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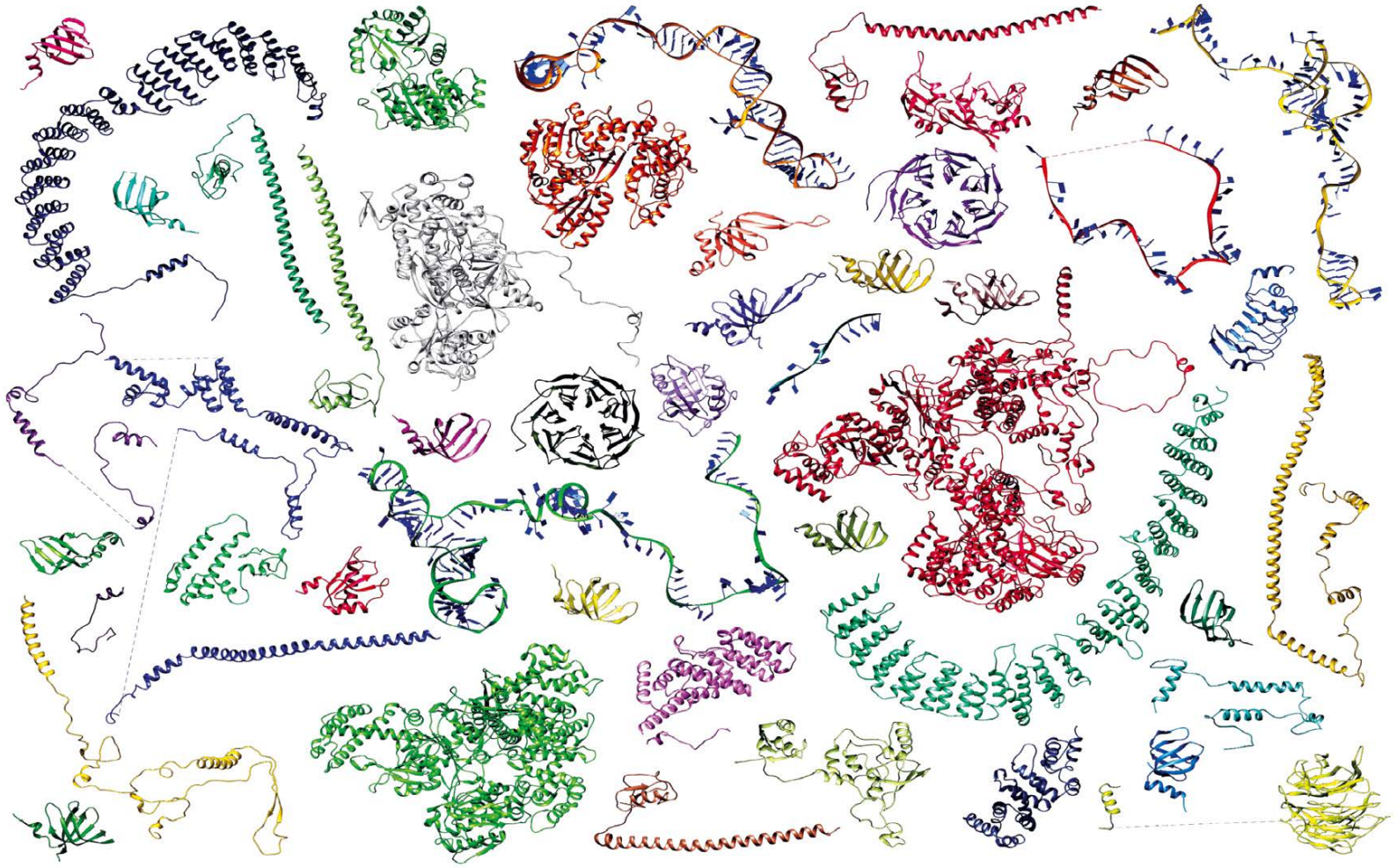

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Bioanalytische Massenspektrometrie

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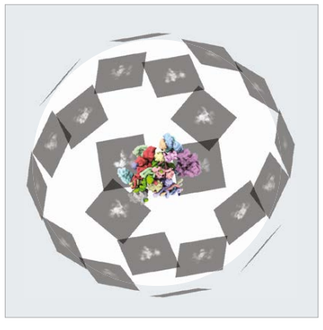


4 ***Protein cross-linking to support structure determination in electron cryo-microscopy of macromolecular complexes***

14 ***Melina Schuh erhält wichtigsten deutschen Forschungspreis***

18 ***Peter Lenart leitet neue Facility zur Mikroskopie lebender Zellen***

24 ***Die nächste Nacht des Wissens in Göttingen ist am 26. Januar 2019***

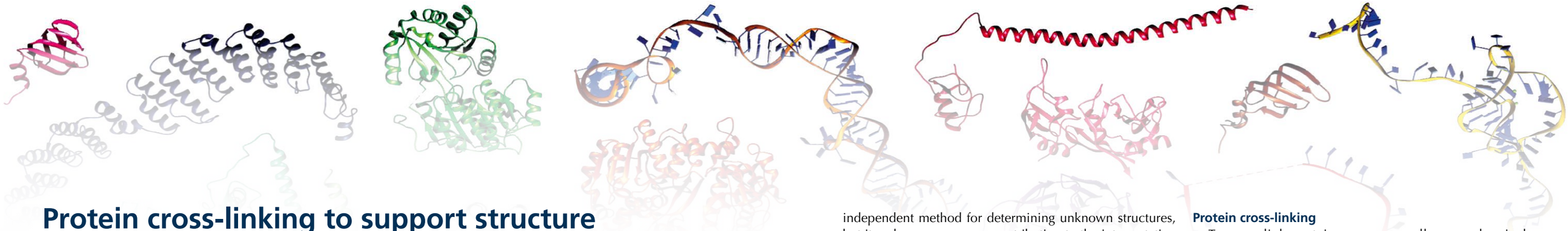
GÖTTINGEN CAMPUS AKTUELL

AUS DER MAX-PLANCK-GESELLSCHAFT

Titelbild: Einzelne Porteine lassen sich mittels ***cross-linking*** in Kombination mit Massenspektrometrie zur 3D-Struktur eines makromolekularen Komplexes anordnen. ***(Abbildung: Karl Bertram und David Haselbach / MPI-BPC)***

Cover image: Individual proteins can be arranged within the 3D structure of a macromolecular assembly by cross-linking combined with mass spectrometry ***(Image: Karl Bertram and David Haselbach / MPI-BPC)***

Hinweis: Obwohl aus Gründen der Lesbarkeit im Text die männliche Form gewählt wurde, beziehen sich die Angaben stets auf Angehörige beider Geschlechter.



Protein cross-linking to support structure determination in electron cryo-microscopy of macromolecular complexes

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Cryo-electron microscopy (cryo-EM) can solve structures of highly dynamic macromolecular complexes. To characterize less well defined regions in cryo-EM images, cross-linking coupled with mass spectrometry (CXMS) provides valuable information on the arrangement of domains and amino acids. CXMS comprises covalent linkage of protein residues close to each other as well as identifying these connections by mass spectrometry. Here, we exemplify the advances of CXMS and its integration with cryo-EM for structural reconstruction.

Proteins are dynamic molecules, and they often join up with ligands and other proteins to form functional macromolecular complexes in the cell. Discovering the three-dimensional (3D) structures of such complexes is a huge challenge. Classical methods of structure determination, such as X-ray crystallography and nuclear magnetic resonance (NMR), are restricted by the size, the structural flexibility, and the heterogeneity of most macromolecular protein complexes.

Currently, cryo-EM is the method of choice for elucidating the structures of macromolecular complexes. In cryo-EM, 3D structures are reconstructed from 2D projections; to make this possible, the complex under investigation is embedded in amorphous ice, so that its structure is kept as close to the native state as possible. Thanks to technical improvements in electron microscopes and to the development of appropriate software, we can today reach impressive spatial resolution, often down to 3 Å or even below (1-4). Examples are structures of ribosomes, proteasomes, complexes involved in transcribing DNA to RNA, spliceosomes, nuclear pores, and mitochondrial membrane import complexes (5).

Nevertheless, this level of resolution has only been realized for a few of these structures. More than 90 % of the structures published so far have had a resolution of 3-5 Å or even less (*https://pdbj.org/emnavi/stat.php*). The most important reason for this is the freedom of movement of some protein components within the macromolecular complex, or of some regions within a protein. Moreover, the quality of the samples, the quality of the 2D images, and the statistical methods employed for reconstructing the 3D model all play a part. The major problem lies in the visibility of individual amino acid side chains, which cannot be seen when the resolution is poorer than 4 Å, rendering the location and the assignment of proteins in cryo-EM structures extremely difficult.

Here, the method of chemical protein cross-linking in combination with mass spectrometry (CXMS) comes to our help. CXMS makes it possible to find out which protein domains in macromolecular complexes are attached to one another, once they have been cross-linked chemically and the cross-linked protein regions have been identified and sequenced by mass spectrometry (6-8). Thus, CXMS is not an independent method for determining unknown structures, but it makes an enormous contribution to the interpretation of structures. This is especially the case in certain specific situations: (i) when no independent structural information about the arrangement of the proteins in a complex is to be had, (ii) when the proteins in the complex contain highly dynamic domains, the structures of which cannot be seen by crystallography or NMR and are invisible in cryo-EM, (iii) when the complex under study can only be investigated structurally in the presence of part of its normal protein complement, so that the positions of the missing proteins in the complex's structure cannot be determined, or (iv) when a structural model for a protein or complex has been proposed and requires validation. Moreover, CXMS makes it possible to identify different conformations of an individual protein in a complex – for example, if the protein's position changes when other proteins become bound to the complex, then this will affect its cross-linking pattern.

