept on getting stronger, until they lightened up the way ahead. We supported each other in the times before our final exam, until finally, all of us passed our master's examinations with great grades! The Molbio office wanted to help us celebrate our success, thus we had the chance to go on the first ever Molbio master's students retreat! The beautiful city of Goslar was chosen as our destination!

A city of breathtaking beauty on the slopes of the Harz mountain, Goslar is a small town in Lower Saxony. Having two UNESCO World Heritage sites, the Old Town and the Rammelsberg mining museum, Goslar is very rich in its cultural and historic background. On our first day right after arrival, we had a very nice guided city tour. Although it was rainy and we were not fully prepared for the cold weather, we decided to fully indulge in the German culture, and as the German saying goes "Wir sind ja nicht aus Zucker", or "We are not made of sugar" in English, whoever had an umbrella and/or extra jackets shared it with everyone else and we continued our tour, enjoying to the highest extent the weather can let us.

The mesmerizing Old Town of Goslar has many of those crooked, narrow, and cobblestone streets that take you to another century. We visited many landmarks including the Siemens family house which was built in 1693. This beautiful mansion was well-preserved and it was both the residency of the family and its business location. It had a beer brewing room that took us way back, where people in another century gathered and enjoyed their time together. In the market square if one stands close to the cen-

The light through the tunnel (continued)

tral fountain that has the largest bronze cast from the Romanesque period, one could hear right at noon the carillon bells and observe the beautiful short show of the figures that tell the story of Rammelsberg mining from its discovery to modern times. After our tour, we went back to the hotel where we had lunch and started to present our third lab rotation projects to our peers. We engaged in an interesting conversation concerning our findings and our progress. In the evening, we had a social gathering where we finally celebrated the success of our master's studies completion.

The next morning, we started our day with a trip to the World Heritage Rammelsberg Mining Museum right after breakfast. Walking in a tunnel with rough walls literally in the depths of a mountain, one could only imagine how thrilling the experience was. Although it was a bit dark and cold, we were very interested in witnessing and understanding the mechanics behind mining. We were walking through the same path the water needed to power different operations flowed. Through our journey, we could see the different phases of modernization, where at some point only wooden pulleys and swings were used and at another metal mechanical equipments were also incorporated. Learning about the work of miners, we could really appreciate how hard it was for them. It was fascinating to see some of the metals shining in the walls and, as scientists, it was also fascinating how time and humidity can add a lot of further details to the life in these same walls.

Along our time inside of the tunnels, I realized something very sweet: while going up and down different steps and stairs, we were always offering help to each other and we kept giving each other reassuring words and this made me think about my bigger journey until now in Germany. The friendships that evolved throughout this year, throughout all the hardships that happened, while pursuing one of the most challenging master's programs in Germany in the middle of a pandemic, were only possible because we provided a strong support network for each other.

I always heard from older batches that some of the greatest gifts this program offers us are the connections and the networks one can form with other Molbios, and after more than one year spent in the program, I completely agree! And it's even more wonderful when these connections turn into beautiful friendships.

Visit of the UNESCO World Cultural Heritage Rammelsberg Mining Museum

Monica Gobran from Egypt is a Molbio MSc student of the 2020/21 class. Because of COVID-19-related delays of her visa she could join her classmates in Göttingen only at the end of January 2021.

MSc double graduation and commencement

The graduation of MolBio master students and the simultaneous welcoming of the new batch is usually one of the central and most anticipated events of each MolBio year. Unfortunately, the ongoing Covid-19 pandemic had prevented this beloved celebration from happening last year, leaving my batch (class of 2018) without a proper graduation. Luckily, with available vaccinations and testing services as well as incredible organizational effort from Kerstin and Steffen, the event could finally take place in October 2021.

The Molbio MSc graduates of the 2019/20 class

In the meantime, the class of 2019 had also finished their master's projects leading to the first-ever double graduation event in MolBio history. Despite several travel-related problems like an old World War II bomb being defused in Göttingen, students having moved to different countries, and of course, the ever-present pandemic, the vast majority of us made it back to the city where our MolBio journey began. This clearly showed how much everyone was looking forward to meeting their friends again and that MolBios are not just a bunch of students but a family.

