# 19TH HORIZONS IN MOLECULAR BIOLOGY

## International PhD Student Symposium
## and
## Career Fair for Life Sciences

12-15th September 2022
Göttingen, Germany

Booklet by Horizons Organizing team 2022,
InDesign template provided by Sara Osman, Katharina Seitz,
InDesign Layout: Atmika Paul
Cover Design by: Carmela Cruz, Atmika Paul
Edited by: Atmika Paul, Naintara Jain, Jannis Anstatt
Group Pictures: Irene Böttcher-Gajewski, MedienService, MPI-BPC

## Acknowledgements

The decision to reintroduce Horizons as an in-person conference was finalised in October of 2021, and gave us a very exciting yet challenging goal to work towards. For some of us it brought back memories of participating in Horizons as new students in Göttingen and the wonderful experience it had been – seamlessly planned and meant to provide a place for students to talk to and learn directly from established scientists in a relaxed yet scientifically charged environment. While many of us had previously helped organise the Horizons held online during the COVID-19 pandemic in 2020 and 2021, none of us had actually experienced the behind-the-scenes logistics required for an in-person Horizons catering to over 250 participants and guests! In our journey over the last 12 months, we have learnt and grown, stumbling and falling, and finally finding our way. This journey would have been impossibly hard without the support of many, and we would like to thank everyone whose contribution helped us on the way!

To begin with, we thank Dr Steffen Burkhardt and Kerstin Grüniger from the IMPRS Molecular Biology Coordiation office, without whose experience and advice, Horizons would not be what it is. They helped us give shape to our vision of Horizons and to plan and execute each step on the journey to reach the final outcome today. Thank you both for all your inputs and problem-solving help!

As you can see in the booklet, we have support from many people and companies whose encouragement and financial aid make Horizons possible. Their support allows us to invite a large number of participants each year and provide food, prizes, and even this booklet itself! We are also proud that Horizons is privileged to be the recipient of the patronage of the Federal Ministry of Education and Research, represented by Federal Minister Stark-Watzinger. Such support reinforces the importance of student participation in international scientific conferences.

We would like to thank the Georg-August University of Göttingen and the Max Planck Institute for Multidisciplinary Sciences, for their support and help, as well as letting us use their facilities and resources for the Symposium. We appreciate the support of Michael Hartig and Peter Lösel, without whom we would have no technical setup, and a very empty foyer. We would also like to thank the MPI-Nat Media Service, especially Irene Böttcher-Gajewski and Johannes Pauly, for their help and contribution in taking wonderful (and fun) photographs of Horizons over the years, printing our posters, schedules, name tags, coupons and banners, as well as putting our events on the screens in the MPI-Nat foyer. We would also like to thank Uwe Krüger for serving us a delicious spread during the conference. The Happy Hour Community also has our gratitude for letting us share this tradition with our conference participants and helping us organize a joint MPI-Horizons Happy Hour on 15th September. We would also like to share our appreciation for the MPI-fahrbereitschaft, who are kind enough to help transport our speakers so that we can enjoy their knowledge and company.

We would like to take a moment and share our appreciation for past organizers and friends who have supported us. Thank you for guiding us and giving advice when we needed it the most. Thanks also to our labs and colleagues for supporting us so that we could give our best to Horizons. Last but not the least, a big thank you to the entire organizing team for their commitment, creativity and sheer grit! We gave it our best, learnt a lot and are now ready to march forward towards Horizons, welcoming all our guests, and hoping to have a wonderful event!

*From the Horizons Organizing Committee 2022*

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***Greetings from the Horizons Organizing Committee 2022 !***

## Welcome to the 19th Horizons in Molecular Biology!

Horizons in Molecular Biology was conceived as a symposium by PhD students, for PhD students. Established by the students of the *International Max Planck Research School for Molecular Biology*, it was meant to provide a platform for young researchers to learn about the cutting-edge advancements taking place in the field of Molecular Biology beyond their own niche area. Further, it provided an opportunity to interact with leading scientists and network in an informal and fun environment.

After two years of keeping the spirit of Horizons alive online, this year we are happy to welcome the participants back to Göttingen in-person. The 19th Horizons promises a 4-day festival with scientific talks, career fair, poster sessions, a panel discussion and lots of opportunities to socialize and engage with scientists at all stages of their career.

While some of our distinguished speakers will be joining us from around the globe via video-conferencing, most of our guests will be present in Göttingen to share not only their amazing research, but will also be available for students to engage, possibly during the poster sessions, social activities and even the plentiful number of coffee breaks planned.

For those who are more focused on the next steps in their career, our career fair offers many talks as well as workshops. Special speed dating sessions further give students a chance to network and personally interact with the guests from different fields.

This year we also want to address the topic ***"Who gets the credit - how does recognition for scientific discoveries work"*** in our panel discussion and hear opinions from different perspectives – PIs, Post-docs and students. The discussion follows a highly dynamic format, and time permitting, allows for a great amount of audience participation.

As Horizons is a student symposium, we would like to encourage and motivate our peers. The awarded talks and poster sessions provide students an opportunity to share their work with peers and experts alike. Amongst the many awards being offered for poster presentations, we have a popular vote award, where all participants are welcome to vote for their favorite poster!

Our endeavour is to provide an opportunity for all participants to network and interact with graduate students from across the globe and enjoy themselves during the social events! We hope all our guests enjoy the symposium and take back with them not only new discoveries and friends (and maybe the exciting lottery gift!), but fond memories and unforgettable experiences as well!

*From the Horizons Organizing Committee 2022*

## Organizing Committee

The 19th PhD Student Symposium Horizons in Molecular Biology is organized by a group of PhD students of the International Max Planck Research School for Molecular Biology in Göttingen.

**Jannis Anstatt**
MPI for Multidisciplinary Sciences,
Nano-Biophotonics

**Monica Gobran**
MPI for Multidisciplinary Sciences,
Cytoskeletal Dynamics in Oocytes

**Gantavya Arora**
MPI for Multidisciplinary Sciences,
Physical Biochemistry

**Vaishali Goyal**
MPI for Multidisciplinary Sciences,
Physical Biochemistry

**Nilanjan Ghosh Dastidar**
MPI for Multidisciplinary Sciences,
Physical Biochemistry

**Naintara Jain**
University Medical Center Göttingen,
Cellular Biochemistry

**Nesil Eşiyok**
German Primate Center,
Degenerative Diseases

**Delong Li**
IMPRS Molecular Biology
Master Student

**Mareike Lohse**
MPI for Multidisciplinary Sciences,
Molecular Neurobiology

**Dimitra Tsouraki**
MPI for Multidisciplinary Sciences,
Genome Organization and Regulation

**Annabel Maisl**
MPI for Multidisciplinary Sciences,
Tissue Dynamics and Regeneration

**Çağıl Urhan**
University Medical Center Göttingen,
Cellular and Molecular Immunology

**Sumeru Panta**
MPI for Multidisciplinary Sciences,
Structural Dynamics

**Malena von Elling-Tammen**
University Medical Center Göttingen,
Translational Epigenetics

**Atmika Paul**
University Medical Center Göttingen,
Molecular Oncology

**Ana Vučković**
IMPRS Molecular Biology Master Student

## Partners

The 19th International PhD Student symposium ”Horizons in Molecular Biology” is financially supported by the following institutions through the International Max Planck Research School for Molecular Biology:

GEORG-AUGUST-UNIVERSITÄT GÖTTINGEN IN PUBLICA COMMODA SEIT 1737

MAX-PLANCK-GESELLSCHAFT

## Donors

The PhD Student Organizing Committee would like to thank the following companies and organizations for their support:

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| Career Fair | | Plenary Lectures | | | | | |
|---|---|---|---|---|---|---|---|
| Monday: 12th September | | Tuesday: 13th September | | Wednesday: 14th September | | Thursday: 15th September | |
| 10:00 am | Opening Ceremony | 09:00 am | Opening Ceremony | 09:00 am | Nina Papavasiliou | 09:00 am | Dimple Notani |
| 10:15 am | Chiara Pastore | 09:15 am | James Rothman | 09:45 am | Chris Proud | 09:45 am | Tamal Das |
| 10:45 am | Coffee Break | 10:30 am | Coffee Break | 10:30 am | Coffee Break | 10:30 am | Coffee Break |
| 11:00 am | Bishoy Hanna | 10:45 am | Konstanze Winklhofer | 10:45 am | Tom Rapoport | 10:45 am | Tal Dagan |
| 11:30 am | Coffee Break | 11:30 am | Alexey Amunts | 11:30 am | Luca Scorrano | 11:30 am | Kushagra Bansal |
| 11:45 am | Satya Prakash Dash | 12:15 pm | Lunch Break | 12:15 pm | Lunch Break | 12:15 pm | Lunch Break |
| 12:15 pm | SPEED DATING I | 02:30 pm | Shiv Pillai | 01:00 pm | Kerstin Göpfrich | 02:30 pm | Cassandra Extavour |
| 12:45 pm | Khalil Abou Elardat | 03:15 pm | Azim Surani | 01:45 pm | Student Talk 1 | 03:15 pm | Marieke Oudelaar |
| 01:00 pm | Lunch Break | 04:00 pm | Coffee Break | 02:05 pm | Student Talk 2 | 04:00 pm | Coffee Break |
| 02:00 pm | Oliver Rinner | 04:15 pm | Prerana Shrestha | 02:25 pm | Student Talk 3 | 04:15 pm | Orly Laufman |
| 02:30 pm | Coffee Break | 05:00 pm | Alice Ting | 02:45 pm | Group Picture | 05:00 pm | Sonja Lorenz |
| 02:45 pm | Claudia Walther | 05:45 pm | Coffee Break | 03:00 pm | Tyler Jacks | 05:45 pm | Coffee Break |
| 03:15 pm | Coffee Break | 06:00 pm | Panel Discussion | 03:45 pm | Olivier Duss | 06:00 pm | Barbara Treutlein |
| 03:30 pm | Marc Gerauer | | | 04:30 pm | Coffee Break | 06:45 pm | Closing ceremony |
| 04:00 pm | SPEED DATING II | | | 04:45 pm | Meytal Landau | | |
| Workshops | | Poster Sessions | | | | | |
| Workshop 1 : 10:00 am - 01: 00 pm | | Poster Session 1 | | Poster Session 2 | | Poster Session 3 | |
| Workshop 2: 02:00 pm - 05: 30 pm | | 12:15 pm - 02:15 pm | | 05:30 pm - 07:00 pm | | 12:15 pm - 02:15 pm | |

| Social Hours | | | |
|---|---|---|---|
| Monday | 12th September | 8:00 pm | Cafe & Bar Celona |
| Tuesday | 13th September | 8:00 pm | Deutsches Theatre |
| Wednesday | 14th September | 6:00 pm | Wine & Cheese |
| Thursday | 15th September | 7:00 pm | Happy Hour at Faßberg |

# GENERAL INFORMATION

## Admission to Plenary Lectures

Admission to plenary lectures is free and restricted to registered participants.

## Poster Sessions

If you are presenting a poster you will be given your poster number during registration. The number will serve as an identification mark for our poster committee.

| Poster sessions | | |
|---|---|---|
| **13th September** | 12:15 pm - 02:15 pm | **Poster session 1** |
| **14th September** | 05:30 pm - 07:00 pm | **Poster session 2** |
| **15th September** | 12:15 pm - 02:15 pm | **Poster session 3** |

## Poster Prizes

Four poster prizes – three jury adjudged best posters and one popular vote - will be awarded for posters presenting innovative research at the symposium. All registered participants presenting a poster are eligible for the prize. The participants must however be available and present their poster during one of our poster sessions to the jury. Our exciting prizes for this year are €50 Amazon vouchers.

## Social Hours

***Monday - Join us for a beer! -*** *8pm, BarCelona (Weender Landstraße 3)*
The organizers invite everyone, both participants and speakers, to join us for a beer - or any other beverage of your choice. Food and drinks are self paid.

***Tuesday - Conference Dinner & Party -*** *8pm, Deutsches Theater (Theaterplatz 11)*
For one of the traditional highlight of Horizons, the organizers invite all conference package holders and speakers for a dinner and party in the cellar of the Deutsches Theater. Food and water are provided, other drinks are self paid.

***Wednesday - Wine and Cheese Poster Session -*** *5:30 pm, MPI-Nat*
Dive into the diverse research presented by young scientists through their posters in an informal setting framed by wine and cheese.
Wine and cheese are provided.

***Thursday - Closing HappyHour -*** *7pm, MPI-Nat*
Celebrate the end of another Horizons in Molecular Biology Symposium by joining us for a traditional MPI-Nat HappyHour including pizza, beer, and great company!
Pizza is provided, beer is self paid.