Protein cross-linking

To cross-link proteins, one generally uses chemical reagents that possess *N*-hydroxysuccinimide (NHS) ester as reactive groups. These react with the primary amino group of the amino acid lysine and with the N-terminus of the protein (Fig. 1A). NHS esters are relatively stable when dissolved in water, and they react at neutral pH values. Moreover, lysines are found mostly at the surfaces of proteins, making lysine residues ideal points of attack for a cross-linking reagent. The NHS ester cross-linker possesses two reactive groups separated by a "spacer" of adjustable length: For example, the most frequently used reagent disuccinimidylsuberate (DSS) links ε-amino functions of lysines that are about 30 Å apart (strictly speaking: whose C-alpha atoms are 30 Å apart). Following chemical cross-linking, the proteins are digested by using endoproteinases (usually trypsin) and the cross-linked peptides thus obtained are sequenced in the mass spectrometer. The peptides' sequences allow the cross-linked amino

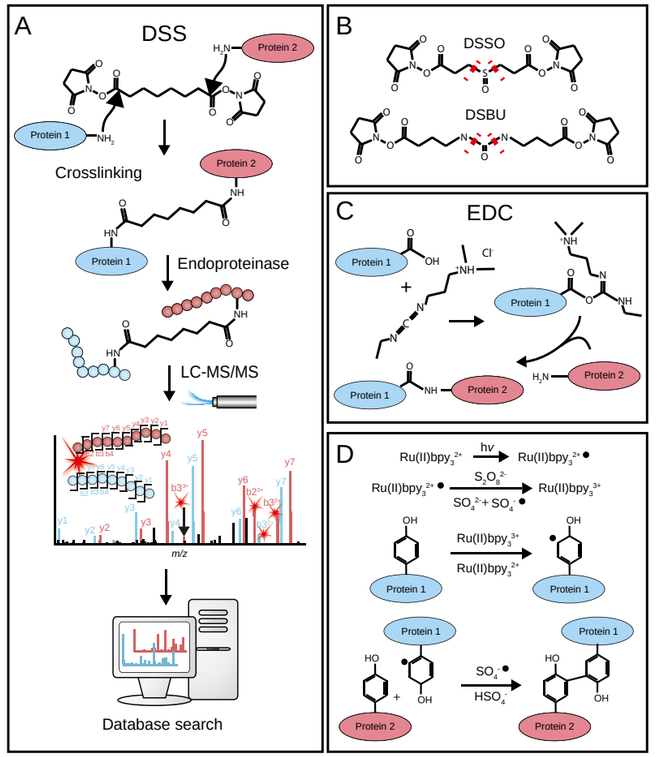

Figure 1: Overview of protein-protein cross-linking reagents used in mass spectrometry for elucidation of protein interactions in macromolecular complexes. **(A)** Schematic depiction of the chemical cross-linking reaction between proteins and disuccinimidylsuberate (DSS), with subsequent digestion with endoproteinases and mass-spectrometric analysis of the cross-linked peptides. The NH_2 groups of the proteins' lysines react with the ester groups of the cross-linker: the N-hydroxysuccinimide (NHS) part splits off and stable amide bonds are formed. Thus, if two proteins are closely adjacent to one another, they become covalently cross-linked. After enzymatic digestion, the cross-linked peptides are sequenced in the mass spectrometer (LC-MS/MS) and the proteins from which they came are identified by dedicated database search. This allows one to deduce which proteins and which protein regions are close to one another in a complex. **(B)** NHS-ester based cleavable cross-linkers that are fragmented in the gas phase of the mass spectrometer and hence facilitate the identification of cross-linked peptide pairs (see text for details). **(C)** Reaction scheme of the cross-linking reagent EDC that links lysine and glutamate or aspartate residues in proteins. **(D)** $Ru(II)bpy_3$ as example of a photoactivatable reagent which leads to the covalent link mainly between tyrosine and/or methionine residues in close vicinity to each other.

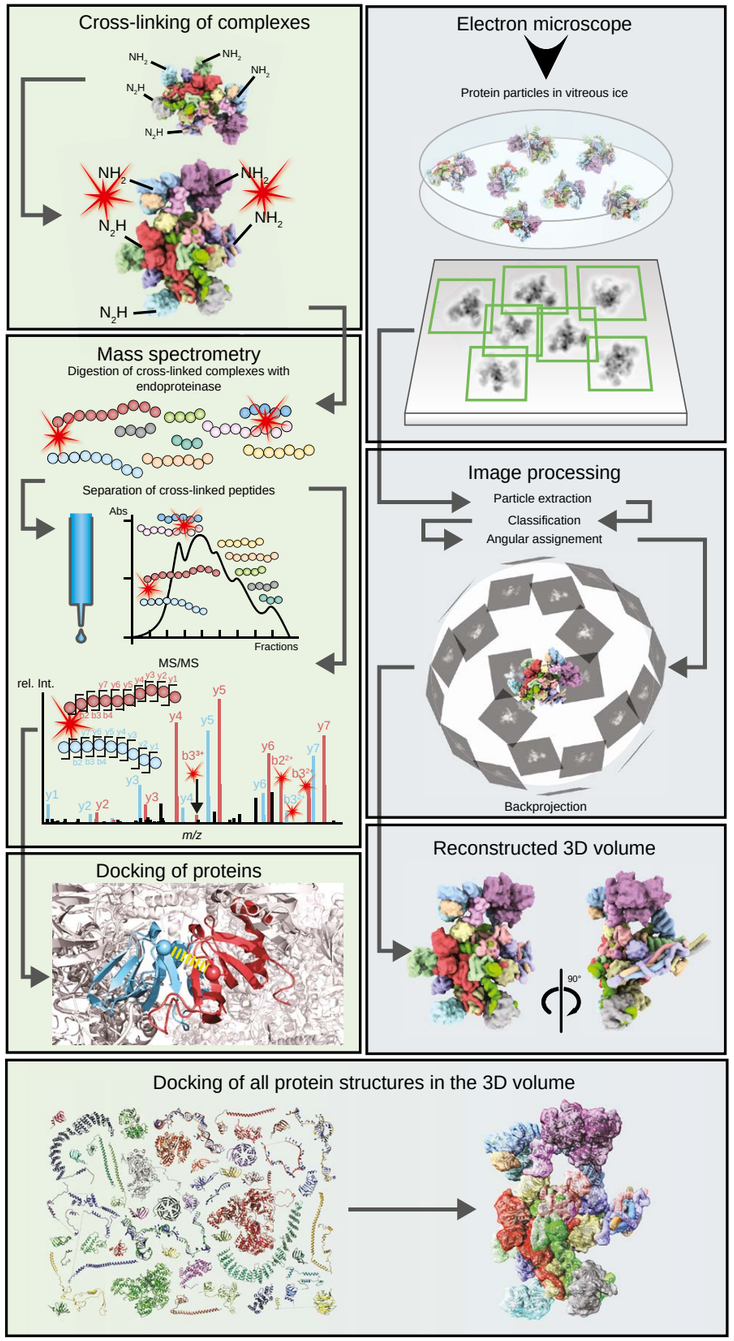

Figure 2: Example of the procedures followed in structure determination of a macromolecular protein complex by CXMS and cryo-EM. For the CXMS (left), the purified macromolecular protein complex is treated with cross-linker and thereafter all its proteins are broken down into peptides with endoproteinases. The cross-linked peptides are separated from the non-cross-linked ones by gel filtration and sequenced in the mass spectrometer. If structural models of the proteins already exist, then the cross-linked protein regions can be matched up. For cryo-EM (right), protein complexes are embedded in amorphous ice and two-dimensional images of the complexes are produced. These are then processed in a multi-step procedure to give a three-dimensional image ("density volume"). This contains the protein structures; if the resolution is high enough these are visible, and if not then the CXMS results and any available structure models are used to place the individual proteins in the 3D volume. Figure from (5)

acid (for example lysine), and from this the cross-linked protein to be identified by searching through data bases after the sequencing has been completed. In fact, in this case the sequencing and identification of the cross-linked peptides in the mass spectrometer presents an enormous challenge (unlike for example in established MS-based proteomics). It requires highly specialized software that is able to handle not just a single sequence but the sequences of both the cross-linked peptides and takes into account the mass of the cross-linker. It must be able to locate these among all the possible combinations of all the peptide sequences that come into question in the complex under investigation, and to compare all of these with the sequences in the database.

To simplify the database search, cleavable cross-linkers have been developed, as shown in Figure 1B (9-11). Cross-linkers such as DSSO or DSBU can be cleaved in the gas phase, within the mass spectrometer. This procedure has the advantage that the two peptide sequences (after cleavage in the MS) can be identified separately (again, while taking account of the mass of the cross-linker) in a "classical" database search.

Further cross-linkers react with the carboxyl groups of amino acids, like 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC, Fig. 1C), in order to connect glutamate or aspartate with lysine residues. There also exist protein-cross-linkers that are activated by ultraviolet light, like Tris(bipyridine)ruthenium(II) chloride (Ru(II)bpy$_3$; Fig. 1D). Since Ru(II)bpy$_3$ generates radicals, these can react with any amino acid (with a preference for tyrosine of methionine residues), which encumbers the mass-spectrometric work-up to some extent, as the type of the cross-linked amino acid is then not known in advance.

Figure 2 (left panel) illustrates how CXMS of protein complexes is carried out. Isolated macromolecular protein complexes are incubated together with cross-linking reagents, so that proteins lying close to one another become cross-linked (forming "inter-links"). At the same time, parts of the same protein can become cross-linked (forming "intra-links"). Cross-linked complexes are digested with trypsin, after which the cross-linked peptide pairs are enriched, for example by gel filtration. The enriched fractions are then analyzed in the mass spectrometer and the cross-linked peptide pairs are sequenced. The sequences thus found allow one to identify the cross-linked proteins and to pinpoint the cross-linked amino acid. Specially developed software makes it possible to visualize the cross-link points identified, both at the protein-sequence level and in models of the protein's 3D structure.

The cross-linked points in the amino acid sequences of proteins can be matched up with the structural models derived from cryo-EM. Figure 2 (right panel) shows schematically the course of a single-particle cryo-EM experiment that leads to a 3D model of the complex investigated. First, a very large number of 2D electron-microscopic images is acquired. For each image, its orientation is determined, and the information from all the images is then combined in the computer to generate a 3D picture of the structure sought. To recast the structure thus obtained as an atomic model then requires either (i) a similar structure model, already known, or (ii) a *de novo* construction. However, reliable *de novo* modelling of a protein demands a resolution of around 3 Å or better, allowing nearly all the protein side chains to be seen in the cryo-EM structure. As most of the cryo-EM structures presently available have lower resolutions than this, CXMS offers the possibility of assigning protein components on the basis of cross-linking results and of fitting these, by homology, into the overall structure. Moreover, CXMS allows the course of the so-called "intrinsically disordered" regions of a protein in the protein ensemble to be mapped, even if their dynamics prevent them from being visible in the reconstructed 3D volume. The structural models of proteins are fitted into the 3D volume of the cryo-EM model and the relative orientation of the proteins is adjusted with the help of the CXMS results.

Manual fitting and modelling of proteins into the 3D volumes on the basis of CXMS results is very time-consuming and requires detailed knowledge of all the available biochemical and genetic information about the protein(s) involved. Consequently, an increasing number of research groups are addressing the task of creating algorithms to automate such processes.

Spliceosomes and pre-mRNA transcription complexes – prime examples of the use of CXMS in structure determination

The use of CXMS to determine the locations of proteins in 3D structures determined by cryo-EM is convincingly illustrated by the recently solved structure of the spliceosome (12-16) and Polymerase II-dependent pre-mRNA transcription complexes (17-25) here at the MPI-BPC.