Two generations of MSc graduates together with the Molbio newcomers, family and friends

The event kicked off with a warm introductory speech by program spokesperson Prof. Marina Rodnina who welcomed all graduates as well as the next generation of MolBios. Initial technical problems forcing Prof. Rodnina to use her best improvisation skills also could not stop us from streaming the event to a larger audience, including many family members and friends who could not attend in person.

MSc graduation speech by the student representatives Frederike and Marcel

Next, we as the student representatives of the 2018 and 2019 classes took everyone on a ride to relive the best memories of the past years, along with many entertaining stories and hilarious pictures. While the technical problems had been finally fixed, the flower shop also seemed to have conspired against us, leading to a lack and subsequent recycling of bouquets during the handover of graduation certificates.

A highlight of the evening was a joint musical performance by members of the 2018 and 2019 classes featuring Aybeg, Rohan, and Jannis. They introduced us to an amazing oriental love song, teaching us about love and suf-

MSc double graduation and commencement (continued)

fering, something quite closely resembling our enthusiasm and struggles with science itself.

Afterwards, the newly arrived students of 2021 had the opportunity to introduce themselves, wishing all the best to the graduates, and looking forward to joining and connecting with the MolBio community. The ensuing, small speech by newcomers Svenja and Zahra took a beautiful approach on recapitulating the MolBio journey with biology itself - the newcomers are now starting as unfolded peptide chains hoping to become fully folded proteins like us graduates. As with every journey, the people helping us along the way are the most important ones. Our chaperones like Steffen, Kerstin, and many faculty members who ensure the correct folding through their invaluable support, made and will make this maturation process a great experience for all students.

The Molbio newcomers - commencement speech by Zahra and Svenja

Following the ceremonial part of the evening, a wonderful reception by the MPI-BPC canteen team greatly satisfied the small hunger after the event and allowed us to catch up with each other and meet the next generation of students. Numerous stories were shared, and a lot of pictures were taken.

Nevertheless, this was not yet the end of the evening. Many culture nights of the past decades have established that MolBios certainly know how to party and many of us missed these amazing events dearly over the past two years. Trying to revive this spirit as much as possible, we decided to organize a small after-party. After the events at MPI-BPC, most attendees joined us for a Covid-19-adapted party at Bar Celona, allowing us to celebrate old times, our success, and many more great years to come.

Marcel Werner, Frederike Maaß

Musical perfomance by Jannis (piano), Aybeg (vocals) and Rohan (sithar)

MolBio PhD Retreat at last!

2020 was the year of cancelled meetings, and 2021 was the year of online meetings. There is a certain joy in attending lab meetings and conferences at the comfort of your house. But staring at a fixed grid of floating muted heads can become tiresome very easily.

So, it was no surprise that Steffen's plans to organize the next PhD retreat in-person came like a breath of fresh air. It is without doubt that such retreats are much anticipated by the PhD students as they combine exceptional science with career planning and fun social activities. It had also been what felt like ages since we had a culture night and the Molbios got to know each other in a relaxed setting. Everyone was thrilled that we could experience such an event again!

The first-ever Molbio PhD In-house Retreat fills the Manfred-Eigen Lecture Hall

Poster session at the end of Day 1

Due to the ever-changing nature of pandemic, we decided that the retreat would take place in Göttingen. Now came the planning of the retreat. This task came naturally to us with the training from the organization of Horizons symposia in the past. The acquired skills immediately re-awakened: schedule of the speakers and the poster session, arrangement of the coffee and lunch breaks, brainstorming on social activities… and of course having a great time. Steffen arranged a brilliant line-up of alumni speakers with diverse careers in academia, industry, science communication, management, and entrepreneurship. After fruitful meetings of the organization team, we managed to create a promising plan: almost 60 participants, 16 of which would give an oral presentation and 13 would present a poster during the poster session. Surprisingly, except the usual scientific projects, we were excited to welcome an interesting venture by the MSc student Camilo Torres to present his dueling card-game inspired by the battle between humans and pathogens during infection.