## Awarded Student Talks

**Awarded Talk 1:**

**Florian Kabinger (Poster P30)**
*MPI-NAT (Wed., September 14, 13:45-14:05)*

**Awarded Talk 2:**

**Alejandro Aguilera Castrejon (Poster P40)**
*Weizmann Institute of Science (Wed., September 14, 14:05-14:25)*

**Awarded Talk 3:**

**Francesca Lugarini (Poster P14)**
*MPI-NAT (Wed., September 14, 14:25-14:45)*

## History of Horizons

December 4th, 2003. The seminar room in Göttingen Center for Molecular Biosciences was bustling with activity. Organizers darted in and out of the room, making sure everything was in order and as it should be. Speakers attempted to look through their talking points, whilst entertaining the many curiosities of the next generation gathered around them. The graduate students themselves, whispered to each other and waited apprehensively, with thinly veiled excitement, for the program to begin. There were just under a hundred eager minds crowded into that one room. Students and researchers; all brought together by a shared passion: a passion for science. This was the inaugural Horizons in Molecular Biology Conference: An International PhD Student symposium!

The conference has come a long way since then. Over the years, the number of participants grew steadily and increased in variety. Horizons now regularly attracts around three hundred participants from over thirty countries. The symposium has featured numerous renowned researchers, representing a wide range of fields in the life sciences. This exhaustive list also included several Nobel Laureates, namely: Martin Chalfie, Sir John Walker, Ada Yonath, Thomas Südhof, Kurt Wüthrich, Carol Greider, Venki Ramakrishnan, Sir John Gurdon, Tim Hunt, Michael Rosbash, Richard Henderson, last year, Christiane Nüsslein-Volhard and this year James Rothman.

Horizons has also evolved continuously as each new batch of student organizers brings a fresh perspective and new ideas, proving consistently that you can make a good thing better! In 2006, the organizers introduced a Poster Session accompanied by Student Talks. PhD students presented over a hundred posters and a select few were given the chance to present their work to an audience of peers and professors. Building on this, in 2007, Horizons launched its first Career Fair in conjunction with the conference. The fair offered budding scientists an opportunity to connect with industry and network with life science professionals with different backgrounds and perspectives. Representatives from over twenty companies were present at the inaugural Career Fair, conducting live interviews and CV checks. Today, the Career Fair has adopted a major role in the conference, offering workshops held by professionals, and interactive discussions with key figures in the modern life science industry. All catered to the needs of a young scientist.

At the heart of Horizons, is an idea: An International Scientific Conference from PhD students for PhD students. Organized by students from Göttingen's International Max Planck Research School for Molecular Biology, Horizons in Molecular Biology provides an interactive experience in a relaxed environment. It aims to bridge the gap between young scientists and experienced researchers and bring together experts and novices from various fields of the life sciences to engage in a productive dialogue and exchange information. Modern discovery is persistently progressing from exploring rainforests in faraway lands to observing the nature of life under a microscope. We are the modern explorers, and are committed to keep progressing forward, in the pursuit of science, towards the Horizon.

## IMPRS for Molecular Biology

For the 19th time, the Horizons symposium is organized by students of the International Max Planck Research School (IMPRS) for Molecular Biology at the University of Göttingen. The Molecular Biology Program is jointly conducted by various departments of the University of Göttingen, the University Medical Center Göttingen, the Max Planck Institute for Multidisciplinary Sciences, and the German Primate Center. The common aim is to offer an intensive, research-oriented education in order to prepare the students for a professional career in the life sciences. This broad spectrum of topics is mirrored in the fields covered by Horizons. In addition to the small classes and specialized hands-on laboratory courses, the intercultural experience is extraordinary. Excursions, culture nights and workshops with students from all over the world naturally become a "seminar" on intercultural communication.

Students can join the program after completing their Bachelor studies. During the first year, students receive a broad education in molecular biology through lectures, lab rotations and methods courses delivered by the participating institutions. From the second year, the students conduct their own research during their MSc or PhD thesis projects and receive further training in specialized methods and skills courses within the Göttingen Graduate Center for Neurosciences, Biophysics and Molecular Biosciences (GGNB), which is funded by the German Excellence Initiative.

In September 2000 the first brave students from as far away as Ghana, China, Mexico and Malaysia came to Göttingen to join the new International MSc/PhD Molecular Biology Program. Today, with the twenty-second of twenty students joining the IMPRS, the program has become very successful as demonstrated by excellent evaluations, awarded prizes, and applications from all over the world. By now, more than 175 students have successfully defended their PhD theses within the program and kissed the Gänseliesel. Kissing this statue that stands on a fountain on the marketplace in the middle of the city and giving her flowers is an old tradition for Göttingen PhD students.

For more detailed information about the International MSc/PhD Molecular Biology Program in Göttingen, please take a look at our website:

*www.gpmolbio.uni-goettingen.de*

## About Göttingen

The renowned university town of Göttingen lies in the center of Germany in southern Niedersachsen (Lower Saxony) between the Harz mountains and the Weser river. Its establishment dates back to 953, it was chartered in 1210 and flourished as a member of the Hanseatic League.

A glimpse of this hanseatic opulence is still present today in the medieval Town Hall, the splendid churches and quaint half-timbered houses in Gothic, Renaissance and Baroque styles. Göttingen's landmark is the "Gänseliesel", an art nouveau statue of a girl herding geese on top of the fountain on the market square, outside the Old Town Hall. Traditionally, all new doctoral graduates of the University kiss the cheeks of the statue after passing their examinations, making her "the most kissed girl in the world".

The Georg-August University was founded in 1734 and today has 14 faculties with 24,000 students. The university sends forth many famous scientists – amongst its alumni are 42 Nobel laureates. Especially many famous mathematicians come from Göttingen: Carl Friedrich Gauss, Bernhard Riemann and David Hilbert, to name only a few.

Apart from the university, the city is also home to many research institutes, such as Max Planck Institutes, and international companies.

Nearly untouched by bombings in World War II, the city center is now an attractive place to live in with many shops, small cafes and chic bars. Consequently, many students live here, giving Göttingen a young face: in 2003, almost half of the population of the inner city was between 18 and 30 years of age. Today Göttingen has approximately 120,000 inhabitants including 31,000 students, giving it the charm of a small and lively university city.

## Practical Information

**Certificates of attendance**
Certificates of attendance will be emailed upon request at the registration desk.

**Insurance**
The Organizing Committee accepts no responsibility for accidents or damage to participants' private property. Please make your own arrangements for all the necessary insurance.

**Internet**
Free Wi-Fi internet (eduroam) is available throughout the symposium in the lecture facilities. If you do not have access to eduroam, please contact the registration desk.

**Parking**
Participants can use the parking lots available near the MPI for Multidisciplinary Sciences Faßberg campus.

**Buses**
The buses numbered 21, 22 and 23 to the city center leave just outside the symposium venue at the bus stop "Faßberg". Bus schedules are available at the registration desks.

**Taxi**
Taxis to the city center can be arranged by calling one of the many Göttingen taxi companies:

- Göttinger-Funk-Taxi-Zentrale: 0049-0551 69300
- Puk minicar: 0049-0551 484848

Please note that taxis are considerably more expensive than public transport, and only accept cash.

**Organizers**
In case you have any difficulties, you are always welcome to ask for help from one of the organizers. Just look out for students wearing a Horizons t-shirt and get in touch with us regarding your issue.

**Services**
Registered participants are entitled to the following: Admission to plenary lectures, conference material (certificate of participation, name badge, conference bag) and refreshments during coffee breaks.

Participants who opted for the conference package, in addition to the above, get vouchers for lunch, city tour, conference dinner and party as well as a hard copy conference booklet.

# CAREER FAIR


## Career Fair - Schedule

### Monday: 12th September

| | | |
|---|---|---|
| 10:00am | Opening Ceremony | 10:00am |
| | | |
| Career Fair: | | |
| | | |
| 10:15am | Chiara Pastore | |
| | | |
| 10:45am | Coffee Break | |
| | | Workshop 1 |
| 11:00am | Bishoy Hanna | |
| | | |
| 11:30am | Coffee Break | |
| | | |
| 11:45am | Satya Prakash Dash | |
| | | Academic writing: How to create good texts |
| 12:15pm | SPEED DATING: | |
| | Chiara Pastore/ Bishoy Hanna/ Satya Prakash Dash | |
| 12:45pm | Khalil Abou Elardat | |
| | | |
| 1:00 pm | Lunch Break | 1:00 pm |

| | | |
|---|---|---|
| | | |
| 2:00 pm | Oliver Rinner | 2:00 pm |
| | | |
| 2:30 pm | Coffee Break | |
| | | Workshop 2 |
| 2:45 pm | Claudia Walther | |
| | | |
| 3:15 pm | Coffee Break | |
| | | |
| 3:30 pm | Marc Gerauer | |
| | | Academia as springboard into other sectors |
| 4:00 pm | SPEED DATING: | |
| | Oliver Rinner/ Claudia Walther/ Marc Gerauer | |
| | | |
| | | |
| | | |
| | | 5:30 pm |

## Welcome to the 16th Career Fair for Life Sciences

Your PhD is the starting point of your career. But have you ever wondered: what is a career in science? A Post-Doc and tenure track to become a group leader? A position in a big biotech company? What are my options?
The answer is that with a PhD in the natural sciences, you have an ocean of options. Certainly, more than two! During your PhD you will acquire skills and a mind-set sought after everywhere.
In this year's Horizons Career Fair, you'll have the chance of meeting six inspiring people, all with a background in the natural sciences, now having diverse careers in publishing, patent law, science management, start-ups, or industry. They will share their experience about making important career choices, alternative career paths, leadership, promoting gender equality, sustainable innovations and many more.

In addition, we offer you to take part in 2 different workshops, that will allow you to hone your scientific writing skills and guide you to use academia as a springboard for a future into other sectors.
Join the Horizons Career Fair 2022 and broaden your Horizons!

Career Fair Organizers

## Chiara Pastore

*Senior Editor,*
*Nature Nanotechnology*

Monday
10:15 am

Chiara has a first degree and a PhD in chemistry, obtained from the University of Pisa and from Scuola Normale Superiore, Pisa. During her PhD she focused on the structural biology and biochemistry of iron binding proteins, carrying out research in Pisa, at EMBL in Heidelberg and at the National Institute for Medical Research in London. She then moved to Columbia University in NYC to work on protein-RNA interactions at then back to the UK, at Imperial College London, where she studied viral proteins. She started her editorial career in October 2015 at Nature Communications & joined Nature Nanotechnology in June 2017, where she handles papers in the areas of nanobiotechnology and nanomedicine. Chiara is based in London.

In her presentation, she will introduce her job as a scientific editor in one of the journals of the Nature family. She will talk about her day-to-day tasks, from assessing manuscripts to looking for referees and interacting with the community. She will try to highlight what are the skills required and the personal qualities that will make the job easier. She will further talk about the highs and lows of being an editor and will go through the path she followed to become one.

## Bishoy Hanna

*Global Medical Affairs Lead, Merck*

Monday
11:00 am

By acting as a link between R&D and health care professionals and key opinion leaders, the medical affairs unit plays a key role in drug development. Are you interested in learning more about the role of medical affairs? Are you wondering what a typical day for a medical affairs lead looks like? Would you like to know which skills are essential to succeed in medical affairs? If your answer is yes, you are more than welcome to join my talk. My name is Bishoy Hanna. I am an alumnus of the Molecular Biology program, Göttingen. In my current role, I am part of the Global Medical Affairs team at Merck KGaA. I will be happy to share with you more about my role and answer your questions about medical affairs. Looking forward to meeting you!

Medical Affairs is a function that plays a key role in drug development by generating impactful insights to help shape the company's medical strategy. In his current position as a consultant working closely with the Global Medical Affairs team at Merck Healthcare KGaA, Bishoy has the chance to contribute to drug development and make an impact on the patients' journey. Bishoy Hanna is originally from Egypt. He completed his Master's in 2017 at the MSc/PhD Molecular Biology, Georg-August-Universität Göttingen, Germany. He was later awarded a Marie-Curie fellowship to pursue his PhD studies in the group of Professor Thomas Helleday at Karolinska Institute, Sweden. During his PhD studies, Bishoy focused on studying the oxidative DNA damage response in cancer and inflammatory conditions and how to exploit it using novel small-molecule inhibitors. Bishoy's strong scientific background together with his passion for medical affairs enable him to support the development of Merck's oncology portfolio in the field of DNA damage response (DDR) and ultimately help bring it to the clinic.