The spliceosome is one of the most dynamic multifactorial ribonucleoprotein complexes in eukaryotic cells. It catalyzes the excision of the introns and the ligation of the resulting exon ends of pre-mRNA to generate the mature mRNA. It consists of five small nuclear (sn) RNA molecules and up to 170 proteins. The spliceosome assembles on the pre-mRNA to be spliced and passes through several functional stages, which differ substantially in both RNA-RNA interaction pattern and in protein compositions. The spliceosome's dynamics, the flexible nature of its proteins, and its massive molecular weight long impeded structural research into its functional states. However, in the past two years cryo-EM

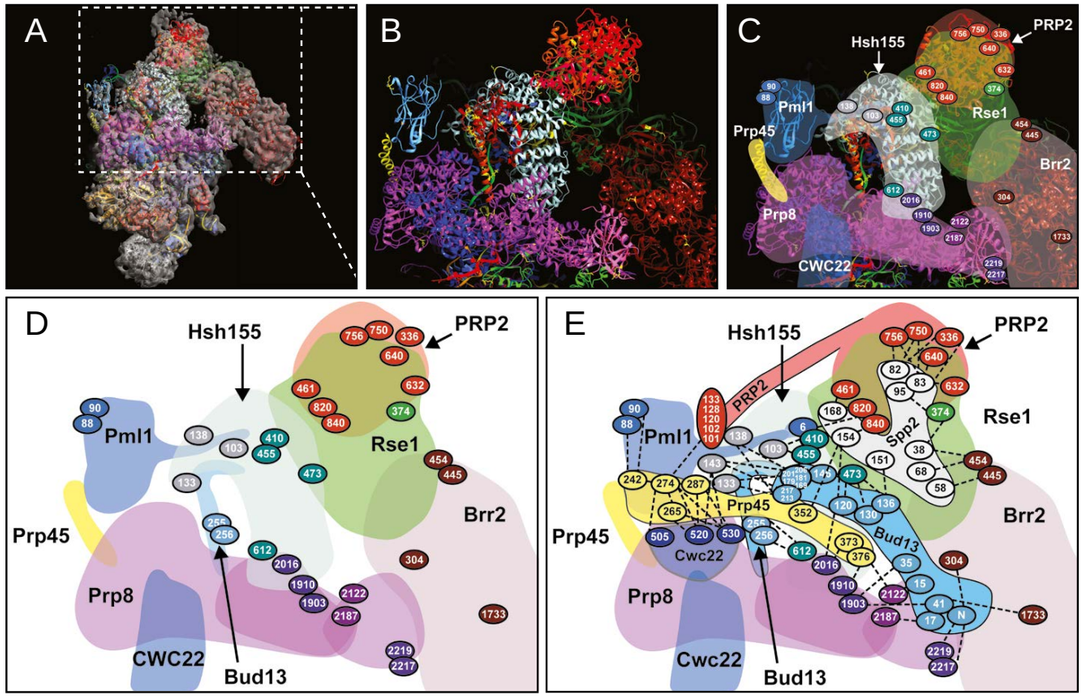

Figure 3: Modelling of non-folded protein regions of the spliceosomal proteins Prp2, Bud13, Prp45, and Spp2 within the activated spliceosome (B^{act}) using information obtained by CXMS. **(A)** 3D structure of the B^{act} spliceosome at a resolution of about 6 Å. With this resolution, the structures of spliceosomal proteins with defined protein domains can be located. However, proteins and domains with large non-folded regions remain invisible. **(B)** The region of the spliceosome without density volume, showing the structures of the spliceosomal proteins CWC22, Prp45, Pml1, Hsh155, Prp2, and Brr2. **(C)** Here, the proteins are represented as colored areas and the amino acids that were found by mass spectrometry to be cross-linked are indicated (lysines, in colors corresponding to their proteins). **(D)** As (C), but without the structure models of the proteins. **(E)** Schematic representation of the unstructured regions of the proteins Cwc22, Prp45, Prp2, Spp2, and Bud1, showing those amino acids that became cross-linked to other proteins in the complex. The cross-links identified allow the location of the non-folded regions of proteins Cwc22, Prp45, Prp2, Spp2, and Bud1 in this region of the spliceosome.

has brought to light impressive 3D structures of intact, functional spliceosomes. To locate proteins more precisely in the spliceosome's various functional states, and to define their positions precisely, we use CXMS. Figure 3 illustrates a procedure of this kind, using the 3D volume model of the activated spliceosome, the B^{act} complex (13) as obtained at a resolution of 5.8 Å (Fig. 3A). The structures of the individual proteins – those that were available – were fitted into the 3D volume of the spliceosome. Because of the limited resolution, the non-folded regions of the spliceosomal proteins Prp2, Bud13, Prp45, and Spp2 could not be assigned clearly enough. However, it is precisely these regions that are of greatest interest for understanding the spliceosome's structure and function, as they interact sequentially with several other proteins. CXMS was used to assign these regions to their positions in the 3D structure of the B^{act} complex. Figure 3B shows a part of the complex at higher magnification (not in 3D) and only those proteins that show defined elements of secondary structure. Figures 3C and 3D show these proteins as simple colored areas with correspondingly colored amino acids that were identified as cross-linking to the non-folded regions of the proteins Prp2, Bud13, Prp45, and Spp2. Figure 3E shows the corresponding amino acids and, schematically, the unfolded regions of the proteins Prp2, Bud13, Prp45, and Spp2, which were placed there on the basis of information derived from cross-linking. An extensive network of protein-protein interactions is revealed. This network is functionally important, as precisely these interactions are believed to "clamp" the non-folded regions of protein Prp2 so that it can exert its catalytic function and thus propel the B^{act} complex into the next functional state of the spliceosome, the catalytically activated B* complex.

Figure 4 illustrates further examples for the combination of CXMS and cryo-EM. Here, protein-protein cross-linking networks of Polymerase II-dependent pre-mRNA transcription complexes are shown with selected protein structures, which are placed in the corresponding 3D volumes of the complexes obtained by cryo-EM. In this manner, we were able to locate and orientate specific protein structures with the 3D structure of the corresponding pre-mRNA transcription complexes in a more precise manner, in particular within those parts of the 3D volume where the resolution of the corresponding complex is not sufficient to allow for unambiguous orientation of the proteins.

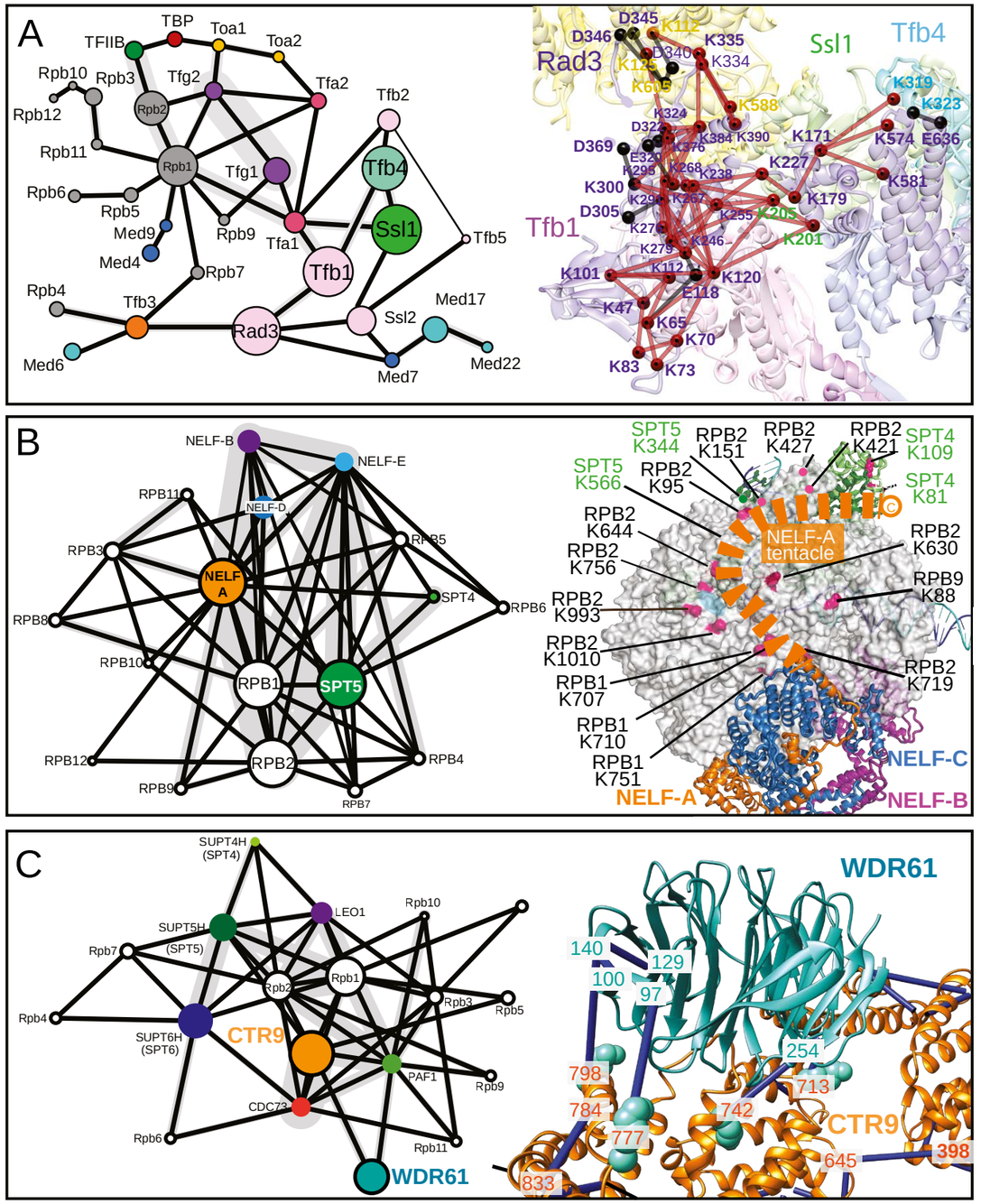

Figure 4: Cross-linked protein networks and selected protein structures of the RNA Polymerase II Pre-Initiator-Complex (PIC) (A) and paused Polymerase II elongation complexes (B and C). **(A)** EDC-derived inter-subunit cross-links between selected subunits in the PIC-cMed complex. Ribbon representation of Tfb1 and the surrounding domains of Rad3, Ssl1, and Tfb4. BS3- and EDC-derived cross-links are depicted in red and black, respectively. The displayed cross-links aided modelling of the proteins and their anchor domains into the cryo-EM 3D volume. **(B, C)** Protein cross-linking network of paused and activated transcription elongation complexes with their specific proteins. NELF-A tentacle interaction with the Polymerase II is based on CXMS data (B) and the orientation of WDR1 relative to CTR9 (C) was possible because of the CXMS analyses of cross-linked amino acid residues of the respective proteins.