Despite the overall motivation, we did not forget to comply with the ongoing regulations concerning the Covid-19 pandemic: all participants were fully vaccinated or recovered (2G rule) and tested negative from the Campus-Covid-Screening, a collaborative attempt of the University and the Max Planck Institutes. Therefore, this double-sieve status was the entry ticket to the retreat for all the participants, without exception. With a tight control of the safety and organization, we looked forward to the retreat!

Day 1: The morning of the first day was spent in joy and excitement! Setting up the poster holders, printing signs and schedules, arranging the technical setup and welcoming participants and alumni at the venue reminded us of the good old days when we organized the Horizons symposium. The retreat started shortly after noon. The first day was entirely devoted to PhD project presentations and the poster session. Exciting PhD projects were presented, spanning from structural biology to biochemistry and cell biology (many of which have already been published in scientific journals), and were accompanied by constructive

Molbio PhD Retreat at last! (continued)

questions and discussion from the audience. Despite it being the first time for many of us to present in front of a large audience in person, all the talks were very engaging.

In the evening, the poster session continued at the same joyful vibe with two hours of vivid discussions around 13 interesting posters of cutting-edge research. The impromptu discussions ebbed and flowed into dinner time. Apart from the tasty (and free) dinner, catching up with old friends and meeting new ones was the highlight of the dinner. The advent of virtual meetings has chewed off the fun social aspects of doing science. So we tried our best to transform the evening into a mini culture night of its own. There was groovy music, people dancing and of course a splendid cocktail bar with our Molbio mixologist Valentyn. Kicker and Flunkyball also helped break the ice between the Molbio batches. Later in the night Rohan and Aybeg gave a captivating musical performance fusing Indian, Persian and Turkish cultures. A truly spellbinding night!

Musical performance by Rohan (left) and Aybeg

Kicker contest

Day 2: The second day included more talks by PhD students but also talks by alumni of the program. Sinem Saka (EMBL), Koray Kirli (DKFZ), Mandy Hanemann (Octapharma Biopharmaceuticals), Victor Bustos (Apollo Health Ventures) and Manuel Maidorn (MPI-DS). They unveiled their individual professional pathways into academia, industry, entrepreneurship and science communication. Later during the speed dating sessions, the PhD students had the chance to further dig into details of the pathways of their interest. All the alumni were very frank and friendly which made career planning seem less daunting. They gave honest and valuable advice on how to maximize our opportunities and find the right job for us.

Putting it all together, the first in-house PhD retreat after the Covid-19 outbreak was an unrivalled success. Despite the restrictions and necessary precautions that had to be taken under consideration, the quality of the retreat was not even slightly compromised. For this, we are grateful, first and foremost, to Steffen and Kerstin who initiated it, despite the challenges that constantly emerge for the MSc and PhD students. We would also like to thank all the organizers, participants, and alumni that complied responsibly with the regulations and engaged into making this event memorable. Without the interesting talks and the social bonding that characterizes the Molbio students throughout generations, this event would not have met the expectations. On that note, we hope that in-person meetings would be possible and the Molbio PhD retreats will once again become the event to look forward to each year!

Round-table discussions with Molbio alumni Manuel, Sinem and Victor. Two other round tables in parallel with Koray and Mandy.

Panagiotis Poulis, Ninadini Sharma

Ninadini Sharma and Panagiotis Poulis are PhD students at the MPI for Biophysical Chemistry under the supervision of Melina Schuh (Ninadini) and Marina Rodnina / Sarah Adio (Panagiotis).

My PhD research a bottomless pit?

Report on a new Molbio pilot project on stress prevention

Have you recently asked your PhD students whether they are happy with the progress of their research? No doubt you did. Have you received a polite answer that everything seems to be okay and only a few issues should be discussed to keep the project on track? Would you expect the same answer when your PhD students meet with an external coach in a confidential meeting?