## Satya Prakash Dash

*CEO BITS BioCyTiH Foundation &*
*Founding & Former Head Strategy*
*BIRAC*

Monday
11:45 am

Dr Satya Dash is a national innovation ecosystem designer, technology strategist, policy and implementation expert. He contributed to the growth of Indian biotech & medtech innovation landscape by designing, implementing & driving 17 national programs which have cumulatively supported more than 2000 startups/innovators & 60 incubators. He also built 12 partnerships for BIRAC (Nesta, WISH Foundation, TiE, Indian Angel Network & others). Previously he was COO ABLE (nodal biotech industry body) and former Director Global Innovations at PATH & Consultant to Nesta. Recently he joined as the Founding CEO of BITS BioCyTiH, hosted by BITS Pilani across 3 campuses, funded by the Government of India, to push innovations in bio-cyber-physical systems. He is a Board Member at Venture Center, Pune, India's largest S&T incubator, advises several startups & is a Honorary Trustee at Surabhi Foundation (a creative arts focused entity).

***Embedding and navigating my journey to drive systems' change, build & transform an architecture of biomed innovation in India***

How does one fashion and design a meaningful career in national and international innovation policy and implementation? What role does personal interests, environment, mentorship, serendipity, health and other factors play when charting a career path where things seem hazy and unclear? My talk will cover the directions and turns (& tribulations) from my days in academic labs to driving "systems change" in biomedical innovation in India & personal reflections on "what next questions", "epiphany", "being a nomad" & career "nirvana".

## Oliver Rinner

*Founder, CEO, Biognosys AG, Switzerland*

Monday
02:00 pm

Oliver is cofounder of Biognosys AG, a leading company in next generation proteomics tools and services. A biochemist and psychologist by training, he founded the company as a spin-off from ETH Zurich, where he was working as a post-doc in the lab of Prof. Ruedi Aebersold. Oliver will discuss his motivation to move from academia into entrepreneurship, the first steps in founding a company, and important learnings on the way. He will also give insights into financing and commercialization.

Oliver was a co-founder of Biognosys in 2008 and is leading the company as CEO, starting as a spin-off from ETH Zurich to a market-leading inventor and provider of proteomics technology that Biognosys is today. He holds a diploma in Psychology and Biochemistry from the University of Zurich and did his Ph.D. in psychophysics and behavioral molecular genetics at the ETH Zurich. In his post-doctoral studies in the group of Ruedi Aebersold (ETH), he developed algorithms and methods for quantitative mass spectrometry, which formed the basis for the technology that Biognosys develops today.

## Claudia Walther

*Advisor,*
*Boehringer Ingelheim Fonds*

Monday
02:45 pm

For nearly 14 years, until the end of June 2022, Dr. Claudia Walther was the Managing Director of the Boehringer Ingelheim Fonds, Foundation for Basic Research in Biomedicine, in Mainz (Germany), a non-profit organisation internationally known in particular for its PhD programme and the International Titisee Conferences. In a honorary capacity, she is also responsible for the Siblings Boehringer Ingelheim Foundation for the Humanities; from 2009 to June 2020 she was also Managing Director of the Boehringer Ingelheim Foundation. Before joining the three charities, she worked for the vfa in Bonn, the German association of research-based pharmaceutical companies, and for the German Cancer Research Center in Heidelberg. She pursued her PhD and postdoctoral research in molecular developmental biology with Prof. Peter Gruss at the former Max Planck Institute for Biophysical Chemistry in Göttingen (Germany). She studied biology, physics and chemistry at the Universities of Heidelberg and Sussex (UK).

Studying sciences and completing a PhD is an excellent jumping-off point to a fulfilling career in many different areas and walks of life. During this long and intense education and training phase one has not only become an expert in a particular subject matter and built a network in one's scientific community. Many other skills have been developed and honed: e. g. analytical and critical thinking skills, dealing with and systematically solving complex problems, persistance and frustration tolerance, processing an overwhelming amount of information and pursuing a longterm goal. Communication and interpersonal skills as well as professional project management are usually not sufficiently trained during a PhD but are often as important. Bottom line: Given all those skills there are many possible „pathways" in particular since the „war on talent" between companies is on (and one can change if the first choice did not fulfil expectations!).

Monday
03:30 pm

## Marc Gerauer

*Partner, Patentanwalt,*
*European Patent Attorney,*
*Kraus & Weisert*
*Patentanwälte PartGmbB*

***From medication to application***

The talk will give inventors who were yet not frequently involved with patents a first overview over the patent application proceedings. Anyone who has an innovative idea should consider filing a patent application to safeguard the rights to the idea. However, it is a long way from the idea to a patent. Not all ideas can be protected by a patent and the examination procedures at the Patent Offices are in many cases time-consuming and complex. It will be explained what kind of protection is achievable with a patent, and the requirements which an idea has to fulfil to get a patent will be described.

Gerauer studied chemistry at the Heinrich Heine University Düsseldorf. He received his doctorate at the University of Dortmund and the Max-Planck-Institute of Molecular Physiology. He has published in several high impact journals, like Cell and Nature Chemical Biology. From 2008 to 2010, Dr. Gerauer trained in the field of intellectual property at a patent law firm and qualified as a German Patent Attorney in 2011, subsequently joining Isenbruck Bösl Hörschler LLP. Dr. Gerauer qualified as a European Patent Attorney in 2013 and joined Kraus & Weisert in 2017. For several years now, his primary practice has been focused on patents in the technical fields of organic chemistry, polymers, biochemistry, pharmaceutical chemistry, and related areas. Dr. Gerauer provides advice in the area of patent and trademark law with particular focus on questions regarding national and international prosecution and the defence and enforcement of protective rights against third parties.

## Dr. Khalil Abou Elardat

*Head of Application Support Department, Singleron Biotechnologies*

Monday
12:45 am

Dr. Khalil Abou Elardat has been working in the field of biology for 17 years and analyzing next generation data for 9 years. He earned his MSc in biology from the American University of Beirut in 2006 and a PhD in applied biological sciences from Ghent University in 2011. He currently heads the Application Support Department at Singleron Biotechnologies, GmbH. Additionally, Khalil works as a bioinformatician analyzing single-cell RNA sequencing data from various organs and species

***Dimensionality reduction of my life***

In his short talk, Dr. Khalil Abou Elardat will share with us his career journey - from his PhD, to his current employment at Singleron Biotechnologies.

# WORKSHOPS

**Bartlett Warren-Kretzschmar**

*Teacher of Environmental Planning,*
*Leibniz University Hannover,*
*Coach for scientific communication*
*at Golin Wissenschaftsmanagement*

*Monday*
*10:00 am*

## Academic writing: How to create good texts

### WORKSHOP 1

Bartlett Warren-Kretzschmar, Hanover, was born in New York and studied Landscape Architecture and Environmental Planning at Cornell University. She has been teaching courses in landscape architecture and environmental planning at both American and German universities for the past forty years. At the Leibniz University in Hanover, she has taught and researched for 30 years. Moreover, she was a guest professor in the international Master of Landscape Architecture programme at the Anhalt University of Applied Sciences in Bernburg and professor in the Bioregional Planning Programme at Utah State University, where she also offered courses in research skills and scientific writing, as well as communication and rhetoric.

For many young scientists writing is the most difficult part of research work. Poor structure, breakneck formulations and unclear argumentation lead to texts which are not too user friendly. However, for the success of academics it is essential that the content is successfully conveyed to the relevant target groups – from the subject community to the wider public.

In this workshop the process of academic writing is highlighted from the first idea through the structuring and formation of the text to its completion. The participants engage with the content related, formal and organisational aspects of writing. The following topics are covered:

- **Abstract, article, thesis:** Text types and reasons for writing in academia
- **From idea to text:** Topic selection, structure, argumentation
- **Writing as a process:** Utilising creative bursts – avoiding blocks
- **Academic writing:** My next steps

*Monday*
*02:00 pm*

**Dr. Gaby Schilling**

*Business Coach, Kepos, Düsseldorf*

## Academia as springboard into other sectors

### WORKSHOP 2

This workshop is designed to give the participants an insight into the sometimes unknown world of private businesses.

The following questions will be addressed in this short workshop: What are the cultural differences between private industry and academia? What are the advantages/disadvantages of public and private business? What kind of jobs are out there and what sort of personality/mindset is necessary to be successful in industry? How can I apply for a job if I don't even understand what the job offers mean? And where shall I start looking for a job?

Gaby earned her doctorate in chemistry and holds a B. Sc. in psychology.
For more than 17 years she held various leading positions in an internationally operating DAX 30 company in Germany and the US and was heading teams of experts and managers in research, product development and product safety. She has thus gained profound first-hand experience in all phases of collaboration with employees – from recruitment over career development and promotion to change of career.
Qualifications to business coach and team coach complement her practical experience. Since 2012 Gaby has been working as coach and consultant for natural scientists. She also runs workshops and trains groups whereby the main focus is on the transition from science into industry and taking over leadership tasks.

## Speed Dating

Along with talks and exciting workshops, we have a ‘Speed Dating’ event in the line-up. Here, the participants get a chance to talk to the speakers of choice face to face. During the lunch break, this event gives you an opportunity to interact with the speakers in a personal and informal environment. In small groups, you will get to meet two speakers and discuss for half an hour each all the questions that pop in your heads.

# PLENARY LECTURES

Developmental Biology 

Immunology 

Cell Biology 

Molecular Medicine 


Genome Biology 

Biochemistry & Biophysics 

## Plenary Lectures - Schedule


### Plenary Lectures

| Tuesday: 13th September | | Wednesday: 14th September | | Thursday: 15th September | |
|---|---|---|---|---|---|
| 09:00 am | Opening Ceremony | 09:00 am | Nina Papavasiliou | 09:00 am | Dimple Notani |
| 09:15 am | James Rothman | 09:45 am | Chris Proud | 09:45 am | Tamal Das |
| 10:30 am | Coffee Break | 10:30 am | Coffee Break | 10:30 am | Coffee Break |
| 10:45 am | Konstanze Winklhofer | 10:45 am | Tom Rapoport | 10:45 am | Tal Dagan |
| 11:30 am | Alexey Amunts | 11:30 am | Luca Scorrano | 11:30 am | Kushagra Bansal |
| 12:15 pm | Lunch Break | 12:15 pm | Lunch Break | 12:15 pm | Lunch Break |
| 02:30 pm | Shiv Pillai | 01:00 pm | Kerstin Göpfrich | 02:30 pm | Cassandra Extavour |
| 03:15 pm | Azim Surani | 01:45 pm | Student Talk 1 | 03:15 pm | Marieke Oudelaar |
| 04:00 pm | Coffee Break | 02:05 pm | Student Talk 2 | 04:00 pm | Coffee Break |
| 04:15 pm | Prerana Shrestha | 02:25 pm | Student Talk 3 | 04:15 pm | Orly Laufman |
| 05:00 pm | Alice Ting | 02:45 pm | Group Picture | 05:00 pm | Sonja Lorenz |
| 05:45 pm | Coffee Break | 03:00 pm | Tyler Jacks | 05:45 pm | Coffee Break |
| 06:00 pm | Panel Discussion | 03:45 pm | Olivier Duss | 06:00 pm | Barbara Treutlein |
| | | 04:30 pm | Coffee Break | 06:45 pm | Closing ceremony |
| | | 04:45 pm | Meytal Landau | | |

### Poster Sessions

| Poster Session 1 | Poster Session 2 | Poster Session 3 |
|---|---|---|
| 12:15 pm - 02:15 pm | 05:30 pm - 07:00 pm | 12:15 pm - 02:15 pm |

# PLENARY LECTURES

**Tuesday, 13th September**

©Alena Soboleva

Prof. Dr. James Rothman

*Yale School of Medicine*

Tuesday
09:15 am

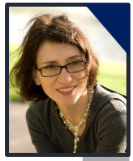
## Molecular choreography of synaptic vesicle fusion revealed by cryo-electron microscopy and cell-free reconstitution

Sub-millisecond release of neurotransmitters sets the pace of information processing in the brain, and represents evolution to the limits of physical chemistry. The key physical principle is mechanical coupling of SNARE proteins embedded in locally rigid bilayers. Theory suggest that as few as 3 and not more than ~6 such SNAREs will trigger fusion in <1 millisecond. Cryo-electron tomography of synapses reveals there are exactly six SNAREpins under each synaptic vesicle, spaced equally in a ring. Reconstitution shows that the calcium ion sensor and SNARE-clamping protein Synaptotagmin self-assembles into rings of a similar diameter, and the effects of mutations suggest that the *in vivo* rings depend on the ability of Synaptotagmin to oligomerize. Preventing oligomerization de-synchronizes release and increases spontaneous release. High resolution cryo-electron microscope crystallography of the central SNAREpin assembly chaperone Munc13 bound between lipid bilayers reveals unexpected oligomeric arrangements, including a hexameric ring that would be expected to template six circularly symmetrical SNAREpins. This suggests a tightly choreographed process of vesicle capture and activation as Munc13 ratchets the vesicle successively closer to the plasma membrane, coordinating the components that assemble to generate a ready-release vesicle.