Polymerase II-dependent pre-mRNA transcription is the first essential step in eukaryotic gene expression by using double strand DNA as template for generating a pre-mature mRNA. Polymerase II consists of twelve different protein subunits. It cannot bind on its own to a promoter region for a protein-coding gene on the DNA to initiate transcription. It rather needs to be assembled with other protein factors (transcription factors TFIIA, B, D, E, F, and H) on the promoter, hence forming the pre-initiation complex (PIC). A so-called mediator complex (PIC-med) further stabilizes the interactions with DNA sequences upstream of the promoter region. Very recently, the group of Patrick Cramer solved the structure of the PIC-med including detailed structural information of TFIIH (23). In particular the spatial orientation of the essential TFIIH protein complex within the PIC-med has never been described owing to the dynamic nature of this complex. Here, we used cross-linking of the holoenzyme with EDC, which connects lysine and glutamate/aspartate residues. Importantly, EDC cross-linker connects residues that have a much shorter distance restrain as for example DSS so that TFIIH with its subunits can be more precisely located in the 3D volume of the holoenzyme. Figure 4A shows the EDC-derived cross-linking network of the PIC and highlights the cross-linking of the TFIIH proteins Rad3, Ssl1, Tfb1, and Tfb4.

After initiating, the transcription complex starts elongating the nascent RNA (that is, by forming a transcription elongation complex), but after a few nucleotides (25-150 base pairs) can stably pause in the promoter-proximal region. This step is used as an additional checkpoint to control gene expression, namely to determine whether Polymerase II is removed from DNA or is activated by co-factors to proceed with elongation. During pausing, the Polymerase II is stabilized by two protein complexes, DSIF and NELF. NELF must be removed by phosphorylation so that an active Pol II-DSIF (along with other proteins) elongation complex (EC*) can be formed. The Cramer group has solved the structures of a paused transcription complex containing NELF and the EC* using cryo-EM (24, 25). We have applied CXMS in order to define the orientation of the disordered regions in NELF subunits, particularly for the NELF-A subunit (Fig. 4B). NELF-A possesses an unstructured "tentacle" that is required for its association with DSIF and for pausing of Polymerase II. The NELF-A tentacle is also heavily phosphorylated when NELF is evicted from Polymerase II. In the cryo-EM maps, density for the NELF-A tentacle was discontinuous making it impossible to model. Using CXMS, we were able to determine how the NELF-A tentacle snakes along the surface of Polymerase II and which region of NELF-A associates with DSIF to stabilize pausing. In the EC* complex, CXMS was applied to locate peripheral proteins like WDR61, LEO1, CTR9, DSIF SPT4, and DSIF SPT5 with its domains KOW1and KOWx-4, as well as SPT6 relative to the core of EC* (Fig. 4C). Although the overall resolution of the cryo-EM map for EC* was high (3.1 Å), peripheral densities had resolutions in the 4-12 Å range. CXMS was used to unambiguously place WDR61 in the correct orientation, as it is a highly symmetrical beta propeller protein and at low resolution could be placed in multiple positions that would satisfy the density. We also used CXMS to aid *de novo* modeling of the CTR9 protein.

In summary, protein cross-linking combined with mass spectrometry (CXMS) currently is the method of choice to support cryo-EM studies on macromolecular complexes. CXMS also bears the possibility of visualizing conformational changes of large assemblies using cross-linkers that are differentially isotopically labeled. Changes in the cross-link profiles between separately probed functional states may even yield semi-quantitative information on the abundances of the constituents' different conformations. However, when complexes are analyzed by CXMS in parallel using cryo-EM, the entire mixture – with a certain heterogeneity (for example subcomplexes through disassembly, and/or various functional states, which could not be separated biochemically) – will be cross-linked. Therefore, it is difficult to distinguish if a set of cross-links represents only the most abundant conformation, or rather results from a less abundantly present subcomplex or a different functional state. Conversely, cryo-EM offers this possibility through classification of collected images and can distinguish between various assembly and/or functional states in a single sample preparation. Improving quantitative cross-linking approaches can be expected to allow the description of entire sets of various conformational states even in macromolecular and heterogeneous complexes, while software development and improvements in computational power should enable cryo-EM to provide different conformational states of macromolecular assembly.

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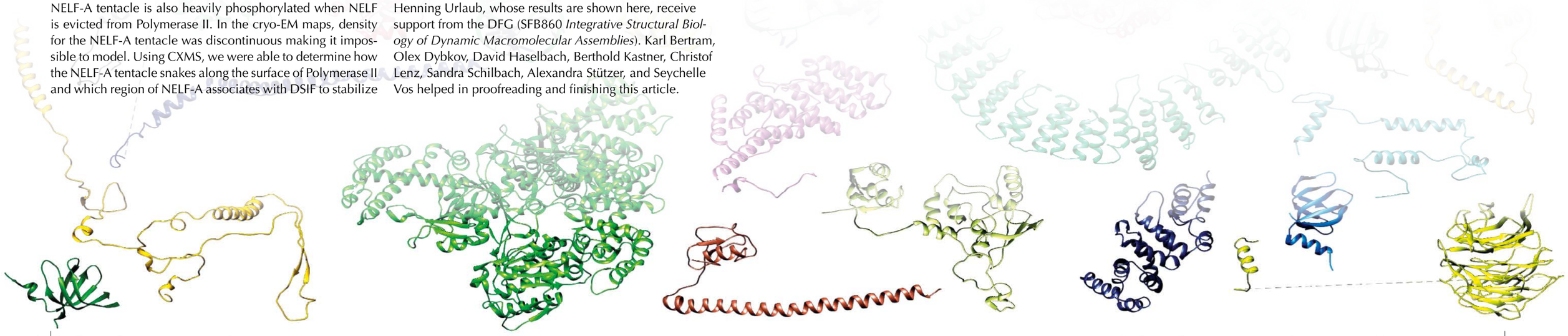

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Der Wurm *C. elegans* schläft, um seine Zellen vor Alterung zu schützen. Im Gegensatz zum Wurm, der geschlafen hat (links), zeigt der schlaflose Wurm (rechts) Schäden an der grün gefärbten Muskulatur. *(Foto: Yin Wu, Henrik Bringmann / MPI-BPC)*

Hungernde Fadenwürmer schützen ihre Zellen vor Alterung, indem sie schlafen

Wer ausreichend schläft, lebt gesünder – davon ist die Schlafmedizin heute überzeugt. Doch kann Schlaf auch verhindern, dass wir altern? Zumindest bei Fadenwürmern ist das der Fall, wie Wissenschaftler am MPI-BPC jetzt gezeigt haben: Der Fadenwurm *Caenorhabditis elegans* schläft ein, wenn er hungern muss, und verlangsamt so das Altern seiner Zellen. Die Forscher weisen damit erstmals einen direkten Zusammenhang zwischen Schlaf und Alterungsprozessen nach, der so auch beim Menschen bestehen könnte. *(Current Biology, 8. November 2018)*

Der Schlaf ist alt, sehr alt. Vermutlich ist er vor über 500 Millionen Jahren entstanden, als die ersten Tiere ein Nervensystem entwickelten. Im Tierreich ist er entsprechend weit verbreitet – Säugetiere schlafen ebenso wie Fische und sogar Quallen. Schlaf scheint also eine unverzichtbare Funktion zu erfüllen.

Wir Menschen müssen schlafen, damit unser hochkomplexes Gehirn Erfahrungen und Gelerntes verarbeiten und sich regenerieren kann. Schlafentzug kann für uns tödlich enden. Aber wieso schlafen selbst vergleichsweise primitive Tiere, die nur über ein paar Hundert Nervenzellen verfügen? Und unter welchen Bedingungen ist Schlaf überlebenswichtig? Diese Fragen wollte der Biologe Henrik Bringmann mit seiner Max-Planck-Forschungsgruppe *Schlaf und Wachsein* am MPI-BPC beantworten. Für ihre Untersuchungen nutzten die Wissenschaftler den Fadenwurm *C. elegans* als Modellorganismus. Der etwa ein Millimeter lange Wurm besitzt lediglich 302 Nervenzellen und durchläuft in seiner Entwicklung vier Larvenstadien mit wiederholten Schlafphasen. Er ist somit bestens geeignet, um grundlegende Eigenschaften von Schlaf zu erforschen.

Henrik Bringmann *(Foto: ibg)*

„Wie wir herausgefunden haben, sind die Larven von *C. elegans* auf Schlaf angewiesen, um Hungerphasen zu überleben“, fasst Bringmann die Ergebnisse zusammen. „Dabei schlafen die Würmer offenbar nicht nur, um Energie zu sparen, sondern auch, um schädliche Alterungsprozesse aufzuhalten. Der Schlaf stellt für den Wurm unter diesen Bedingungen also eine Art Anti-Aging-Strategie dar.“

Die Göttinger Wissenschaftler hatten zunächst analysiert, inwiefern *C. elegans* überhaupt schlafen muss. Während Schlafentzug bei erwachsenen Würmern keine Auswirkung auf ihre Lebensdauer habe, würden schlaflose Larven sterben, erläutert Yin Wu, Doktorandin in Bringmanns Forschungsgruppe. „Wir wollten wissen, warum da so ist.“