A recent survey with an emphasis on satisfaction of PhD students with their situation as a doctoral researcher, launched by a group of GGNB students, revealed that despite a general appreciation of their PhD supervision, about one fourth of the survey participants indicated that they had not enough time to recover from work, foster non-scientific interests or have enough time for friends, family or themselves. The open discussion round with Molbio and Neuro students during our Internal Quality Review (internal accreditation) last summer pointed in the same direction, but is it not a challenge for all of us working in demanding jobs, you could ask.

When talking to their PhD supervisors, many students tend to pretend that everything is under control, while many supervisors tend to look back on a rather positively colored and slightly idealized picture of their own doctorate – the time before the "real" hard work, coming with additional responsibilities at an advanced stage of their scientific career, made life more challenging. But in hindsight we always seem wiser don't we? What we may underestimate, however, is how easily vaguely defined milestones or expectations leave some students with the feeling that they never do enough while being on a continuously accelerating hamster wheel.

Source: iStock

The work environment of PhDs is characterized by a strong performance orientation under competitive pressure, no matter how well team work and a social network is established in the lab. The lack of regular social events and scientific interaction at conferences, retreats, culture nights or other events during the pandemic has certainly added to this challenge. In addition, there is the frequent frustration unfortunately common in scientific research due to sometimes less successful experiments or mistakes when following novel avenues. Consequently, mental health issues are widespread among academics but, fortunately, more openly discussed since a few years, which is definitely a big step forward, however certainly not enough.

To what extent should a graduate program respond and support its students? What would be the right measures? Apparently, supervisors and TAC members should offer help and have an open eye and ear for these problems. If it comes to mental health issues, however, PIs are not supposed to be intrusive in the personal feelings of students. Nevertheless, most faculty member would agree that the PhD students should certainly feel invited to approach their PIs/TAC members in case of problems. The GAUSS website offers an up-to-date overview of contacts recommended for critical situations and mental health issues, also pointing to established services of the Psychosoziale Beratungsstelle of the Studentenwerk and the Psychotherapeutische Ambulanz für Studierende of the UMG. Over the past two years, GAUSS/GGNB has expanded its course program significantly towards workshops on resilience and mental health issues and there are more to come. Other service/support measures such as the "Employee and Manager Assistance Program" of the Max Planck Society (an external, anonymous and free service by the Fürstenberg Institute available to all IMPRS students) have evolved as well. Moreover, it seems obvious that stress prevention and personal counseling should provide valuable support to manage the hurdles on the ways to your PhD.

To address this important topic, the Molbio program started a pilot project in fall 2021, inviting all its PhD students to individual coaching sessions with an occupational psychologist. Thanks to the invaluable logistic support by the MPI for Biophysical Chemistry and the dedicated commitment by two psychologist, these preventive stress check-ups took place in December 2021. Preceded by a short online questionnaire testing work-related behavior and experience patterns, the coaching sessions aimed at

My research a bottomless pit? (continued)

reflecting on the personal work-related stress level, discussing possible preventive measures, which could be applied, and thus strengthening the personal recovery skills of the students. For this first round, 26 out of 52 Molbio PhD students have signed up. The interest was highest in the first year (67%) and second year (58%) of their PhD compared to 50% in the third year and only 17% in the fourth (and final) year".

What have we learned from this pilot project on stress prevention so far? According to a general summary from the two psychologists, the feedback of the advised PhD students at the end of the individual sessions was overall very positive, appreciating the opportunity to discuss their personal challenges with an independent professional expert. Many student stated that the counseling helped them to gain new insights and were confident that their situation will improve as a result of the measures discussed in the coaching sessions. A common theme of these confidential meetings appeared to be frustration caused by high motivation and expectations of success on the one hand, and on the other hand disregarding external factors such as luck or fortunate timing highly influencing the outcome. Experimental failures are often interpreted as caused by a lack of own effort. Long working hours of experienced scientists or other PhDs at the institute are interpreted as an expectation of one's own presence.