James E. Rothman is the Sterling Professor of Cell Biology at Yale University and chairs Yale School of Medicine's Department of Cell Biology. His research has elucidated the molecular mechanisms and machinery governing vesicle traffic in the cell, explaining such diverse processes as the secretion of hormones like insulin, the action-potential controlled release of neurotransmitters in synaptic transmission, and the propagation of membrane compartments of the cytoplasm during cell growth and division. This work has been recognized by many awards, including the Albert Lasker Award for Basic Biomedical Research (2002), the Kavli Prize for Neuroscience (2010), and the Nobel Prize in Physiology or Medicine (2013). Rothman graduated from Yale College (1971) with a BA in Physics, then attended Harvard Medical School (1971-1976) as an MD-PhD student, leaving before completing the MD program. Before returning to Yale in 2008 he held professorships at Stanford, Princeton, and Columbia Universities, and was Vice-Chairman of the Sloan-Kettering Institute for Cancer Research.

Prof. Dr. Konstanze Winklhofer

*Ruhr-University Bochum*



Tuesday
10:45 am

## Mitochondria as a platform for ubiquitin signaling

Mitochondria are increasingly recognized as cellular hubs to orchestrate signaling pathways that regulate metabolism, redox homeostasis, and cell fate decisions. Mitochondria also play a role in innate immune signaling, however, the mechanisms of how mitochondria affect signal transduction are poorly understood. Our recent research revelaed that the NF-κB pathway activated by the tumor necrosis factor (TNF) employs mitochondria as a platform for signal amplification and shuttling of activated NF-κB to the nucleus. TNF induces the recruitment of HOIP, the catalytic component of the linear ubiquitin chain assembly complex (LUBAC), and its substrate NEMO to the outer mitochondrial membrane, where M1- and K63-linked ubiquitin chains are generated. NF-κB is locally activated and transported to the nucleus by mitochondria, resulting in an increase in mitochondria-nucleus contact sites in a HOIP-dependent manner. Notably, TNF-induced stabilization of the mitochondrial kinase PINK1 contributes to signal amplification by antagonizing the M1-ubiquitin-specific deubiquitinase OTULIN.

Dr. Winklhofer is a cell biologist interested in the pathomechanisms underlying development of neurodegenerative diseases. Her research activities are focused on ubiquitin signaling at the interface between stress protection and immune responses, regulation of the proteostasis network and mitochondria as signaling organelles. Dr. Winklhofer studied Pharmacy at at the Ludwig Maximilians University (LMU) Munich, Mayo Medical School Rochester, USA, and University of Zurich, Switzerland. She performed her doctoral studies in molecular virology at the Max Planck Institute for Biochemistry, Martinsried. She trained as a postdoctoral fellow at the Max Planck Institute for Biochemistry, and got her Habilitation from the Faculty of Chemistry and Pharmacy at the LMU Munich. She continued her studies as a group leader at the LMU, and at German Center for Neurodegenerative Diseases in Munich. After a research stay at the National Institutes for Health, National Institute of Neurological Disorders and Stroke, Biochemistry Section, Bethesda, USA she moved to Bochum, where she is chair of the Molecular Cell Biology Department at the Ruhr University Bochum since 2013.

Prof. Dr. Alexey Amunts

*Science for Life Laboratory*

Tuesday
11:30 am

## How genes become machines in mitochondria

The mitoribosome translates specific mitochondrial mRNAs and regulates energy production that is a signature of all eukaryotic life forms. We present cryo-EM analyses of its assembly intermediates, mRNA binding process, and nascent polypeptide delivery to the membrane. To study the assembly mechanism, we determined a series of the small mitoribosomal subunit intermediates in complex with auxiliary factors that explain how action of step-specific factors establishes the catalytic mitoribosome. It features a mitochondria-specific protein ms37 that links the assembly to translation initiation. A delivery of mRNA is then performed by a 150kDa protein LRPPRC that forms a stable complex with a small binding partner SLIRP. In mammals, LRPPRC stabilises mRNAs co-transcriptionally, thus it links the entire gene expression system. Through the translation cycle, a nascent polypeptide is delivered to the mitochondrial inner membrane, and we report the mitoribosome structure bound to the insertase OXA1, which elucidates the basis for protein synthesis coupling to membrane delivery. Finally, comparative structural and biochemical analyses reveal functionally important binding of cofactors NAD, ATP, GDP, iron-sulfur clusters and polyamines. Together with experimental identification of specific rRNA and protein modifications, the data illuminate principal components responsible for the translation of genetic material in mitochondria.

Alexey Amunts earned his PhD from Tel Aviv University for work on a plant Photosystem I, and did a postdoc at the Laboratory of Molecular Biology in Cambridge on cryo-EM studies of a mitoribosome that became known as the 'Resolution Revolution'. In 2016, he established an independent group at Stockholm University focusing on mechanisms of mitochondrial translation and bioenergetics, and since 2020 he is an Associate Professor. The group studies mitochondrial protein synthesis and energy production at the molecular and cellular level, and examines how these fundamental processes are affected by natural selection and disease.

The talk presented by Alexey Amunts for Horizons is an EMBO Young Investigator Lecture

Prof. Dr. Shiv Pillai

*Harvard Medical School*

Tuesday
02:30 pm

## Human extrafollicular and memory B-cell subsets in vaccination and disease

T-dependent B cell responses occur in two geographic locations, extra-follicularly and in the germinal center. The relevance of both these locations to immunity and memory B cell formation will be discussed in the context of vaccination, COVID-19 and human autoimmunity. How the immune system is altered by infections such as COVID-19 and how aberrant immune responses can result from infectious insults will also be a topic that will be broadly covered.

Shiv Pillai MD PhD is a Professor of Medicine and Health Sciences and Technology at Harvard Medical School. He is the director of the Harvard PhD and MMSc Immunology programs and of the HMS-HST MD student research program. He is also the program director of an NIH-funded Autoimmune Center of Excellence at Massachusetts General Hospital. Dr. Pillai coined the term "surrogate light chains" for proteins that he identified as part of the pre-B receptor, that drives early B cell development. His laboratory postulated and provided evidence for the first ligand-independent signaling model during lymphocyte development and showed that BTK, the product of the gene mutated in X-linked agammaglobulinemia, is functionally linked to the pre-B receptor and the B cell receptor. His laboratory is currently located at the Ragon Institute of MGH, MIT and Harvard and his group studies T cell-B cell collaboration and its relevance to autoimmune and inflammatory diseases including IgG4-related disease, systemic sclerosis, common variable immunodeficiency and COVID-19.

Prof. Dr. Azim Surani

*University of Cambridge*

Tuesday
03:15 pm

Azim Surani received his PhD at Cambridge University (1975) under Robert Edwards, established his lab at the Animal Research Station in Cambridge (1979) and was elected Marshall-Walton Professor at the Gurdon Institute (1992) and later Director of Germline and Epigenetics Research (2013). His research led to the discovery of genomic imprinting (1984), which is critical for totipotency and mammalian development, and pivotal for advances in epigenetics, including the unique epigenetic resetting of the mammalian germline. Surani also elucidated the hitherto unknown genetic basis of previously unknown germ cell specification in humans (2015) and other mammalian species. His awards include a Royal Medal, McEwen Award by the ISSCR, Rosenstiel Award, Genetics Society's Mendel Medal and the Gairdner International Award. He is a Fellow of the Royal Society.

## Genomic imprinting, human development and the 'immortal' germline

The germline generates the totipotent state at fertilisation, where the parental genomes make an equal genetic contribution. However, the mammalian parental genomes exhibit an epigenetic asymmetry with distinct functions due to genomic imprinting. Genomic imprinting is an essential component of mammalian evolution and placental viviparity, accompanied by a significant change in the strategy for vertebrate development. Development in mammals includes two epigenetic resetting events that commence with the specification of primordial germ cells (PGC) for totipotency and during preimplantation development for pluripotency. Parental genomes and epigenomes play an essential role in development, balancing embryonic growth and development, mammalian physiology, behaviour and metabolism. Advances in human germline and early development require animal proxies and stem cells derived *in vitro* models for mechanistic studies.

Prof. Dr. Prerana Shrestha

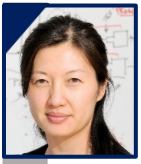
*Stony Brook University*

Tuesday
04:15 pm

## Cell type-specific nascent protein synthesis during memory consolidation

Long-term memories are often formed when the event involves a threat and triggers survival behaviour. As a consequence, sensory cues present during the threat can form a long-term association with it. While it is known that transformation of associative memories from labile state to long-term form requires new protein synthesis in discrete brain regions, the specific neural pathways that are recruited during memory consolidation and the mechanisms that control the dynamics of protein synthesis in these pathways are not yet understood. This knowledge is important not only for gaining a deeper understanding of spatiotemporally resolved protein synthesis in memory processes but also for targeted therapeutic intervention in disorders of emotional memories such as PTSD. Using Pavlovian and instrumental threat conditioning paradigms in mice, we aim to understand the neurobiological substrates for modulation of emotional memories by threat intensity and volitional control. Two key modes for protein synthesis, namely the eukaryotic initiation factor 2 (eIF2) and eIF4E dependent translation, are thought to be crucial for associative emotional memories. By regulating these modes of translation in specific cell types in the brain we aim to understand the molecular players that govern consolidation of long-term memories in both healthy and diseased brain states.

Prerana Shrestha is an Assistant Professor in the Department of Neurobiology & Behavior at Stony Brook University in the Renaissance School of Medicine. Her lab studies cell type-specific protein synthesis dynamics during memory processes in both healthy and diseased brain states. Prerana received her Ph.D. in Life Sciences from The Rockefeller University. She did her postdoctoral work at NYU Center for Neural Science, where she developed novel chemogenetic strategies to block nascent protein synthesis with cell type specificity and applied them to probe protein synthesis requirement in memory consolidation. She has received several accolades for her work – she was named the Molecular and Cellular Cognition Society (MCCS) Scholar in 2017, and more recently she has been named a Sloan Research Fellow in 2022. Prerana is also a recipient of the Anuradha Rao Memorial travel award, and a NARSAD Young Investigator grant.



Prof. Dr. Alice Ting

*Stanford University*

Tuesday
05:00 pm

Alice Ting is Professor of Genetics, Biology, and by courtesy, Chemistry at Stanford University. She was born in Taiwan, raised in Dallas, Texas, and received her degrees from Harvard (AB) and UC Berkeley (PhD), training with EJ Corey, Peter Schultz, and Roger Tsien. Alice started her independent laboratory at MIT in 2002, and was recruited to Stanford in 2016. Alice's work straddles the interface of chemistry and biology and the molecular technologies she has invented, such as proximity labeling, have transformed the study of cells and neurons. She has received the NIH Pioneer Award, the Arthur Cope Scholar Award, and the McKnight Technological Innovations in Neuroscience Award. Alice has been a Chan Zuckerberg Biohub investigator since 2017.

## Chemogenetic and optogenetic technologies for probing molecular and cellular networks

In my talk, I will describe molecular recorders that we are developing for scalable, single cell recording of past cellular events (calcium, protein localization, extracellular antigens, etc). I will also describe proximity labeling-based methods to map proteome trafficking and dynamics in living cells.

# PLENARY LECTURES

**Tuesday, 14th September**

Prof. Dr. Nina Papavasiliou

*German Cancer Research Center*

Wednesday
09:00 gm

Prof. Dr. Papavasiliou has a long-standing interest in molecular processes that generate informational diversity in a cell or organism. These include DNA mutation and RNA editing and modification, both crucial for the establishment of an optimal immune response. Equally, such processes are also at work in organisms (like the African trypanosome) that have evolved to evade the immune response. She has studied DNA mutation (in the context of mammalian antibody diversification), and RNA editing and modification (in innate immune cells), to understand the benefit of diversity for the immune response both in health and disease. Her lab has studied with equal intensity how parasites like the African trypanosome have evolved similar diversification mechanisms to evade the immune response (and has furthermore used the trypanosome as a tool to manipulate immune responses).

## RNA editing in Immunotherapy

RNA deamination (also known as editing) is a frequent epitranscriptomic modification. Here, we explore its contribution to cancer pathogenesis (Diffuse Large B Cell Lymphoma). We demonstrate that DNA mutations and RNA editing events are often mutually exclusive, suggesting that tumors can modulate pathway outcomes by altering sequences at either the genomic or the transcriptomic level. We further show that in DLBCL, RNA editing targets transcripts within known disease-driving pathways. Finally, using targeted RNA base editing tools to restore editing to specific transcripts in ADAR1-deficient cells, we demonstrate that editing is causal to an increase in the downstream signaling output of the transcript-encoded protein. I will discuss these data as well as potentially ADAR-based “therapeutic” approaches in cancer immunotherapy.