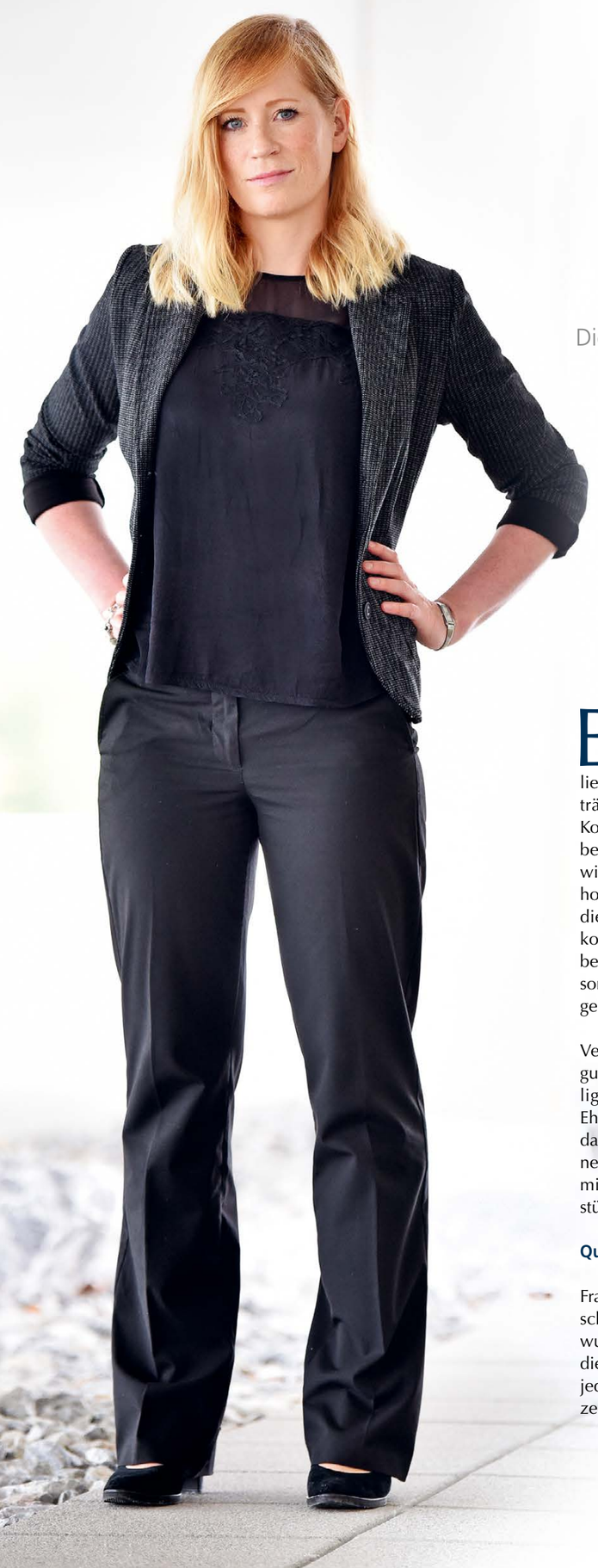
Weitere Experimente offenbarten, dass das Nahrungsangebot für die Larven wesentlich über deren Schlafmenge entscheidet: Je weniger Futter sie finden, desto mehr schlafen sie. Dieser Schlaf diene allerdings nicht ausschließlich dazu, Energie zu sparen, betont Florentin Masurat, ehemaliger Doktorand von Bringmann. Stattdessen legen die Ergebnisse der Forscher nahe, dass es – zumindest bei *C. elegans* – mindestens ebenso sehr darauf ankommt, die Körperzellen vor dem schädlichen Einfluss des Hungerns zu schützen: „Schlaflose Würmer sterben nämlich, weil ihre Zellen zugrunde gehen“, wie Bringmann erklärt. „Ihre Muskelfasern werden abgebaut und in den Zellen sammeln sich schädliche Proteine. Dieser Prozess ähnelt dem Altern und lässt sich durch Schlaf verlangsamen.“

Doch ist Schlaf nur für hungernde Würmer ein Jungbrunnen? Oder lassen sich aus den Erkenntnissen von Bringmanns Team auch Schlüsse für komplexere Tiere ziehen? Schließlich müssen alle Organismen mit längeren Hungerperioden umgehen können und haben entsprechende Überlebensstrategien entwickelt. „Wir vermuten, dass die molekulare Verknüpfung von Hunger auf der einen sowie Alterung und Schlaf auf der anderen Seite schon früh in der Geschichte des Tierreichs entstanden ist“, so Bringmann. „Es ist daher durchaus möglich, dass Schlaf auch beim Menschen Alterungsprozesse beeinflusst.“ (fk)

Originalveröffentlichung

Wu Y, Masurat F, Bringmann H: Sleep counteracts aging phenotypes to survive starvation-induced developmental arrest in *C. elegans*.
Current Biology, doi: 10.1016/j.cub.2018.10.009 (2018)

Yin Wu (links) und Florentin Masurat *(Foto: ibg)*



Leibniz-Preis 2019 für Melina Schuh

Die Deutsche Forschungsgemeinschaft (DFG) zeichnet die Biochemikerin am MPI-BPC damit für ihre wegweisenden Arbeiten zur Entwicklung befruchtungsfähiger Eizellen aus. Der wichtigste deutsche Forschungsförderpreis ist mit bis zu 2,5 Millionen Euro dotiert.

Es ist ein großartiger Erfolg für Melina Schuh, dass sie für ihre bahnbrechenden Forschungsarbeiten nun mit dem renommierten Leibniz-Preis ausgezeichnet wird“, gratulierte der Geschäftsführende Direktor Dirk Görlich der Preisträgerin. „Wir freuen uns außerordentlich mit unserer Kollegin über diese tolle Anerkennung! Ihre Forschung darüber, wie sich befruchtungsfähige Eizellen entwickeln, ist wissenschaftlich äußerst interessant und gesellschaftlich von hoher Relevanz! Wie entsteht neues Leben? Und was sind die Folgen, wenn es in der Eizell-Entwicklung zu Fehlern kommt? Melina Schuhs Arbeiten haben maßgeblich dazu beigetragen, dass wir heute besser verstehen, wie Chromosomen-Anomalien beispielsweise zu Down-Syndrom, Fehlgeburten und Unfruchtbarkeit führen können.“

Mit einem Anruf rund eine Stunde vor der öffentlichen Verkündung der Preisträger hatte die DFG Melina Schuh die gute Nachricht übermittelt. „Die Auszeichnung hat mich völlig überrascht und ich freue mich sehr über diese große Ehre“, berichtet die frisch gekürte Preisträgerin. „Ein Riesendank geht an meine bisherigen und jetzigen Mitarbeiterinnen und Mitarbeiter sowie die fantastischen Mentoren, die mich im Laufe meiner wissenschaftlichen Karriere unterstützt haben.“

Qualität von Eizellen nimmt ab, wenn Frauen älter werden

In einer Partnerschaft stellt sich früher oder später die Frage nach dem Kinderwunsch. In unserer Gesellschaft entscheiden sich zunehmend mehr Paare erst spät für Nachwuchs. Doch dieser Aufschub ist nicht frei von Risiken: Denn die Qualität unreifer Eizellen – die bereits von Geburt an bei jeder Frau angelegt sind – nimmt mit deren Alter ab. Gleichzeitig steigt die Wahrscheinlichkeit für Fehlgeburten oder ein Kind mit chromosomalen Anomalien wie dem Down-Syndrom. Doch warum ist das so?

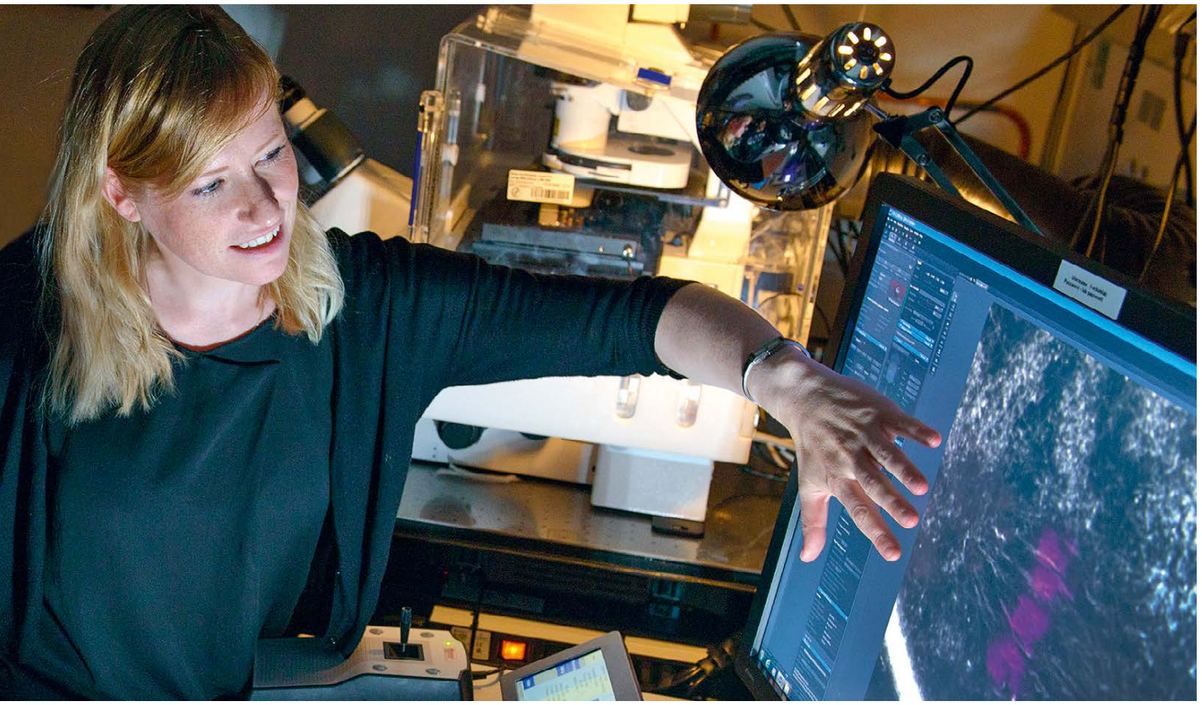
„Die häufigste Ursache dafür sind Fehler während der Reifeteilung der Eizelle, Meiose genannt, bei der die Eizelle ihren doppelten Chromosomensatz halbiert“, erläutert Schuh. Nur einer der beiden Chromosomensätze verbleibt in der reifen Eizelle, während der andere aus dem Zellplasma ausgeschleust wird. Erst dann kann die Eizelle mit einer Samenzelle verschmelzen. Zusammengehörige (homologe) Chromosomen ordnen sich vor der Teilung der Eizelle zunächst mithilfe sogenannter Spindelfasern in der Zellmitte an. Dort werden sie getrennt und der Spindelapparat transportiert je eine Kopie zu den beiden Zellpolen.

Die Biochemikerin konnte mit ihrem Team zeigen, dass zusammengehörige Chromosomen in unreifen Eizellen bei Frauen über 35 Jahren schlechter aneinanderlagert sind als bei jüngeren. Weiter fand sie heraus, dass Chromosomen oft nicht korrekt an den Spindelapparat gebunden sind. Beides trägt zur Fehleranfälligkeit der Meiose bei und bewirkt, dass reife Eizellen eine falsche Chromosomenzahl enthalten können. „Wird eine solche Eizelle befruchtet, kann sich die Chromosomenanomalie negativ auf den Verlauf der Schwangerschaft und die Gesundheit des Kindes auswirken“, so die Max-Planck-Direktorin.

Chromosomenanomalien durch Fehler in der Meiose

Wie solche Fehler bei der Halbierung des Chromosomensatzes zustande kommen, erforscht die Biochemikerin in ihrer Abteilung *Meiose* am MPI-BPC unter anderem mithilfe leistungsstarker Lichtmikroskope. So gelang es ihrem Team jetzt, den Prozess der Chromosomentrennung direkt live in unbefruchteten menschlichen Eizellen zu beobachten. Um

Melina Schuh am Mikroskop mit ihrer Doktorandin Katarina Harasimov
(Fotos dieser Doppelseite: Frank Vinken / Max-Planck-Gesellschaft)



Melina Schuh an einem der leistungsstarken Mikroskope der Abteilung *Meiose (Foto: ibg)*

den Vorgang der Chromosomentrennung bis ins molekulare Detail zu verstehen, entwickelte Schuh mit ihrer Gruppe auch eine neue Methode namens *Trim-Away*, mit der sich bestimmte Proteine innerhalb weniger Minuten aus den Eizellen entfernen lassen. Durch Analyse der resultierenden Effekte können die Forscher aufdecken, welche Aufgaben die entsprechenden Proteine während der Meiose haben.