Although many offers to support PhDs already exist or are planned, the psychologists recommended continuing to focus more on counteracting this self-overload, building resilience and promoting mutual social support. Regular constructive feedback, also pointing out how common failures and setbacks in research are, may take out some of the perceived pressure. Mentoring, a buddy program and stress management program, as well as social and scientific networking events, can be equally helpful as increased leisure activities, apparently combined with sufficient time to rest.

Source: iStock

This pilot project will be carefully evaluated in the upcoming weeks with respect to the perceived benefit for the students, possible adjustments and recommended follow-up measures.

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Extension of the IMPRS for Genome Science approved

When the International Max Planck Research School for Genome Science (IMPRS-GS) was established in 2017, it secured funding until December 2022 by the Max Planck Society. The aims of the IMPRS-GS are to train doctoral researchers in experimental and computational genome science and to establish and strengthen the growing area of genome science that had been underrepresented at Göttingen. The program was also established to facilitate collaborative research projects that rely on cutting-edge techniques from both experimental and computational disciplines. Another aim is to increase the international visibility of Göttingen in this dynamic field and enable the recruitment of excellent students from all over the world.

In spring 2021 the school applied for a further six years of funding and underwent an evaluation process with four external experts. Due to COVID-19 restrictions the evaluation took place as an online event. Based on the very positive external evaluation, the IMPRS Evaluation and Selection Committee of the Max Planck Society and the German Rectors' Conference decided to continue funding of the IMPRS-GS for another six years until the end of 2028. Congratulations!

The Journey towards Horizons…

Planning for the 18th Horizons in Molecular Biology to be held in September 2021 began immediately after the successful completion of the 17th Horizons, which was held online. We began on a particularly optimistic note, with discussions of hosting the first ever Hybrid Horizons. However, as Germany entered a lockdown in December, which would continue till the middle of 2021, our plans grew and shifted towards an online conference with a promise of increasing participation and interaction between our invited guests and the attending students and researchers. Towards this goal, we hunted for online platforms which would combine practicality and convenience with an interactive atmosphere. We chose to continue streaming the talks on Big Marker and used Gather.Town as a virtual conference space to hold interactive poster sessions and allow for participant interaction. As September rolled in, we were ready with our online platforms and were also able to arrange for in-person screening under 3G rules in the Manfred Eigen Lecture Hall for people from MPI-BPC and the IMPRS students, especially the newbie MolBios!

The Horizons 2021 organizing team

The 18th Horizons in Molecular Biology, a 4-day conference organized by PhD students of the IMPRS Molecular Biology program, began on the 13th of September 2021 with the Career Fair. Our invited speakers came from a wide variety of non-academic science-related careers to share their experience and advice. We had researchers from industry join us to discuss their job profiles and individual scientific journeys, as well as people from non – academic fields like science communication and science policy. Elizabeth Steib, Head of Text and Research at Kurzgesagt, the much loved science communication channel on Youtube, gave a much anticipated talk and shared with us not only all the work which goes into their beautiful and engaging videos, but also her passion for taking science directly to people. Adam Ruben, a writer, comedian, storyteller, and molecular biologist, joined us from the USA and gave a very engaging talk full of anecdotes and personal stories on "alternative science careers". The Career Fair also included speed dating sessions for participants to get specific answers and advice, as well as workshops to help improve their communication and presentation skills.