Wednesday
09:45 am

Prof. Dr. Chris Proud

*South Australian Health and Medical Research Institute*

## CAPturing the control of mRNA translation

The control of protein synthesis (mRNA translation) plays crucial roles in shaping the proteome. It is tightly regulated by signaling pathways, including mTORC1 and oncogenic MAP kinases. Faulty control of mRNA translation causes cancers and neurological diseases. Translation requires binding of mRNAs' m7G-cap to initiation factor eIF4E. We developed a novel method (capCLIP) to comprehensively capture and quantify the mRNAs associated with eIF4E in living cells, which we term the 'cap-ome'. We applied capCLIP to examine the control of the cap-ome in specific settings. First, we explored the effect of rapamycin (inhibits mTORC1) on the eIF4E cap-ome. Rapamycin is thought to inhibit translation of so-called TOP (terminal-oligopyrimidine) mRNAs by displacing eIF4E from their caps. capCLIP confirmed that rapamycin does indeed decrease representation of TOP mRNAs in the cap-ome, validating our methodology and refined the requirements for a functional TOP sequence. We then applied capCLIP to probe the consequences of eIF4E phosphorylation, which is controlled by MAP kinase signaling. capCLIP shows phosphorylation of eIF4E reduces its overall association with mRNAs and preferential dissociation of mRNAs with short 5′-UTRs. capCLIP is a valuable new tool to probe impact of specific signaling pathways on the cap-ome. It can reveal novel insights into the control of gene expression.

Professor Chris Proud studies the intracellular signaling pathways that control protein synthesis (mRNA translation). Recent research concerns the regulation of protein synthesis in neuronal cells, cancer cell biology and the molecular mechanisms involved in diet-induced obesity. A particular focus are protein kinases that control the protein synthesis machinery, i.e., mammalian target of rapamycin, elongation factor 2 kinase and the MAP kinase-interacting kinases. Between 2005-2008, Chris Proud was Head of the Department of Biochemistry & Molecular Biology at the University of British Columbia and served as co-Director of UBC's Life Sciences Institute. At the University of Southampton (2008 – 2014), he led a substantial research team studying the control of protein synthesis and ribosome biogenesis in settings such as cancer and neurological disorders. In 2014, Chris Proud moved to Adelaide to become Theme Leader: Nutrition and Metabolism at the SAHMRI. In 2019, Chris Proud was appointed to the position of Theme Leader: Lifelong Health.

Prof. Dr. Tom Rapoport

*Harvard Medical School*

Wednesday
10:45 am

Dr. Tom Rapoport received his Ph.D. from Humboldt University (Berlin) and then joined the Zentralinstitut für Molekularbiologie der Akademie der Wissenschaften der DDR in Berlin. In 1995, he became a Professor of Cell Biology at Harvard Medical School in Boston, and in 1997, a Howard Hughes Medical Institute Investigator. Tom Rapoport is a member of the National Academies of USA and Germany.

In early work, Tom Rapoport developed the Metabolic Control Analysis (MCA) (with Reinhart Heinrich). Subsequently, he elucidated the mechanism of protein translocation across the endoplasmic reticulum (ER) membrane, which culminated in the determination of the first structure of a protein-conducting channel (together with Steve Harrison). He also studies the mechanism of ER-associated protein degradation (ERAD), recently determining the structure of the retro-translocon and elucidating the function of the Cdc48/p97 ATPase. Rapoport also studies how the ER is shaped and how proteins are imported into peroxisomes.

## Mechanism of protein import into peroxisomes

Peroxisomes are ubiquitous organelles whose dysfunction causes fatal human diseases. Most peroxisomal enzymes are imported in a folded state from the cytosol by the receptor PEX5, which interacts with a docking complex in the peroxisomal membrane and then returns to the cytosol for the next import cycle. We have used Xenopus egg extract to demonstrate that PEX5 accompanies cargo completely into the lumen, utilizing WxxxF/Y motifs near its N terminus that bind a lumenal domain of the docking complex. PEX5 recycling is initiated by an amphipathic helix that binds to the lumenal side of a membrane-embedded, heterotrimeric ubiquitin ligase complex. Biochemical data and a cryo-EM structure indicate that the N terminus of PEX5 inserts into an open pore of the ligase complex, positioning a conserved cysteine for monoubiquitination by one of the three RING fingers of the ligase complex. Finally, PEX5 is extracted from the lumen, resulting in the unfolding of the receptor and cargo release. Current efforts are directed towards an understanding of how folded cargo is imported into peroxisomes.

Prof. Dr. Luca Scorrano

*University of Padova and Veneto Institute of Molecular Medicine*

Wednesday
11:30 am

## Keeping mitochondria in shape: a matter of cell life and death

In the last years, mitochondrial ultrastructural and morphological changes have been implied in the control of several physiological and pathological changes, including the progression of apoptosis, inflammation, differentiation, tumorigenesis. However, the role of mitochondrial dynamics in the control of complex cellular cues and in response to reversible and irreversible cellular damage is not yet clarified. We will overview the key experiments that shed light on the role of mitochondrial shape and ultrastructure in cell physiology, pathology and in disease and offer a personal perspective on the missing pieces of the puzzle that await to be studied.

Luca Scorrano is Professor of Biochemistry at the Department of Biology, University of Padua (Italy). He completed his Medical Degree (1996) and his PhD in Molecular and Cellular Biology and Pathology (2000) at the University of Padua with Paolo Bernardi. From 2000 to 2003 he was Human Frontier Science Program (HFSP) postdoctoral fellow at Dana-Farber Cancer Institute, Harvard Medical School in Boston (USA), in the lab of the late Stanley J. Korsmeyer, a founding father of the field of apoptosis. In 2003 he was awarded an Assistant Scientist position at the Dulbecco-Telethon Institute, in 2006 he was recruited as Full Professor at the University of Geneva (Switzerland). In 2013 he moved to the University of Padova as Professor of Biochemistry (appointed by chiara fama) and from 2014 to 2020 he served as Scientific Director of the Veneto Institute of Molecular Medicine.

He was elected EMBO Member in 2012 and Member of the Academia Europaea in 2019 and he is among the Clarivate Highly Cited researchers in 2021.

Dr. Kerstin Göpfrich

*MPI for Medical Research*

Wednesday
01:00 pm

## Synthetic cells: *De novo* engineering with DNA nanotechnology

Can we construct a cell from non-living matter? In search for answers, bottom-up synthetic biology has successfully encapsulated functional sets of biomolecules inside lipid vesicles, yet a “living” synthetic cell remains unattained. Instead of relying exclusively on biological building blocks, the integration of new tools can be a shortcut towards the assembly of active and eventually fully functional synthetic cells. This is especially apparent when considering recent advances in DNA nanotechnology. DNA nanotechnology allowed us to engineer various functional parts for synthetic cells, which, meanwhile have found diverse applications as biophysical probes in cell biology. Recently, we engineered functional DNA-based mimics of a cytoskeleton. These cytoskeletons are capable of stimuli-responsive reversible assembly, cargo transport and can deform giant unilamellar lipid vesicles (GUVs) from within. We further demonstrate the division of GUVs based on phase separation or spontaneous curvature increase and osmosis rather than the biological building blocks of a cell’s division machinery. We derive a parameter-free analytical model which makes quantitative predictions that we verify experimentally. Ultimately, by coupling GUV division to their informational content and their function, we aim for a prototype of a synthetic cell capable of evolution.

Kerstin Göpfrich is the Max Planck Research Group Leader of the "Biophysical Engineering" group at the Max Planck Institute for Medical Research in Heidelberg, Principal Investigator in the Cluster of Excellence "3D Matter Made to Order" at KIT and Heidelberg University, and Fellow of the Max Planck School "Matter to Life". Her research focuses on the construction of artificial cells from custom-engineered components. With the help of DNA/RNA nanotechnology, functional components are created that equip lipid vesicles with properties of living cells. For example, the team succeeded in producing artificial cytoskeletons or controlling the division of synthetic cells. Kerstin Göpfrich received, among others, the Women Interactive Materials Award and the Hector Career Development Award. She was awarded a Marie Skłodowska Curie Fellowship and received one of the prestigious Gates Cambridge Fellowships from the Bill & Melinda Gates Foundation.

Wednesday
03:00 pm

## Prof. Dr. Tyler Jacks

*Massachusetts Institute of Technology*

This presentation will focus on the use of genetically engineered mouse models of cancer to examine key questions in tumor evolution and tumor immunology. Through the use of gene targeting technologies, CRISPR-based gene editing and other methods, the Jacks laboratory has constructed a series of models of lung adenocarcinoma, pancreatic cancer and colon cancer. These models have been subjected to deep molecular profiling, including at the single cell level, to reveal details of tumor progression and intra-tumoral heterogeneity. Furthermore, these models have been modified to express one or more tumor antigens, which allows for the investigation of anti-tumor immune responses as well as mechanisms of immune escape. Tumor-immune interactions have also been explored using immunopeptidomic studies in both mouse models and human samples.

Tyler Jacks, PhD, is the Founding Director of the Koch Institute for Integrative Cancer Research at MIT, the David H. Koch Professor of Biology at MIT, and head of the Lustgarten Pancreatic Cancer Research Laboratory at MIT. Dr. Jacks is also President of Break Through Cancer, a foundation committed to supporting multi-disciplinary teams of researchers with a goal of finding new solutions to the most intractable challenges in cancer. He was a long-time Investigator of the Howard Hughes Medical Institute (1994 – 2021). He received his bachelor's degree in Biology from Harvard College, and his doctorate from the University of California, San Francisco, where he trained with Nobel Laureate Harold Varmus. He was a postdoctoral fellow with Robert Weinberg at the Whitehead Institute before joining the MIT faculty in 1992. Dr. Jacks received the AACR Outstanding Achievement Award, the Amgen Award from the American Society of Biochemistry and Molecular Biology, the Paul Marks Prize for Cancer Research, and the AACR Princess Takamatsu Memorial Lectureship.

Dr. Olivier Duss

*European Molecular Biology Laboratory*

Wednesday
03:45 pm

## Real-time tracking of transcription-translation coupling

In prokaryotic cells, transcription and translation occur in the same compartment, enabling a functional interaction between both gene expression machineries. Several studies, including recent high-resolution structures, demonstrate a physical link that establishes coupling between both machineries either mediated by direct interactions between the RNAP and the ribosome or by factor-mediated interactions via the transcription factors NusA and NusG. In contrast, recent work challenges the notion that transcription and translation are generally coupled. To understand what promotes coupling and how it is regulated, we reconstituted *in vitro* the complete active transcription-translation coupling system and developed multicolor single-molecule fluorescence microscopy assays to track in real-time how single RNA molecules are actively transcribed (Duss et al., Cell, 2019) and simultaneously translated by the ribosome. Furthermore, by site-specifically labeling the ribosome and the RNAP, we can detect the direct physical coupling between both machineries. Overall, by tracking the conformation and interaction dynamics of individual molecules over time, these methods allow us to investigate how different macromolecular machines cooperate to fine-tune gene expression.

Olivier Duss studied Chemistry at the ETH Zurich. After traveling for 6 months, teaching Chemistry at a high school and doing a research stay with Kurt Wüthrich, he did a PhD in the group of Prof. Fred Allain at the ETH Zurich developing integrative structural biology approaches (combining NMR with electron paramagnetic resonance) for structure determination of dynamic protein-RNA complexes and investigating how bacterial non-coding RNAs regulate translation initiation (Duss, Alain, Nature, 2014). In 2014, he then moved to California to do a joint-postdoc in the labs of Jamie Williamson at Scripps Research and Jody Puglisi at Stanford University where he developed single-molecule fluorescence microscopy approaches to study co-transcriptional ribosome assembly (Duss, …, Puglisi, Williamson, Cell, 2019). Since the end of 2020, he has been a group leader at the European Molecular Biology Laboratory in Heidelberg, where he studies how RNA folds and how protein-RNA complexes assemble in context using a combination of single-molecule techniques, structural biology and biochemistry.

Prof. Dr. Meytal Landau

*Technion – Israel Institute of Technology*

Wednesday
04:45 pm

## Virulent and Antimicrobial Amyloids in Infections and Neurodegeneration

Amyloids are protein fibers with unique and strong structures, known mainly in the context of neurodegenerative diseases. Surprisingly, amyloid fibers are secreted by species across kingdoms of life, including by microorganisms, and help their survival and activity. Our laboratory published the first molecular structures of functional bacterial amyloid fibrils, which serve as key "weapons" making infections more aggressive. This exposed new routes for the development of novel antivirulence drugs. Moreover, we revealed that amyloids secreted by bacteria highly abundant in the microbiome and food sources show similarities in molecular structures to human amyloids involved in neurodegenerative diseases such as Alzheimer's and Parkinson's. This might raise concerns about the involvement of microbes in facilitating these diseases, similar to prion proteins transmitted by contaminated meat that elicit the Creutzfeldt-Jakob disease. In addition, we identified peptides produced across species that provide antimicrobial protection that form amyloid fibrils and determined their first high resolution structures. This amyloid-antimicrobial link signifies a physiological role in neuroimmunity for human amyloids.