Weitere große Vorteile der Methode: Mit *Trim-Away* können Wissenschaftler erstmals die Funktion direkt auf Proteineben untersuchen, und nicht wie bisher durch Eingriff auf DNA- oder RNA-Ebene. Die Methode ist zudem in vielen anderen Zelltypten einsetzbar.

„Unsere Erkenntnisse tragen dazu bei, besser zu verstehen, wie befruchtungsfähige Eizellen entstehen und warum Kinder älterer Frauen häufiger unter Chromosomenanomalien leiden als die jüngerer. Dieses Wissen könnte zukünftig helfen, Frauen in ihren späten 30ern und frühen 40ern ihren Kinderwunsch zu erfüllen“, hofft die Leibniz-Preisträgerin.

Neben Melina Schuh wurden in diesem Jahr neun weitere Forscher ausgezeichnet, darunter die beiden Max-Planck-Direktorinnen Ayelet Shachar vom MPI für multireligiöse und multikulturelle Gesellschaften sowie Brenda Schulman vom MPI für Biochemie. Mit dem neuesten Leibniz-Preis haben bisher 14 Wissenschaftler, die am MPI-BPC forschen oder geforscht haben, den renommierten Preis erhalten. (cr)

Melina Schuh

studierte Biochemie an der Universität Bayreuth und wurde 2008 nach mehrjährigen Arbeiten am *European Laboratory of Molecular Biology* (EMBL) in Heidelberg von der Universität Heidelberg promoviert. Im Anschluss wechselte sie nach Cambridge (England), wo sie von 2009 bis Ende 2015 als Gruppenleiterin am renommierten *MRC Laboratory of Molecular Biology* forschte. Seit Januar 2016 ist sie Direktorin am MPI-BPC und leitet dort die Abteilung *Meiose*. Für ihre Arbeiten wurde sie bereits vielfach ausgezeichnet, zuletzt erhielt sie die *EMBO Gold Medal*.

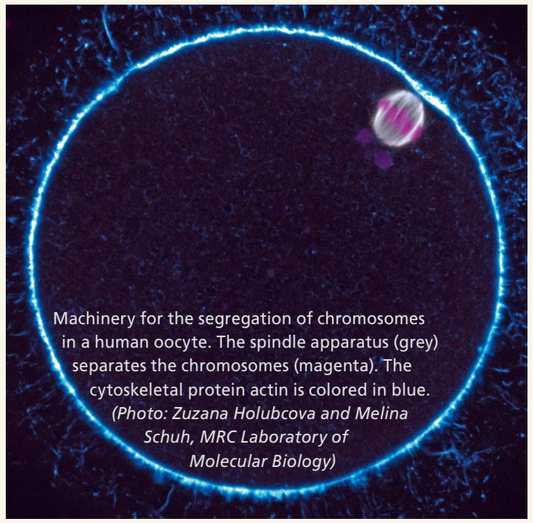
Über den Leibniz-Preis

Ziel des 1985 eingerichteten Leibniz-Programms ist es, die Forschungsmöglichkeiten der Preisträger zu erweitern, sie von administrativem Arbeitsaufwand zu entlasten und ihnen die Beschäftigung besonders qualifizierter junger Wissenschaftler zu erleichtern. Die Ausgezeichneten erhalten je ein Preisgeld von 2,5 Millionen Euro. Diese Gelder können sie bis zu sieben Jahre lang nach ihren eigenen Vorstellungen und ohne bürokratischen Aufwand für ihre Forschungsarbeit verwenden. Verliehen werden die Gottfried Wilhelm Leibniz-Preise am 13. März 2019 in Berlin.

Leibniz Prize 2019 for Melina Schuh

The German Research Foundation (DFG) honors the biochemist at the MPI-BPC for her pioneering research on the development of fertilizable oocytes. The most important German research prize is endowed with up to 2.5 million euros.

It is a great success for Melina Schuh that she has now been awarded the renowned Leibniz Prize for her groundbreaking research," Managing Director Dirk Görlich congratulated the prizewinner. "We are extremely happy for our colleague! Her research on how fertilizable oocytes develop is scientifically extremely interesting and highly relevant to society! How does new life come into being? And what are the consequences if errors occur in egg cell development? Melina Schuh's work has contributed significantly to our today's understanding of how chromosomal abnormalities can lead, for example, to Down's syndrome, miscarriages, and infertility."



Machinery for the segregation of chromosomes in a human oocyte. The spindle apparatus (grey) separates the chromosomes (magenta). The cytoskeletal protein actin is colored in blue. *(Photo: Zuzana Holubcova and Melina Schuh, MRC Laboratory of Molecular Biology)*

Quality of eggs decreases as women get older

Sooner or later in a partnership the question arises whether to have children or not. In our society more and more couples decide to become parents later. However, this postponement is not free of risks: The quality of immature oocytes – which are already present in every woman from birth – decreases with the woman's age. At the same time, the probability of miscarriages or a child with chromosomal abnormalities such as Down's syndrome increases. But what are the reasons for this?

"The most common cause are errors that occur during the egg cell's maturation, called meiosis, in which the egg halves its double set of chromosomes," Schuh explains. Only one of the two sets of chromosomes remains in the mature egg, while the other is exported from the cell. Only then can the oocyte fuse with a sperm cell. Before the egg cell divides, related (homologous) chromosomes are first arranged in the cell center using so-called spindle fibers. There, they are separated and the spindle apparatus transports one copy each to the two cell poles.

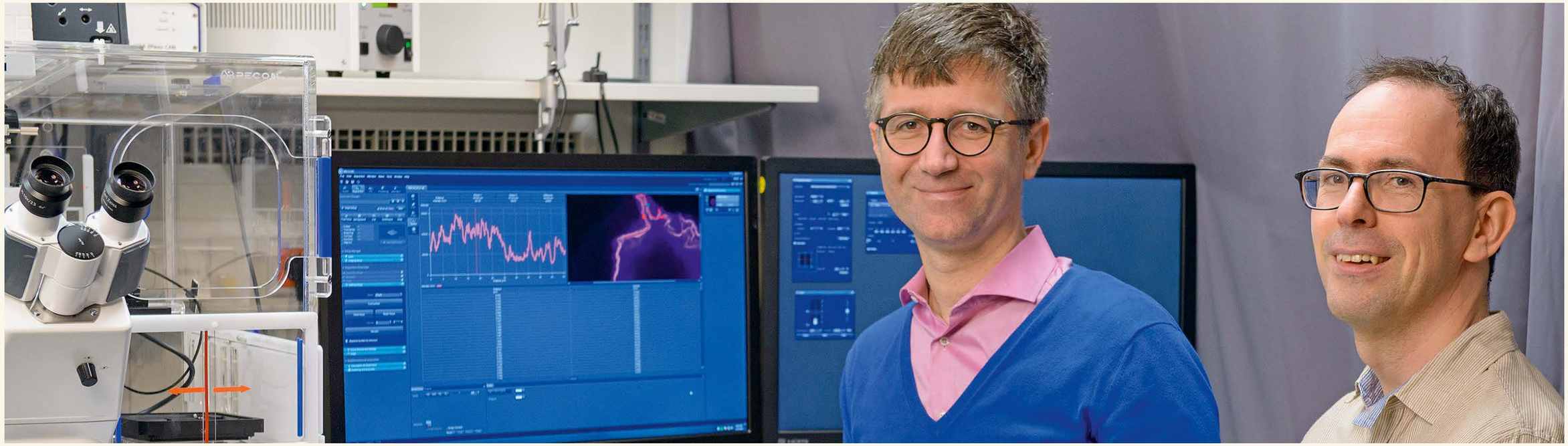
Chromosomal aberrations due to errors in meiosis

The biochemist and her team were able to show that the chromosomes of immature oocytes belonging together are less stably attached to each other in women over 35 than in younger ones. She also found that chromosomes are often not correctly bound to the spindle apparatus. Both factors contribute to the susceptibility of meiosis to errors and lead to mature oocytes with a wrong number of chromosomes. "If such an egg is fertilized, the chromosomal aberration can have a negative effect on the course of pregnancy and the child's health," says the Max Planck Director.

In her Department of *Meiosis* at the MPI-BPC, the biochemist uses powerful light microscopes to investigate how such errors occur when the chromosome set is halved. Her team has now succeeded in observing the process of chromosome segregation live in unfertilized human oocytes. To understand the process of chromosome segregation in detail, Schuh and her group also developed a new method called *Trim-Away* which allows to remove defined proteins from the oocytes within a few minutes. By analyzing the resulting effects, the researchers can uncover the functions of the corresponding proteins during meiosis.

"Our findings contribute to a better understanding of how fertile eggs are produced and why children of older women suffer from chromosomal aberrations more often compared to younger ones. In the future, this knowledge could help women in their late 30s and early 40s to have children," the Leibniz Prize winner hopes.

Together with Melina Schuh, nine other researchers were honored with this year's Leibniz Prize, including the two female Max Planck Directors Ayelet Shachar of the MPI for the Study of Religious and Ethnic Diversity as well as Brenda Schulman of the MPI for Biochemistry. In total, 14 scientists who work or have worked at the MPI-BPC have so far received the renowned prize. (cr/translation fk)



Peter Lenart (right) and Antonio Politi in front of one of the facility's microscopes. *(all photos: ibg)*

«We bring together experiment and technology»

The institute's new Facility for ***Live-cell Imaging*** recently opened its doors. Facility head Peter Lenart and operational manager Antonio Politi talked to us about their ideas and the service they provide for users in the institute.

To start with the most obvious question: What kind of services does the new facility offer?
Peter Lenart (PL): Here in the facility we cover the full range of light microscopy, with particular emphasis on imaging living cells. Our service includes help with sample preparation, planning experiments, image acquisition, image processing, and data analysis. Furthermore, we will provide regular training courses in light-microscopy and bio-image analysis.

How are you set up for these services?
PL: Antonio and I are an ideal combination in my view: I am a biologist by training and spent my whole PhD and beyond doing confocal microscopy and imaging live cells. Therefore, I have good expertise in sample preparation and assay development. Antonio complements this nicely because ...
Antonio Politi (AP): ... I have a PhD in biophysics, much experience with microscope automation as well as image processing and thus can help with data analysis. Moreover, I have been in a support role before and know what has to be taken care of. And we have superb help by our third team member Jasmin Jakobi who takes over the technical assistance in cell culture, for example. Thus, our goal is to bring together our user's experiments and technology, which is a particularly complex task in live-cell imaging.