The academic talks were kicked off by our keynote speaker and Nobel laureate, Christiane Nüsslein-Volhard. The invited speakers covered a wide array of topics including developmental biology, biotechnology, structural biology, bioinformatics, epigenetics, and cell biology. Beyond presenting novel research and cutting edge scientific tools, our speakers also had humorous moments and stories to share. Oded Rechavi's story of the PhD student brave enough to freeze *C. elegans*, and the wonderful clip of a Cephalopod shared by Joshua Rosenthal come to mind. The conference also gave a platform for talented PhD students to share their research. Awarded students included MolBio Valentyn Petrychenko from MPI-BPC, Vaithish Velazhahan from the MRC-LMB at the Universi-

Organizers on site during the online meeting

The Journey towards Horizons… (continued)

ty of Cambridge, and David Wiener from the Weizmann Institute in Israel. The panel discussion held this year tackled the "Growing Rift between Science and Society", a topic of great importance, especially against the backdrop of the COVID-19 pandemic. The fruitful discussion had the moderators and panelists share their thoughts and experiences as perspectives of people on both side of the information wall, and lead to a debate on how to tackle such problems in the future as young researchers.

The 18th Horizons saw participation of over 900 people from across the globe. Our mission to continue to uphold the tradition of providing a relaxed background for scientific exchange between established PIs and young researchers was greatly helped by utilizing Gather.Town as a virtual conference space. The poster session allowed people to communicate with the presenters in small, mobile groups to keep the spirit of the presentation alive. Some speakers also joined the organizers for an informal get-together which lead to a wonderful discussion on various hot topics, including COVID-19 and the rise of preprints. A similar event also took place for all the participants on Gather.Town where they could interact with the organizers and each other, discuss their thoughts and also play games with each other! We were also able to have a wonderful in-person IMPRS 2G - get together at Café & Bar Celona after the Horizons closing ceremony!

Despite some technical setbacks, Horizons was met with overall positive feedback and ended on a cheerful note. The triumphant conclusion quickly gave way to the preparations for the 19th Horizons in Molecular Biology, which are already underway! Confirmed speakers for next year include Marieke Oudelaar, Cassandra Extravour, Olivier Duss, Dimple Notani, Alexey Amunts, Luca Scorrano, Tom Rapoport, Tamal Das, Sonja Lorenz, Shiv Pillai, Kushagra Bansal, Maytal Landau and Chris Proud. Stay tuned to know who all will join us for the Career Fair and the workshops – all information will be updated on our website www.horizons-molbio.de. The organizing team looks forward to seeing you at the 19th Horizons in Molecular Biology which will be held from 12th – 15th September, 2022 at Göttingen!

Naintara Jain

In-person screening under 3G rules in the Manfred Eigen Lecture Hall

Horizons speakers 2021

Anna Akhmanova, Buzz Baum, Ron Diskin, Benjamin Engel, Casey Greene, Thomas Helleday, Kalina Hristova, Anthony Hyman, Grant Jensen, Thomas Langer, Ravi Manjithaya, Christiane Nüsslein-Volhard, Andrea Pauli, Ana Pombo, Oded Rechavi, Pamela Ronald, Joshua Rosenthal, Thomas Schwarz, Iva Tolic, Vidita Vaidya, Jessica Whited

New Faculty

Joining the program in 2021

Hauke Hillen pursued his doctoral studies at the Gene Center of the Ludwig-Maximilians-Universität München after he completed his studies of biochemistry at the University of Tübingen and the University of California, Berkeley, USA. Soon after, he started as project leader at the Max Planck Institute for Biophysical Chemistry (MPI-bpc). In 2020, Hauke was appointed W1 (tenure track W2) professor of protein biochemistry at the University Medical Center Göttingen and became an Independent Research Group Leader at the MPI-bpc). The research of Hauke's group aims at understanding the structure and function of molecular machineries in eukaryotic cells and organelles. For this, they combine structural biology methods such as single-particle cryo-electron microscopy, X-Ray crystallography and cryo-electron tomography with biochemical and biophysical approaches to unravel the mechanistic basis of cellular processes. As a new faculty member of the Molecular Biology program, Hauke contributes to the Master's curriculum with a lecture on DNA structure. In addition, Hauke is supervising Molbio PhD students and his group offers lab rotation projects.