Meytal Landau is an Associate Professor at the Technion Faculty of Biology, a visitor group leader at EMBL Hamburg, and an associate member of the Center for Structural Systems Biology (CSSB), Hamburg. Her lab focuses on the assembly of proteins into functional fibrils associated with microbial pathogenicity and infections, and their connection to neurodegenerative diseases via the gut-brain axis. She holds a PhD degree from Tel-Aviv University under the supervision of Prof. Nir Ben-Tal, and conducted her postdoctoral research at UCLA with Prof. David Eisenberg. Prof. Landau holds three patents and has published more than 55 papers in professional journals, cited >4000 times, and was invited to present her work at around 50 international conferences. She has received more than 20 awards and honors, including the Biophysical Society's Margaret Oakley Dayhoff Award (2019) and the Wolf Foundation's Krill Prize for Excellence in Scientific Research (2018).

# PLENARY LECTURES

**Tuesday, 15th September**

Dr. Dimple Notani

*National Centre for Biological Sciences*

Thursday
09:00 am

## Understanding the enhancer code in regulation of transcription

Expression of genes is controlled by DNA sequences that are distal from the promoters known as enhancers.. They regulate target genes by establishing looping with the promoter. There are thousands of enhancers in mammalians genomes and they act in a cell-type specific manner. Although discovered over forty years ago, how enhancers regulate their promoters remains poorly understood. Further, the enhancers that drive cyclic signaling response, are reversibly dynamic as opposed to developmental enhancers, adding another layer of complexity to this conundrum.

Using genomic techniques that quantify the alterations in TF binding, nascent transcription, three-dimensional architecture during the course of estrogen signalling, our work has revealed that chromatin state under basal signaling is the key to signalling response. Certain regions in the genome are bound by estrogen receptor (ERα) even before exposure to ligand. These regions act as a seed to give rise to ERα bound enhancer clusters that drive the signaling response. Further, these and other enhancer clusters do not function as sum-of-all but rely on complex hierarchies that cannot be predicted *in silico*. I will discuss how these enhancers regulate the genome organization, how promiscuous transcription and mutations in these enhancers lead to patho-physiologies including cancer.

After finishing her doctoral degree in India, Dimple moved to San Diego to work in the laboratory of Prof. Michael Geoff Rosenfeld to study the enhancer functions underlying signalling pathways. Her work revealed the crucial roles of ligand induced enhancer RNAs (eRNAs) in gene regulation. Since 2016, she has been a group leader in the National Centre for Biological Sciences in Bangalore, India. Dimple is an EMBO Global Investigator and a Wellcome-DBT India Alliance Fellow.

Her group uses multidisciplinary approaches from single molecule kinetics to genomics to understand the link among three-dimensional chromatin architecture, distal regulatory elements, and associated eRNA in signaling-driven gene regulation events. Recently, her group identified the book-marking of functional enhancers by unliganded receptor under basal signalling and the formation of enhancer condensates in a ligand-dependent manner for robust gene expression. These findings have implications in our understanding of the robust and specific signaling response in eukaryotes.

Dr. Tamal Das

*Tata Institute of Fundamental Research*

Thursday
09:45 am

## Emergent features of collective cell migration at different length-scales

Many key physiological processes involve tens or hundreds of cells coordinating their dynamics in a way that they effectively act like a single entity or a collective. Collective cell migration is the process of many cells moving as a cohesive group, with each individual cell coordinating its motion and its internal organization, with that of its neighbors. It critically influences development of an embryo, healing of a wound, and metastatic migration of cancer cells, to name a few processes. My talk will highlight some of the differences between single cell migration and collective cell migration, especially focusing on the features that are exclusive to collective cell migration and do not exist at the single cell level. These features include crowd following behavior of the migrating cells, emergence of a few selected leader cells, collective cell polarity, and multicellular sensing of gap curvature in the context of epithelial wound healing.

Tamal pursued his doctoral research in the Microfluidics lab at Indian Institute of Technology Kharagpur and graduated in 2010. In 2011, Tamal joined Prof. Joachim Spatz' department at the Max Planck Institute for Intelligent Systems in Stuttgart, Germany as a project leader. In November 2016, Tamal moved to TIFR (Tata Institute of Fundamental Research) Hyderabad and started his own group. Tamal has received the prestigious Intermediate Fellowship by the Wellcome Trust (UK) - India Alliance for this research theme, and his group is recognized as a partner group by the Max Planck Society, Germany

Prof. Dr. Tal Dagan

*Christian-Albrechts-University of Kiel*

Thursday
10:45 am

Tal Dagan had a PhD in Molecular Evolution from Tel-Aviv University. Since 2013, she has been a professor of genomic microbiology at Kiel University.

Her main interests are in field of bacterial genome evolution with a focus on evolution via lateral gene transfer. In recent years, her research was mainly focused on plasmid evolution.

## The Darwinian fitness of extra-chromosomal genetic elements

Plasmids are an important source of raw material for microbial genome evolution outside the mainstream of bacterial chromosomes. Nonetheless, many plasmids found in nature are lacking a clear trait that is advantageous to their host; the determinants of plasmid evolutionary success in the absence of plasmid benefit to the host remain understudied.

Borrowing terminology from evolutionary biology of cellular living forms, the team hypothesizes that Darwinian fitness is key for the plasmid evolutionary success.

In this talk, Dr. Dagan will present recent results from her group on the determinants of plasmid fitness, and how plasmid fitness might change depending on the environmental conditions.

Dr. Kushagra Bansal

*Jawaharlal Nehru Centre for Advanced Scientific Research*

Thursday
11:30 am

## Regulators of genome superstructure in the immune system

The mammalian immune system is a complex network of an assortment of cellular players that function in synchrony to protect the body from potential pathogenic threats. The ability of immune cells to maintain themselves in the absence of pathogenic infection as well as their proficiency to respond to environmental stimuli is dependent on the cooperative activity of various molecular regulators that impact the transcriptional output of these cells.

The lab is currently focusing on two such regulatory group of proteins in the immune cells -topoisomerases and cohesin complex. These molecular regulators control the superstructure of genetic material and have been implicated in various immunological disorders. However, much remains unknown regarding their immune cell-specific function and their association with immunological disease etiology.

The team is seeking to provide a comprehensive understanding of how molecular machines regulating genome superstructure dynamics integrate with gene regulatory machinery in the immune cells and Dr. Bansal will discuss their early work towards this goal.

Kushagra Bansal received his PhD degree in Microbiology & Cell Biology from Indian Institute of Science, Bangalore, in 2010. His doctoral research was focused on the signaling pathways that govern the immune subversive phenotype of macrophages and dendritic cells during pathogenic infections.

Kushagra carried out his post-doctoral research at Harvard Medical School, Boston. During his post-doctoral tenure, Kushagra sought to delineate the molecular basis of immune tolerance mechanisms that operate in the thymus. In 2018, Kushagra joined the Molecular Biology & Genetics unit at Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, as a faculty member. He was awarded Ramalingaswami Re-entry Fellowship of the Department of Biotechnology (DBT), Govt. of India and DBT/Wellcome India Alliance Intermediate Fellowship to jump start his research program. His research group focuses on understanding the mechanistic details of gene regulation in immune cells and aims to unveil dysregulation of these mechanisms in infectious and autoimmune diseases.

Prof. Dr. Cassandra Extavour

*Harvard University*

Thursday
02:30 pm

## Combining quantitative imaging and mathematical modeling to understand nuclear movements in early embryo

Cassandra Extavour obtained her PhD with Antonio Garcia Bellido at the Severo Ochoa Center for Molecular Biology at the Autonomous University of Madrid. She performed postdoctoral work first with Michalis Averof at the Institute for Molecular Biology and Biotechnology in Crete, Greece, and subsequently with Michael Akam at the University of Cambridge.

In 2007, she established her independent laboratory as an Assistant Professor in the Department of Organismic and Evolutionary Biology at Harvard University, where she was promoted to Associate Professor in 2011 and to Full Professor in 2014.

The first step in animal development is to generate an initial tissue layer, called blastoderm, that then becomes multilayered, differentiates, and folds into the ultimate body plan. Despite the broad evolutionary conservation of this embryonic stage, the cellular behaviours that lead to blastoderm formation are poorly understood. In most insects, before blastoderm formation, nuclei divide without cytokinesis, and move within the shared cytoplasm of the embryo, termed syncytium. To form a blastoderm, these syncytial nuclei must move from their scattered positions within the cytoplasm, forming a single layer at the cortex. By quantifying nuclear dynamics during the period of syncytial cleavages and movements in the cricket *Gryllus bimaculatus* we found that, unlike in the fruit fly *Drosophila melanogaster*, (1) cytoplasmic flows do not direct nuclear movement; and (2) division cycles, nuclear speeds, and directions of nuclear movement are not synchronized across the embryo, but instead are heterogeneous in space and time. We developed a novel geometric model that uses local nuclear density to determine division timing, speed of movement, and orientation of movement. Going forward, we will use this model to make precise, falsifiable predictions about the dynamics of blastoderm formation in other insect species.

Dr. Marieke Oudelaar

*MPI for Multidisciplinary Sciences*

Thursday
03:15 pm

## Regulation of gene expression in the three-dimensional genome

Mammalian gene expression patterns are controlled by enhancers, which form interactions with the promoters of their target genes to transfer activating signals. Since these elements can be separated by large genomic distances, the specificity of enhancer-promoter interactions is dependent on the 3D organization of chromatin in the nucleus. However, it is not well understood how chromatin structures are formed and how regulatory elements function within this context to control gene expression. Using a combination of functional genomic tools, I will discuss new insights into the establishment of specific chromatin structures during development, the molecular mechanisms underlying the formation of these structures, and their role in the regulation of gene expression.

Marieke Oudelaar obtained her BSc from the University of Utrecht in Netherlands and her MSc form the Karolinska Institute in Sweden. She did her PhD in the Weatherall Institute of Molecular Medicine (WIMM) at the University of Oxford in the United Kingdom in the laboratories of Doug Higgs and Jim Hughes.

After her PhD, she received a Junior Research Fellowship from University College to continue her research in the WIMM.

In 2020, she moved to Germany, to start the group “Genome organization and regulation” at the Max Planck Institute for Biophysical Chemistry.

Dr. Orly Laufman

*Weizmann Institute of Science*

Thursday
04:15 pm

## When hosts become hostages - Deciphering the replication mechanisms of enteroviruses in human cells

Positive-strand RNA viruses including corona, zika and dengue are a major threat to public health. A critical step in the life cycle of all positive-strand RNA viruses is the replication of their genome on cellular membranes called replication compartments. However, the mechanisms underlying the formation of the replication compartments are not well understood. Enteroviruses are common positive-strand RNA viruses that cause diverse medical complications in humans including myocarditis, meningitis and paralysis.

Combining biochemistry, molecular and cellular biology approaches, the lab studied the mechanisms underlying the formation of enterovirus replication compartments. They discovered that enteroviruses hijack lipid storage organelles called lipid droplets and use the lipids stored within them to generate their replication compartments.

Dr. Laufman will describe the sophisticated mechanisms used by enteroviruses to repurpose lipid droplets for virus needs. Their studies illuminate the mechanisms by which positive-strand RNA viruses rewire host organelles and lipid metabolism to promote their replication and provide a snapshot into the complex replication program of these viruses.

Dr. Orly Laufman earned her BSc (2002) and MSc (2005) degrees in biology, both summa cum laude, from the Technion—Israel Institute of Technology. She completed her PhD (2010) and her postdoctoral fellowship (2011) under Prof. Sima Lev at the Weizmann Institute, studying trafficking of proteins in human cells in health and disease.

In 2019, she completed a postdoctoral fellowship under Raul Andino in the Department of Microbiology and Immunology at the University of California, San Francisco studying the cell biology of positive-strand RNA viruses and afterwards, continued on as an associate specialist.

Dr. Laufman joined the faculty of the Department of Molecular Genetics at the Weizmann Institute in March 2021 and opened a lab dedicated to the studies of RNA viruses. She is the recipient of 2021 Sir Charles Clore Prize for Outstanding Senior Scientist at the Weizmann Institute.