Who can use the facility's service?
AP: Our facility is open to everyone at the MPI-BPC. If labs do not regularly use light microscopy but need this method for a specific project or experiment they can come to us and do their experiments here after a short introductory training. For more experienced users we are happy to provide project-related advice and tips for assay development. Resources permitting, we can also optimize assays and develop image analysis routines for users. Generally, we are happy to help in any way we can, for example, we can offer advice when groups would like to purchase a light microscope for their own lab.

How is the facility equipped?
PL: Our current rooms are sufficient to host eight microscopes in total. Two state-of-the-art confocal microscopes are already installed and in use, one of which is equipped for STED imaging invented by our Director Stefan Hell. One additional space is reserved for the iPAM microscope developed by Tom Jovin and Donna Arndt-Jovin here at the institute that will also be available to the facility's users. The spaces left will be gradually equipped with microscopes to meet the demands at the institute. We purposely keep this flexible to offer our users the technology they need.

In addition, we have a cell culture lab to prepare live samples for imaging. Not least, we also provide lab space for sample preparation.

As you can see here, all our rooms are brand-new. The architect, the institute's building service, and the workshops really did a great job! In addition, the *IT Service* helped us a lot in putting up the IT infrastructure and virtual machines. So we had fantastic support all the way from administration to management in setting up this facility and very much thank all of them for their help!

Who is already using the facility?
AP: We have regular users from Melina Schuh's team, from Dirk Görlich's group, as well as from Gregor Eichele's department, and we got contacted by several more people from all over the institute after our official opening event in early December. One of our current favorites are the brain preparations from Eichele's team: It is a real imaging challenge, and it is simply fascinating to watch the coordinated beating of cilia in the ventricles.

Once people have acquired the images, how can these be processed?
PL: We have central servers for image processing which we maintain together with the *IT Service*. We use virtual machine technology to run image processing software that can be accessed from remote computers. Thus, users can come to our image analysis terminals in the facility, but if they prefer, they can access all services and software from any computer at the institute or even from home. (Interview: fk/cr)

If you would like to use the facility or learn more about it, please contact Peter Lenart and Antonio Politi:
✉ *liveim@mpibpc.mpg.de*, ✆ 1774

Jasmin Jakobi inserts a microinjection needle into a sample.

Einweihung der Facility *Mikroskopie lebender Zellen*

Es gab fast kein Durchkommen mehr in der geräumigen, neuen Facility *Mikroskopie lebender Zellen*, als Peter Lenart die Gäste am Nachmittag des 3. Dezember zur Einweihung willkommen hieß. „Gerade noch rechtzeitig ist unsere neue Kaffeemaschine angekommen, da hatten wir wirklich Glück“, verriet der Leiter der Facility sichtbar froh. Antonio Politi, operativer Manager, hatte diese eigens ausgesucht und bereitete für die Gäste einen Kaffee nach dem anderen im Hochdurchsatzverfahren.

„Nutzer, die häufig zu uns kommen, können neben den Mikroskopen auch eine Einweisung in diese tolle Espressomaschine erhalten“, bot er schmunzelnd an. Mindestens ebenso viel Aufmerksamkeit war den neuen Mikroskopen sicher, die Lenart und Politi unterstützt von der technischen Mitarbeiterin Jasmin Jakobi in kleinen Runden den Besuchern vorstellten. Die Geräte werden im Moment stark von Mitarbeitern aus den Abteilungen *Gene und Verhalten, Meiose* und *Zelluläre Logistik* frequentiert. Weitere Mikroskope sollen – abgestimmt auf die Bedürfnisse der Institutsmitarbeiter – nach und nach angeschafft werden.

Wir wünschen der Facility einen guten Start und viele zufriedene Mikroskopie-begeisterte Nutzer! (cr)

(Foto: ibg)

Lab warming of the Facility for *Live-cell Imaging*

There was almost no getting through in the spacious new Facility for *Live-cell Imaging* when Peter Lenart welcomed the guests to the lab warming in the afternoon of December 3. “Our new coffee machine arrived just in time, so we were really lucky,” the facility head happily releaved. Operational manager Antonio Politi had selected this one personally and prepared one coffee after the other in high-throughput for their guests.

“Users who come to us on a frequent basis can also be introduced to operating this great espresso machine in addition to the microscopes,” he offered smiling. The new microscopes, which Lenart and Politi presented to the visitors in small groups with the support of technical assistant Jasmin Jakobi, also attracted a lot of attention. Currently, the microscopes are strongly frequented by employees from the Departments of *Genes and Behavior, Meiosis,* and *Cellular Logistics*. Further systems are to be purchased gradually, in line with the needs of the institute‘s staff.

We wish the facility a good start and many happy microscopy enthusiasts! (cr)

Thomas Burg appointed professor at the Technical University Darmstadt

The head of the Max Planck Research Group *Biological Micro- and Nanotechnology* assumed his new position on September 1, 2018.

Which experiences and memories will you keep from your time at the MPI-BPC?
The MPI-BPC is unique in its scientific diversity, and the collaborative spirit here at the institute is exceptional. Furthermore, from the start I was impressed by the excellent service and support. Everyone, not only the scientists, but also the staff at the administration, central services, and facilities share an enthusiasm for a joint mission – this is something you do not see like that in many other places.

What convinced you to accept the offer from the TU Darmstadt?
In Darmstadt, I have the opportunity to work on research projects with a long-term perspective. The TU Darmstadt is an outstanding university with great students in my field, so I also look forward to teaching and having contact with students at all levels. It was therefore an easy decision for me to accept the offer.

What are your goals in the next years?
While the lab is gradually migrating to Darmstadt, we will expand our research on microsystems to connect live-cell imaging, cryo-light microscopy, and cryo-electron microscopy. Associated with this are many intriguing challenges that will keep us busy for the next few years. For example, we want to better understand the physical principles that govern the limits of vitrification (ice crystal-free freezing) in cells and tissues of different size and composition. In parallel, we will explore the many opportunities in superresolution light microscopy that emerge from the high stability of fluorescent molecules at cryogenic temperature. Darmstadt is perfect for this type of research due to the interaction between engineering and natural sciences within the Rhein-Main-region. And, of course, I look forward to continuing our many fruitful collaborations in Göttingen and especially at the MPI-BPC, which has been a fantastic home for our group over the past nine years.

What do you like most about your work as a scientist?
It is great that I can work together with young people with whom I share the same interest. It is always a thrill to conceive something and then make it work in the lab. This more than compensates for the inevitable failures you are bound to experience from time to time.

Did you want to stay in Germany? Would you have moved abroad?
I am very happy that I received the offer from the TU Darmstadt, but if it had not worked out I would have applied abroad, as well. However, for my family staying in Germany was definitely the first choice. (Interview: fk)

Thomas Burg
studied physics at the ETH Zurich (Switzerland) and received his PhD from the Massachusetts Institute of Technology (MIT) in Cambridge (United States) in 2005. He has been heading the Max Planck Research Group *Biological Micro- and Nanotechnology* at the MPI-BPC since 2009.

New Campus Seminar series – an experiment to foster multidisciplinary conversation

Research groups and individual scientists sometimes tend to work in isolation. With its innovative concept, the new Campus Seminar series at the Göttingen Max Planck Campus is designed to overcome this isolation and to promote exchange between the scientific disciplines at the institute. The series is organized by eight research group leaders of the MPI-BPC and the MPI for Dynamics and Self-Organization. Three of them – Alex Faesen, Stefan Glöggler, and Juliane Liepe – were interviewed by the representatives of our institute's PhD/Postdoc Community.

(Photo: ibg)

Have you attended a seminar in a different field that enhanced your work or made you land in a new job?

Alex Faesen (AF): I did my PhD in a famous cancer institute, but my background was not biology and I had never heard of p53, an extremely well-studied cancer gene. My PhD laboratory worked only tangentially on cancer. So the only way for me to get a good understanding of cancer research was to attend student and postdoc seminars. I am glad I had that foresight, as having a broad conceptual understanding of scientific fields other than your own is invaluable in later stages of your career. Diversity matters, on many levels.

Stefan Glöggler (SG): I was trained as a chemist and was very much exposed to investigating catalysts and materials during my studies. During talks and seminars of students and postdocs from different departments and research institutions, I discovered my interest in connecting what I have learned as a chemist with questions related to biochemistry and biology. This combination of interests has become a strong drive that motivates my research.

Juliane Liepe (JL): I was initially trained in biochemistry. During the first years of my degree I attended seminars in theoretical physics. To be totally honest, this was not completely voluntary as we had to visit seminars from unrelated fields to be admitted to the exams. During those seminars I realized, however, that there is a different way of thinking specific to every field. In those seminars I was confronted with different approaches and tools. This surely triggered in me the interest to combine approaches from different fields in my later research and it became decisive for my scientific career so far.

How will the audience benefit from this new Campus Seminar series with a mix of two topics in an hour?

AF: The science in our institute is very diverse, so this will introduce an extra challenge when presenting your work. Compared to your normal group meeting or specialized conference, the speaker will have to distill the presentation down to the concepts and principles. Details will be less important. This is an incredible skill to learn, and one that does take practice. Only when you really master your topic, you will be able to explain it simply.

Additionally, science is increasingly multidisciplinary, something that is valued highly during grant applications and by journals. Ideally, collaborations start at the level of students and postdocs, which we hope to catalyze with these meetings. At the very least, the seminar can stimulate exchange of ideas and show the scientists which possibilities there might exist in other disciplines from which your own research question could heavily benefit.

JL: Working in a highly interdisciplinary field, I cannot stress enough how important it is to be able to communicate with experts from different fields despite we all use different languages. With the Campus Seminar we hope to provide a platform to practice both, understanding talks from a different discipline as well as communicating your research to non-experts.

We aim to provide a smart, friendly, and community-based platform to encourage early career scientists to exchange their ideas, thoughts, and concepts. We try our best on the organizers' side to ensure this, but the platform relies on the people who attend.

Is there a chance that some audience will leave after the first talk?

AF: We are all busy people, so it is understandable that sometimes you only have time for that one talk that you really want to see, and we (and the speaker) would be very happy that you did decide to come, despite that the order of speakers will only be decided on the spot. In order to help everyone in their planning, we aim to be relatively strict with the time. However, since you can have lunch while listening to the talks, you potentially do not lose time at all.

We will not police people, but will encourage people to stay by providing an important service and forum to the PhD/Postdoc Community. In the end, we hope that people will see the value of staying and spend that little extra time. Do you really want to be that person that walks out of that room for all (including the next speaker) to see?