https://www.uni-goettingen.de/en/640183.html

Sonja Lorenz received her doctoral degree from the University of Oxford in 2008. From 2009 to 2014, she joined the lab of John Kuriyan at the University of California, Berkeley as a Career Development Fellow and Research Associate. In the following years, Sonja worked as an Emmy Noether Group Leader at the Rudolf Virchow Center for Experimental Biomedicine of the University of Würzburg. Sonja joined the Molecular Biology Program in 2021 when she became an Independent Group Leader at the MPI for Biophysical Chemistry. The major research interest of Sonja's group are (1) catalysis, specificity, and conformational dynamics of the ubiquitination machinery, (2) the function of ubiquitin ligases in neurodevelopmental and infectious diseases and (3) therapeutic exploitation of ubiquitination enzymes. In particular, her group identifies, reconstitutes, and structurally characterizes macromolecular complexes of ubiquitination enzymes to reveal how these assemblies encode substrate and linkage specificity in ubiquitin chain formation. Experimentally, they combine the entire spectrum of high-resolution structural techniques (cryo-electron microscopy, X-ray crystallography, and NMR) with chemical biology-based crosslinking, biophysical, and cell biological techniques. As a new Molbio faculty member Sonja will teach an MSc methods course on proteins and takes over the lecture on ubiquitin.

https://www.uni-goettingen.de/en/644758.html

Current faculty members (University of Göttingen and UMG)

Biology
Sarah Adio, Gerhard Braus, Rolf Daniel, Ivo Feußner, Ralf Ficner, Christiane Gatz, Ufuk Günesdogan, Kai Heimel, Wilfried Kramer, Heike Krebber, Volker Lipka, Burkhard Morgenstern, Stefanie Pöggeler, Jörg Stülke, Kai Tittmann, Marcel Wiermer, Ernst Wimmer

Chemistry
Andreas Janshoff, Claudia Steinem

Physics
Jörg Enderlein, Dieter Klopfenstein

Agricultural Sciences
Bertram Brenig

Medicine
Mathias Bähr, Holger Bastians, Tim Beißbarth, Markus Bohnsack, Matthias Dobbelstein, André Fischer, Uwe Groß, Heidi Hahn, Hauke Hillen, Stefan Jakobs, Tobias Moser, Argyris Papantonis, Peter Rehling, Silvio Rizzoli, Michael Thumm, Henning Urlaub, Jürgen Wienands

Leaving the program in 2021

Till Ischebeck joined the Molecular Biology Program in 2020. At that time, he had already been involved in practical training of and supervision of Molbio MSc students in methods courses and lab rotations. Under his supervision, Franziska Kretzschmar successfully completed her doctoral research in the Molecular Biology Program with a summa cum laude distinction and a very good publication record. The research of Till's group focused on four partly interconnected topics: plant lipid droplets (also referred to as oil bodies or oleosomes), pollen development and pollen tube growth, analytics of small metabolites, and plant-pathogen interactions. The main model organisms for their research were *Arabidopsis thaliana* and *Nicotiana tabacum*, but they also examined less well-studied plants such as tiger nuts (*Cyperus esculentus*, also called earth almond). Their methodological spectrum ranged from molecular biology (e.g. CRISPR/Cas9), over cell biology (e.g. confocal laser scanning microscopy) to biochemistry (e.g. LC/MS-based proteomics) and bioanalytics (e.g. GC-MS, GC-FID). In 2021, Till was appointed as a Heisenberg Professor at the University of Münster, Institute of Biology and Biotechnology of Plants. We thank him very much for his contributions and dedicated support of the Molecular Biology Program and wish him all the best for his new position.