Dr. Sonja Lorenz

*MPI for Multidisciplinary Sciences*

Thursday
05:00 pm

## Structural principles regulating the ubiquitination machinery

The astounding precision by which ubiquitin governs countless cellular processes requires the regulated formation of specific ubiquitin modifications on specific substrates, catalyzed by a cascade of protein-protein interactions. It is thus critical that the protein interfaces formed throughout this cascade are tightly controlled. My talk will focus on the structural principles of ubiquitin recognition by two classes of ubiquitination enzymes: ubiquitin-conjugating enzymes (E2s) and HECT-type ubiquitin ligases (E3s). Both classes of enzymes transfer ubiquitin to substrates via a thioester-linked intermediate and can thus control specificity for modification sites or linkage types during ubiquitin chain formation. In particular, I will highlight work demonstrating that the interactions between the thioester-linked ubiquitin molecule and the respective enzyme confer catalytic efficiency and provide a linchpin for structurally and functionally distinct modes of regulation.

Sonja Lorenz has been an independent group leader at the Max Planck Institute for Multidisciplinary Sciences in Göttingen since 2021. She received a PhD from the University of Oxford/UK working with Iain Campbell and Martin Noble, followed by postdoctoral research with John Kuriyan at University of California in Berkeley, USA.

In 2014, she started her independent research career at the Rudolf Virchow Center in Würzburg. In 2018 Sonja was named an EMBO Young Investigator.

Prof. Dr. Barbara Treutlein

*ETH Zürich*

Thursday
06:00 pm

## Human organoid development through the lens of single-cell technologies

Recent advances in stem cell biology have made it possible to grow *in-vitro* three-dimensional human organoids that model human brain development. We are using these organoid systems in combination with single-cell genomic methods to understand molecular mechanisms underlying fate decisions during human brain development. We deconstruct cellular composition and reconstruct differentiation trajectories over the entire course of human cerebral organoid development from pluripotency, through neuroectoderm and neuroepithelial stages, followed by divergence into neuronal fates within the dorsal and ventral forebrain, as well as midbrain and hindbrain regions. We use lineage recording based on single-cell transcriptome-coupled lineage tracing, nuclei tracking from long-term light sheet microscopy, and spatial transcriptomics to understand lineage commitment and dynamics during cerebral organoid regionalization. Single-cell multiomics measurements in combination with a new computational tool allows us to reconstruct a gene regulatory network underlying fate decisions during early brain organoid development. Using pooled genetic perturbation with single-cell transcriptome readout we assess transcription factor requirement for cell fate and state regulation in organoid and show that our gene regulatory network is predictive of the observed changes.

Barbara Treutlein studied chemistry at the Universities of Tübingen and Mainz and at UC Berkeley in 2001-2007. From 2007-2012, she performed her doctoral research in single-molecule biophysics with Jens Michaelis at LMU Munich, Germany. During her Postdoc with Stephen Quake at Stanford University from 2012-2014, she pioneered the use of microfluidic-based single-cell transcriptomics to dissect the cellular composition of complex tissues, and to elucidate differentiation pathways during lung development and cell reprogramming. 2015-2018, she was a Max Planck Research Group Leader at the Max Planck Institute for Evolutionary Anthropology in Leipzig and held a tenure-track assistant professorship at TU Munich. Since 2019, Barbara is Professor for Quantitative Developmental Biology at the ETH Zürich D-BSSE, Switzerland.

For her work, Barbara has received multiple awards including the Friedmund Neumann Prize of the Schering Foundation and the Dr. Susan Lim Award for Outstanding Young Investigator of the International Society of Stem Cell Research



## Who gets the credit – How does the recognition for scientific discoveries work?

Science usually progresses because scientists from various laboratories each discover small pieces of a big puzzle that constitutes a scientific field. From principal investigators via technicians to PhD students and postdocs, many different people contribute to each single advance. Yet, scientific discoveries are often connected to a single big name and awards are presented to one or a few people while other contributors – competing labs, collaborators or students – are lost and forgotten. In this panel discussion we want to find out how scientific recognition is achieved, identify strategies for a fair acknowledgement of individual contributions, and of course, discuss who really should get the credit.

**Panellists:**

Prerana Shrestha, PhD
Assistant Professor, Stony Brook University, USA

Alexey Amunts, PhD
Associate Professor, Stockholm University, Sweden

Chris Proud, PhD
Professor, South Australian Health and Medical Research Institute, Adelaide, Australia

Goran Kokic, PhD
Postdoctoral Researcher, MPI for Multidisciplinary Sciences, Germany

**Moderators:**

Sumeru Panta
Gantavya Arora
Monica Yasser Gobran
Jannis Anstatt

# POSTER ABSTRACTS

**P01**

**Sexually dimorphic architecture and function of a mechanosensory circuit**

Hagar Setty[1,*], Yehuda Salzberg[1], Shadi Karimi[2], Elisheva Berent-Barzel[1], Michael Krieg[2] and Meital Oren-Suissa[1]

[1] Department of Brain Sciences, Weizmann Institute of Science, Rehovot, Israel
[2] Neurophotonics and Mechanical Systems Biology, ICFO, Institut de Ciencies Fot`oniques, Spain

* Presenting Author; hagar.setty@weizmann.ac.il

How sensory perception is processed by the two sexes of a specie is still only partially understood. Despite some evidence for sexual dimorphism in auditory and olfactory perception, whether touch is sensed in a dimorphic manner has not been addressed. Here we deconstructed the neuronal circuit for tail mechanosensation in *C. elegans* and found it is wired differently in the two sexes and employs a different combination of sex-shared sensory neurons and interneurons in each sex. Reverse genetic screens uncovered cell- and sex-specific functions of the alpha-tubulin *mec-12* and the ion channel *tmc-1* in sensory neurons, and of the glutamate receptors *nmr-1* (NMDA type) and *glr-1* (AMPA type) in interneurons, revealing the underlying molecular mechanisms that mediate tail mechanosensation. Moreover, we show that only in males, the sex-shared interneuron AVG is strongly activated by tail mechanical stimulation, and accordingly is crucial for their behavioral response. Our results provide the first evidence for a sexually dimorphic integration of touch signals and establish a framework to explore this integration in higher organisms, while highlighting the importance of research on sex-differences for future sex-specific therapeutic approaches.

**P03**

**Sequence-based prediction and measurement of pH-dependent protein solubility**

Marc Oeller, Ryan Kang, Pietro Sormanni*, Michele Vendruscolo*

Centre for Misfolding Diseases, Yusuf Hamied Department of Chemistry, University of Cambridge, Cambridge, UK
*Corresponding Authors: mv245@cam.ac.uk, ps589@cam.ac.uk

Computational methods are emerging as powerful complements to laboratory-based approaches for protein developability assessments. They enable to address solubility issues early in the development process and reduce the need of laborious and material-demanding experimental work. In particular, the solubility of proteins is an essential biochemical requirement for their activity, and it is often obstructing developability pipelines. In 2015 we introduced the CamSol method, which enables accurate predictions of the solubility of proteins solely by analysing the physico-chemical properties of their sequences, without any knowledge of their structures. By building on these advances, we have now extended the method to enable the accurate prediction of solubility changes resulting from variations in formulation pH. The optimisation of formulation pH is a crucial step in product development, impacting shelf-life and safety. In parallel, we have also developed a low volume, high-throughput, automated PEG-precipitation assay to measure the relative solubility of proteins with very low material requirements. This assay was used to validate our predictions on a number of proteins and antibodies, revealing very high accuracy. Taken together, our data show that we can reliably predict the solubility of proteins and antibodies at varying pH. This new version of CamSol might therefore be a valuable tool to aid biotherapeutic development and formulation optimisation.

**P04**

**A guard protein mediated quality control mechanism monitors 5'-capping of pre-mRNAs**

Sandra Klama[1], Anna Greta Hirsch[1], Ulla Maria Schneider, Gesa Zander, Anika Seel and Heike Krebber

Abteilung für Molekulare Genetik, Institut für Mikrobiologie und Genetik, Göttinger Zentrum für Molekulare Biowissenschaften (GZMB), Georg-August Universität Göttingen, Göttingen, 37077, Germany
[1] Equal contribution

Maturation of RNA polymerase II transcripts consists of 5'-capping, splicing, and 3'-polyadenylation. These processes can generate faulty transcripts, which have to be prevented from nuclear export and have to be degraded. An mRNA gets exported to the cytoplasm only after having gone through processing successfully, enabling its translation. Faulty transcripts, on the other hand, get degraded by the nuclear degradation machinery. In *Saccharomyces cerevisiae,* the SR-like guard proteins Gbp2 and Hrb1 control splicing and retain unspliced transcripts in the nucleus. The guard Nab2 controls the quality of the 3'-poly(A) tail in a similar way. On correct transcripts, these factors recruit the export receptor Mex67-Mtr2. Only mRNAs which are sufficiently covered with it can pass through the nuclear pore complex (NPC). Passage is controlled by Mlp1, a part of the NPC. For the SR-like protein Npl3, which is highly homologous to Gbp2 and Hrb1, no particular function as a guard protein had been reported so far. Here we show that it acts as a guard in 5'-capping. Npl3 retains uncapped transcripts in the nucleus and recruits the 5'-3'-end degradation factors Rai1 and Rat1 to them. Most importantly, in absence of Npl3 faulty mRNAs are not retained in the nucleus for degradation but escape retention and leak into the cytoplasm. On correct pre-mRNAs Npl3 interacts with the cap binding complex (CBC), the indicator of a correct 5'-cap. Npl3 binds independently of it and their interaction is lost on uncapped transcripts, suggesting Npl3 detects its presence. Similar to the other guards, Npl3 recruits Mex67-Mtr2 to correct, quality-controlled transcripts while also interacting with the CBC. The binding of Npl3 to the CBC and Mex67 and its binding to Rai1, which supports the association of Rat1, is mutually exclusive, indicating that it might act as a switch between degradation and export. The fate of the transcript is most probably decided through the contact between Npl3 and the CBC.

**P06**

**Apigenin Ameliorates Methotrexate-Induced Neurotoxicity and Promotes Hippocampal Neurogenesis in Rats.**

Mohamed Taha[1], Omar Mohsen Eldemerdash[2], Ismail Mohamed Elshaffei[3], Mahmoud Ahmed Senousy[4]

[1]Department of Biochemistry, Faculty of Pharmacy, Cairo University, Egypt
[2]Department of Biochemistry, Faculty of Pharmacy, Misr International University (MIU), Egypt
[3]Department of Biochemistry, Faculty of Pharmacy, Misr International University (MIU), Egypt
[4]Department of Biochemistry, Faculty of Pharmacy, Cairo University, Egypt

Although MTX has been widely used as an anti-cancer, it has been shown to have multiple neurotoxic consequences. MTX-induced impaired neurogenesis remained a possible cause, even though the molecular mechanism is yet unknown. Apigenin (Api), a naturally occurring flavonoid, has recently been exhibited to be neuroprotective. The purpose of this work was to evaluate the possible effect of MTX on the miR-15a/ERK1/2/CREB/BDNF pathway, as well as the neuroprotective effect of Api. Four groups of male Sprague Dawley rats were established. 1) Control group rats were given normal saline i.p. daily and saline i.v. on the 8$^{th}$ and 15$^{th}$ days of the model. 2) Api control: got 20 mg/kg/day of Api orally for 30 days. 3) MTX group: received two injections of MTX 75 mg/kg, i.v. on the 8$^{th}$ and 15$^{th}$ days of the model, followed by four injections of leucovorin (LCV): the first is 6 mg/kg after 18 hours followed by three doses of 3 mg/kg after 26, 42, and 50 hours from MTX injection. 4) Api co-treated: received MTX and LCV doses as in group 3 and daily Api doses as in group 2. The study demonstrated that MTX induced a decrease in neurogenesis, as indicated by a decline in doublecortin levels in the hippocampi. This was linked to a downregulation in miR-15a, which corresponded to an inactivation of the downstream ERK1/2/CREB/BDNF pathway, as well as a change in hippocampal redox status. Memory losses and cognitive impairment were detected by novel object recognition test. Api exhibited neuroprotective effects by correcting the behavioral, biochemical, and histological alterations induced by MTX. Api co-treatment ameliorated the neurotoxicity and memory impairments induced by MTX in rats. These neuroprotective effects may be achieved by regulating the miR-15a/ERK1/2/CREB/BDNF pathway, which promotes hippocampal neurogenesis.

**P07**

**Functional and architectural insights of the human autophagy initiation machinery.**

Nguyen A[1], Hosnani P[3], Lugarini F[1], Patel A[1], Parfentev I[4], Urlaub H[4,5], Meinecke M[3], and Faesen AC[1].