JL: Or, would you like to be the second speaker, who spent time and energy in preparing a non-expert talk, who has to watch part of the audience leaving?

SG: I would like to stress in particular how useful it is to be exposed to a different aspect of research even if it is outside of someone's field. Seminars from different research topics will expose you to a whole new angle of seeing and approaching things. Very often new ideas develop in the process of following such talks, ultimately benefiting your own research. One hour per week to develop and improve your out-of-box-thinking is really well spent and even off-topics may surprise you in the end. So why would you leave half-way through a session that has so much to offer?

What is the best thing that you foresee this initiative will bring?

AF: Our main motivation is to invest into the PhD/Postdoc Community. For me, meetings like these were often the highlight of my week. If you feel inspired, if you have learned something new or even got ideas you can employ in your own research: That would be the best reward.

Interview: PhD/Postdoc Community representatives

As with any experiment, scientists value feedback to move forward; the campus seminar organizers appreciate your feedback and constructive criticism on this initiative. Kindly contact:
Alex Faesen (*afaesen@mpibpc.mpg.de*)
Stefan Glöggler (*stefan.gloeggler@mpibpc.mpg.de*)
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Göttinger Nacht des Wissens 2019

Auch bei der 4. Nacht des Wissens am 26. Januar 2019 können Sie wieder Einblick nehmen in die vielfältige und spannende Welt der Forschung und Lehre am Göttingen Campus. Auf kleine und große Wissenschaftsbegeisterte warten spannende, überraschende Mitmach-Aktionen, Vorträge, Experimente und ein Science Slam. Mitwirkende sind neben der Universität Göttingen die Universitätsmedizin, die außeruniversitären Einrichtungen und die weiteren Hochschulen am Campus.

Unser Institut wird gemeinsam mit dem MPI für Experimentelle Medizin sowie dem MPI für Dynamik und Selbstorganisation erneut im MPI für Sonnensystemforschung seine Aktionen präsentieren. Unser herzlicher Dank geht schon einmal an unsere dortigen Gastgeber, die uns immer so nett aufnehmen – und an unsere Abteilungen und Forschungsgruppen, die sich bei der Nacht des Wissens mit großem Einsatz engagieren!

Am Stand der Abteilung *Theoretische und computergestützte Biophysik* können Sie eintauchen in die Welt der Proteine und bei der Abteilung *Gene und Verhalten* ermitteln, ob Sie Frühaufsteher, Nachteule oder keins von beiden sind. Doch warum müssen wir überhaupt schlafen? Antworten darauf geben die Mitmach-Aktionen der Forschungsgruppe *Schlaf und Wachsein*. Experimente der Abteilung *Meiose* wiederum stehen unter dem Motto: *Am Anfang war das Ei!* Erwachsene können hier ebenso wie die Kleinsten die Geheimnisse der Eizelle erforschen. Und wer noch mehr über Vorgänge in unserem Körper erfahren will, ist beim Vortrag von Jens Frahm *MRT-Filme in Echtzeit — Bewegungen unseres Körpers live verfolgen* um 19 Uhr bestens aufgehoben.

Eine Übersicht aller Angebote bei der 4. Nacht des Wissens finden Sie auf *www.ndw.uni-goettingen.de* (cr)

Göttingen Science Night 2019

The 4th Science Night on January 26, 2019, will once again provide insights into the diverse and exciting world of research and teaching at the Göttingen Campus. Surprising hands-on activities, lectures, experiments, and a science slam await science enthusiasts of all ages. The Science Night is organized by the University of Göttingen, the University Medical Center, as well as the non-university institutions and other colleges in Göttingen.

Our institute, together with the MPI for Experimental Medicine and the MPI for Dynamics and Self-Organization, will again present their research at the MPI for Solar System Research. Our heartfelt thanks go to our wonderful hosts there – and to our departments and research groups who participate in the upcoming Science Night!

At the booth of the Department of *Theoretical and Computational Biophysics* you may dive into the world of proteins and at the Department of *Genes and Behavior* you can find out whether you are an early riser, a night owl, or neither. But why do we have to sleep at all? Answers may be found in the hands-on activities of the Research Group *Sleep and Waking*. Experiments of the Department of *Meiosis*, on the other hand, folllow the motto: *In the beginning there was the egg!* Here, adults as well as the youngest can explore the secrets of the egg cell. And if you want to learn more about what happens in our body, join Jens Frahm's lecture *MRI movies in realtime – following movements in our body live* at 7 pm (lecture in German).

You may find an overview of all events at the 4th Science Night at *www.ndw.uni-goettingen.de* (cr)

Participants and organizers of the *Horizons* meeting 2018. *(photo: ibg)*

Horizons turns 15: Looking back at the scientific fiesta of 2018

Over 250 researchers from 30 countries together with renowned scientists joined us at the MPI-BPC for the special 15th anniversary *Horizons in Molecular Biology* symposium.

Fifteen years ago, *Horizons in Molecular Biology* was conceived by the students of the *IMPRS in Molecular Biology* to widen their own horizons beyond the rut of classes and lab work. The symposium has since grown from a humble idea to one of the most sought-after events in Göttingen. It aims to bridge the gap between young researchers and experienced scientists by providing them a platform for interaction. The four-day long event included a career fair, scientific talks, poster sessions, panel discussions, speed dating, and career workshops. The social events in the evenings offered time to relax and network in informal settings. It was great fun to hear one's favorite scientist's talk in the morning and share the dance floor with them in the evening.

The eclectic career fair had speakers from academia, industry, science communication, consulting, and even modeling. Their unique stories inspired and reassured the audience that there is more than meets the eye for one's future. Daisy Robinton, a scientist as well as a fitness and lifestyle model highlighted the importance of taking opportunities as they come. Ben Glick, the founder of *SnapGene*, revisited the story of how his frustrations from DNA cloning led to a fruitful creation. Interactive workshops on science communication and academia-to-industry transition were a hit and saw many people take part.

Osamu Nureki kickstarted the scientific event with his talk on visualizing CRISPR-Cas9 action in real time. True to the theme of the event, he wore a special DNA tie. Floyd Romesberg explored the curious cases of expansion of the genetic alphabet. Elizabeth Villa's exciting talk presented stunning glimpses inside cells revealed by the cryo-electron tomography tools developed in her lab. Michael Sheehan's witty style kept the audience engaged on his work on evolution of social intelligence in paper wasps. Arguably, one of the most interesting talks was given by Polly Matzinger on her revolutionary *Danger Model of Immunity*. Polly's chalk-and-talk style without any slides but lots of interaction with the audience was appreciated by everyone. The last day saw a stimulating panel discussion on *Troubles of a young scientist: Fantastic ideas and where to find them*, moderated by Mary Osborn of our institute.

A new year has dawned upon us, a new *Horizons* lies ahead of us. Preparations for the 16th edition of the symposium are already underway. Our confirmed speakers include John Briggs, Randy Hampton, Jen Heemstra, Gaia Pigino, and Leonie Ringrose. We are excited to see more enthusiastic faces join us so please save the dates September 9-12, 2019.

Ninadini Sharma on behalf of the Horizons organizing committee

GWDG Info

Samba-Server gehören schon seit mehr als 20 Jahren zum festen Bestand bei der GWDG, haben sich im Einsatz bewährt und sind bis auf Weiteres unverzichtbar. Sie stellen für den Göttingen Campus die zentralen Druckdienste und einen Zugang zu den persönlichen UNIX-Speicherbereichen für Arbeitsplatzrechner bereit, wobei die Nutzung überwiegend unter Windows, aber auch unter macOS oder FreeBSD/Linux erfolgen kann.

Am 23. August 2018 fand das diesjährige, von der GWDG veranstaltete **Treffen der Institutsadministratoren** auf dem Max-Planck-Campus in Göttingen statt. Themenschwerpunkt waren die weitreichenden Änderungen im Bereich Massenspeicher in den vergangenen Monaten.

Das von der DFG geförderte Projekt ***GFBio***, an dem auch drei Göttinger Einrichtungen beteiligt sind, ist im August 2018 in seine dritte Förderphase gegangen. Der Fokus in dieser Phase liegt auf der Etablierung von GFBio als zentrale Kontaktstelle und Dienstleister für mit nationalen Mitteln geförderte Forschende und Forschungsprojekte beim Datenmanagement in der Biologie und den Umweltwissenschaften, der Harmonisierung und Verbreitung der Archivierungs- und Informationsdienste sowie der Sicherstellung als langfristige Infrastruktureinrichtung über die Förderphase hinaus.

Anfang Oktober 2018 fanden in Göttingen mit 30 Teilnehmern die erste **Nutzerschulung auf dem neuen Hochleistungsrechner HLRN-IV** sowie das halbjährliche **Treffen der HLRN-Fachberater** statt. Nach einer längeren Testphase mit nur wenigen Nutzern wurde die erste Phase des HLRN-IV am 11. Dezember 2018 für alle Nutzer geöffnet und ist somit in den Produktionsbetrieb übergegangen.

Weitere Informationen finden Sie in den GWDG-Nachrichten 11/2018 und 12/2018. Alle Ausgaben der GWDG-Nachrichten finden Sie im WWW unter dem URL *www.gwdg.de/gwdg-nr*

Thomas Otto

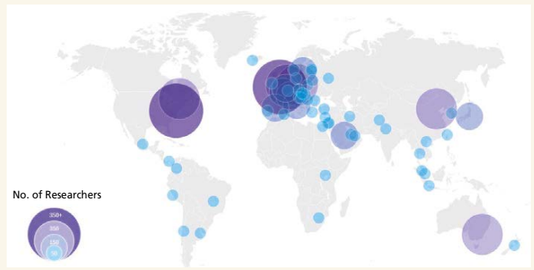
Influential Max Planck authors

76 Max Planck scientists are among the most highly cited researchers 2018. The list also includes 17 Nobel Laureates. One of them is Stefan Hell, Director at the MPI-BPC.

The *Clarivate Analytics* citation analysis, now in its fifth year, provides information about researchers who have published the most highly cited publications in recent years. In addition to the research areas, the corresponding institutions are also listed. With a total of 356 successful scientists, Germany ranks fourth among the scientific locations after the United States, Great Britain, and China. Among the research organizations, the Max Planck Society ranks fifth behind Harvard University (United States), the National Institutes of Health (United States), Stanford University (United States), and the Chinese Academy of Science.

The methodology that determines the who's who of high-impact researchers draws on the data and analysis performed by bibliometric experts from the *Institute of Scientific Information* at *Clarivate Analytics*. The publication and citation data come from the *Web of Science*, a web-based database for scientific and commercial purposes containing the scientific literature of over 30,000 journal titles.

Modified from a press release of the Max Planck Society



Science hotspots: The most successful scientists work in North America, Europe, and China. Australia is catching up. *(Image: Clarivate Analytics)*

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