Michael Meinecke supervised Daryna Tarasenko, who graduated in February 2019, as Molbio PhD student already during his time as an independent group leader. In 2017, he was appointed as professor of membrane biochemistry at the Department of Cellular Biochemistry at the University Medical Center Göttingen. In October 2019, Barbora Knotkova joined his group as another PhD student. Michael's group studied the effects that membrane proteins have on membrane structures. They are also interested in the effects different membrane morphologies have on the distribution and localization of membrane proteins into clusters and microdomains. Taking a multidisciplinary approach, his group uses model membranes to reconstitute the structure and function of organelles in vitro and then correlate these results with *in vivo* imaging techniques. They are particularly interested in ion-channels and apply biochemical and biophysical approaches to study the function and regulation of ion-channels on a single molecule level. As a Molbio faculty member Michael took over the lectures on posttranslational modification and biological membranes, previously taught by Blanche Schwappach. In 2021, Michael accepted an offer by the Heidelberg University Biochemistry Center as Professor for Biochemistry and Molecular Cell Biology. The Molecular Biology Program is grateful for his support of training and supervising our students and wishes him a great start at the new research institute.

Current faculty members (Non-university institutions)

Max Planck Institute for Multidisciplinary Sciences
Sarah Adio, Nils Brose, Patrick Cramer, Alexis Faesen, Dirk Görlich, Christian Griesinger, Helmut Grubmüller, Stefan Hell, Hauke Hillen, Reinhard Jahn, Stefan Jakobs, Peter Lénárt, Sonja Lorenz, Reinhard Lührmann, Klaus-Armin Nave, Marieke Oudelaar, Marina Rodnina, Jochen Rink, Melina Schuh, Johannes Söding, Holger Stark, Alexander Stein, Henning Urlaub

German Primate Center
Rüdiger Behr, Stefan Pöhlmann, Lutz Walter

SAB Visit of the GGNB

In December 2021 the Scientific Advisory Board (SAB) of the Göttingen Graduate Center for Neurosciences, Biophysics, and Molecular Biosciences (GGNB) came for a visit – a virtual visit via Zoom to our regret, as the pandemic didn't allow for a site visit.

As a consequence, the regular format of combining the SAB visit with our GGNB Science Day (scientific keynote, featured students talks or science slam, posters by all advanced GGNB doctoral students) couldn't take place. Nevertheless, our written report to the SAB was extensively discussed with the SAB members in a general meeting open to all GGNB members, as well as in separate closed sessions with the GGNB PhD representatives and the GGNB faculty members. To conclude the visit, the SAB members met with Vice President Brümmer and the GGNB Board to discuss open questions and give detailed feedback on their impressions and recommendations. A written report by the SAB to the President and the GGNB Board is expected soon.

The feedback by the SAB was very positive, highlighting the successful consolidation of the GGNB under the umbrella of GAUSS, the dedicated student-organized events and initiatives, the achievements of the Career Service, and the way how the GGNB managed to cope with the pandemic.

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Current profession and location of our Molbio PhD alumni

Profession

Academia / Research (49%)
Professor, PI, academic staff 7%
Group leader, senior scientist 10%
Postdoc 32%
Science management 1%
Other 1%

Private & Public Sector (40%)
Scientist, team leader, manager R&D 19%
Staff, team leader, manager non-R&D 12%
Science manager/coordinator 4%
Consulting 6%

Other Profession (8%)
Media, publishing 4%
Patent attorney 2%
IT, software development 1%
Self employment 2%

Other (2%)
Other professions, internships, job applications, family management etc. 2%

Country Distribution

Europe (78%)
Austria 2%
Belgium 1%
France 1%
Germany 57%
Luxembourg 1%
Malta 1%
Netherlands 2%
Norway 1%
Poland 2%
Spain 1%
Sweden 1%
Switzerland 5%
Turkey 1%
United Kingdom 5%

North America (16%)
Canada 3%
United States 13%

Asia / Australia (6%)
Australia 1%
China 1%
India 2%
Iran 1%
Qatar 1%
Saudi Arabia 1%
Singapore 1%

Max Planck fusion

The Max Planck Institutes for Biophysical Chemistry and Experimental Medicine have merged as of January 2022. The newly estalished Max Planck Institute for Multidisciplinary Sciences will be the largest institute in the Max Planck Society, covering a much broader spectrum of research, thus promoting disciplinary diversity and collaboration. Patrick Cramer is the Managing Director of this new institute.

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