[1]Max-Planck Institute for Multidisciplinary Sciences, Laboratory of Biochemistry of Signal Dynamics, Göttingen, Germany
[2]Institute of Molecular Medicine I, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany
[3]Universitätsmedizin Göttingen, Institute für Zellbiochemie, Humboldtallee 23, 37073 Göttingen, Germany
[4]Max Planck Institute for Biophysical Chemistry, Bioanalytical Mass Spectrometry, Göttingen, Germany
[5]University Medical Center Göttingen, Institute of Clinical Chemistry, Bioanalytics Group, Göttingen, Germany

Macroautophagy (hereafter autophagy) is a tightly regulated catalytic process in eukaryotes that starving cells use as a major survival mechanism to reallocate nutrients to essential processes. The hallmark of autophagy is the formation of a large double membrane structure - phagophore, which captures surplus or dysfunctional cellular components and recycles them for the most critical processes. The massive membrane remodeling initiates within seconds after starvation and requires an establishment of a membrane contact site (MCS) which connects the source membrane to the phagophore. The MCS then orchestrates a lipid flow from the source membrane to expand the phagophore. Architectural and functional aspects of MCS's assembly, however, remain largely uncharacterized due to the availability of purified full-length recombinant proteins in sufficient quantity and quality. In this study, we successfully produced 9 autophagy (ATG) proteins *in vitro*. Architecturally, we found that the MCS is built upon a core complex of three proteins: ATG9-ATG13-ATG101. The core complex acts as a base for the assembly of a super-complex, including the ULK1 kinase complex and the PI3P lipid kinase complex, which coordinate the production of PI3P - a phospholipid signature that recruits the downstream lipid transfer complex ATG2-WIPI4. After the recruitment, the lipid transfer complex becomes an important structural component of the MCS by bridging and facilitating the lipid flow from the donor membrane to the expanding the phagophore. Interestingly, we found that the lipid transfer activity of ATG2-WIPI4 is significantly accelerated by more than 20 times thanks to the influence of the core complex. Briefly, this study has provided a first model of the architecture of autophagy initiation machinery at the MCS, the contributing factors of lipid transfer acceleration, and the primary constituents for *de novo* autophagic membrane biogenesis.
**Keywords:** autophagy, ATG2, ATG9, ATG13-ATG101, ULK1 complex, PI3K complex, membrane contact site, lipid transfer.

**P08**

**Mutant IDH Inhibitors Induce Lineage Differentiation in IDH-mutant Oligodendroglioma**

Avishay Spitzer[1,*], Simon Gritsch[2,3,*], Hannah R. Weisman[2,3], L. Nicolas Gonzalez Castro[2,3,5], Masashi Nomura[2,3], Nicholas Druck[2,3], Rony Chanoch[1], Christine K. Lee[4], Hiroaki Nagashima[4], Julie J. Miller[5], Isabel Arrillaga-Romany[5], David N. Louis[2], Hiroaki Wakimoto[4], Will Pisano[6], Patrick Y. Wen[7], Keith L. Ligon[6,8,**], Daniel P. Cahill[4,8,**], Mario L. Suvà[2,3,8,**], Itay Tirosh[1,8,**]

[1]Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot 761001, Israel
[2]Department of Pathology and Center for Cancer Research, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114, USA
[3]Broad Institute of Harvard and MIT, Cambridge, MA 02142, USA
[4]Department of Neurosurgery, Massachusetts General Hospital and Harvard Medical School, Boston, MA, 02114 USA
[5]Departments of Neurology and Radiation Oncology, Division of Hematology/Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, 02114, USA.
[6]Department of Pathology, Brigham and Women's Hospital, Boston, MA.
[7]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02114, USA
[*]these authors contributed equally to this work
[**]these authors jointly supervised this work
[8]corresponding authors: Email: Itayt@weizmann.ac.il (IT); Suva.Mario@mgh.harvard.edu (MLS); cahill@mgh.harvard.edu (DPC); keith_ligon@dfci.harvard.edu (KLL)

Recent data showed promising signs of objective tumor responses in subsets of patients with low grade glioma treated with inhibitors of mutant IDH (IDHi). However, the molecular and cellular underpinnings of such responses are not known. Here, we profiled 6,039 transcriptomes by single-cell or single-nucleus RNA-sequencing isolated from three IDH-mutant oligodendroglioma patients with clinical response to IDHi. Importantly, the tissues were sampled on-drug, four weeks from treatment initiation and our dataset includes a matched pre- and on-treatment sample pair. We integrate our findings with analysis of 8,241 transcriptomes from seven untreated samples, 134 bulk samples from the TCGA and experimental models. We find that IDHi treatment induces a robust differentiation towards glial lineages, accompanied by a depletion of stem-like cells and a reduction of cell proliferation. Our study provides the first evidence in patients of the differentiating potential of IDHi on the cellular hierarchies that drive oligodendrogliomas.

**P09**

**YopR is a key component of the SPβ lysis-lysogeny management system.**

K. Kohm[1,2,6], E. Jalomo-Khayrova[3,6], S. Basu[1], W. Steinchen[3], G. Bange[3,4], F. M. Commichau[1,2], L. Czech[3], R. Hertel[1,5]

[1]FG Synthetic Microbiology, Institute for Biotechnology, BTU Cottbus-Senftenberg, Senftenberg, Germany
[2]FG Molecular Microbiology, Institute for Biology, University of Hohenheim, Stuttgart, Germany
[3]Center for Synthetic Microbiology and Department of Chemistry, Phillips-University Marburg, Marburg, Germany
[4]Max-Planck Institute for Terrestrial Microbiology, Marburg, Germany
[5]Satorius AG, Göttingen, Germany
[6]Equally contributing

We are interested in the biology of the temperate phage SPβ that resides as a prophage in the genome of the *B. subtilis* laboratory strain 168. SPβ was discovered half a century ago, but only individual aspects of its biology are known. Recently, several novel players of the lysis-lysogeny system were uncovered, and two independent studies identified YopR as the master repressor of the lytic cycle. Furthermore, a recent analysis identified the core genes of SPβ-like phages and the *yopR*, *yopQ*, *yopP*, *aimR* and *yokI* genes, which are most likely transcriptionally active during the lysogenic cycle. To gain more insides into the lysogeny management system of SPβ, we study the genotype of the c2 mutant. This mutant cannot maintain its lysogenic status upon heat induction, implying alteration of a core regulatory element. Here, we prove that the SPβ c2 phenotype is due to a single nucleotide exchange in the *yopR* gene, rendering the encoded $YopR^{G136E}$ protein temperature sensitive. Thermal shift assays and hydrogen deuterium exchange mass spectrometry analyses uncovered that the G136E exchange renders YopR less stable and reduces its affinity to bind DNA. Structural and biochemical characterization of YopR revealed that the protein is a DNA-binding protein with an overall fold similar to tyrosine recombinases. Finally, a genetic suppressor analysis identified the YosL protein as a novel player in the lysis-lysogeny management system. Further analysis showed that the presence of *yosL* seems to be crucial the heat- and chemical -induction of the lytic cycle of the SPβ c2 mutant. Yet, the protein alone cannot activate the lytic cycle of SPβ.

**P11**

**Understanding the Drought Mediated Regulon of miRNA Biogenesis Machinery in *Oryza sativa***

Tonu Angaila Chithung, Dr. Saurabh Raghuvanshi

Dept of Plant Molecular Biology, University of Delhi, India
angailachithung@gmail.com, saurabh@genomeindia.org

miRNAs are integral nodes of regulation in plant development and stress responses. Their biogenesis process consists of genes/TFs that work in complicated and regulated fashion giving rise to mature and functional forms of miRNAs. We have manually curated the information of 98 genes from literature based only on experimentally verified direct evidence. Most of these genes are found to be directly or indirectly interacting with the core-components of miRNA biogenesis- AGO1, DCL1, HYL1, HEN1, HST, Pol II and SE. Conservation patterns of these genes were identified across plant kingdom. Orthologs of 13 and 8 genes appear to be absent in lower organisms and monocots respectively. Subsequently, attempt was made to characterize the orthologs in *Oryza sativa* on the basis of comparative genomics including sequence variations (SNPs/Indels), transcriptome and epigenomics. Total of 42 genes were significantly differentially expressed (DEGs) in three tissues (flagleaf, inflorescence and root) under drought in two cultivars, Nagina22 (drought tolerant) and IR64 (drought sensitive). Likewise, several genes have DMRs (Differentially Methylated Regions) under drought in all the tissues for both varieties and are marked with histone modifications - H3K4me3, H3K9ac, H3K27me3. We found that 96 and 50 miRNAs in *Oryza sativa* and *Arabidopsis* respectively, are targeting these miRNA biogenesis genes where 10 miRNAs in rice are of high confidence. The study enhances our understanding of the evolution of miRNA biogenesis and its integration with the molecular schema of the cell. It also highlights avenues for further investigations in plant systems beyond *Arabidopsis*.

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**P12**

**Repaglinide as a neuroprotective drug in Parkinson's disease**

Tarek K. Motawi[a], Rawan H. Al-Kady[b], Mahmoud A. Senousy[a] , Sahar M. Abdelraouf [b]

[a]Biochemistry department, Faculty of Pharmacy, Cairo University, Cairo, Egypt
[b]Biochemistry department, Faculty of Pharmacy, Misr International University, Cairo, Egypt

Parkinson's disease (PD) is a rapidly progressing neurological illness with both motor and nonmotor symptoms. These are caused by the death of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpc) in a selective and progressive manner. This is the result of the unfolded protein response (UPR) activated by the intraneuronal aggregation of aberrant protein aggregates, predominantly formed of misfolded α-synuclein, known as Lewy bodies., as well as in response to oxidative stress and inflammation. Persistent UPR activation leads to programmed cell death by autophagy. Autophagy is one of the key systems for maintaining proteostasis and plays a significant part in the development of Parkinson's disease and represents a prospective therapeutic target for the treatment of PD. Repaglinide is an oral antihyperglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus and belongs to the meglitinides class of short-acting insulin secretagogues. Previous studies showed that repaglinide promoted a neuroprotection effect in neuronal loss diseases. Here we provide an experimental design of a rotenone-based neurotoxic model of Parkinson's disease. Our results showed that repaglinide lowered the levels of the autophagic markers beclin 1 and caspase 3, and the inflammatory markers IL-1β and IL-6 with the contaminant increase in the neuron count of SNpc.

**P14**

**Building a survival machinery in time: how HORMA domains regulate human autophagy initiation**

Lugarini F[1], Nguyen A[1], David C[2], Patel A[1], Parfentev I[1], Friedrich A[2], Urlaub H[1,3], Stork B[2] and Faesen AC[1]

[1]MPI for Multidisciplinary Sciences, Göttingen, Germany
[2]Institute of Molecular Medicine I, Heinrich Heine University Düsseldorf, Germany
[3]University Medical Center Göttingen, Institute of Clinical Chemistry, Göttingen, Germany

Autophagy must begin quickly to form cup-shaped structures known as 'autophagosomes' to ensure cell survival under stress and starvation. Autophagosomes rapidly engulf macromolecules, organelles, and the cytosol and then fuse with the vacuole/lysosome for degradation and recycling. The mechanism by which autophagy initiation machinery is rapidly assembled in the ER remains unknown. We investigated this question by biochemically reconstituting the initiation complexes and proposed the formation of the complex composed of ATG13-ATG101 and the lipid scramblase ATG9 (termed the 'core complex') to be the rate-limiting step in autophagy initiation. We discovered that dimerization of ATG101 and ATG13 accelerates the interaction with ATG9 and that, like most HORMA domain proteins, ATG13 can alter its tertiary structure reversibly. This alteration not only controls the dimerization but also affects the HORMA domain proteins protein-protein interaction spectrum. Furthermore, we discovered that ATG13-ATG101-ATG9 connects different initiation subcomplexes that together form a 'super-complex', lending support to the idea that the ATG13-ATG101 interaction with ATG9 is the kinetic bottleneck that controls the assembly of the initiation machinery at the ER contact site, a critical step for autophagosome biogenesis. These findings anticipate the development of quantitative methods for explaining how the autophagy initiation complex promotes autophagosome initiation in space and time.

**P15**

**The roles of Wnt signalling in the maintenance of faithful mitotic chromosome segregation**

Alexander Haas and Holger Bastians

Universitätsmedizin Göttingen, Institute of Molecular Oncology, Section of Cellular Oncology, Griesebachstr. 8, 37077 Göttingen

Chromosomal instability (CIN) is one of the hallmarks of cancer and results from structural or numerical changes to the chromosomal composition leading to genetic variation. Numerical karyotype changes can be triggered through elevated microtubule polymerisation rates during early mitosis and an accompanied increase of lagging chromosomes. Wingless and Int-1 (Wnt)-ligands are a family of secreted signalling proteins that are mainly known for their involvement in cell proliferation and differentiation. In cancer, the canonical Wnt signalling pathway often is hyperactivated, allowing proliferation. In contrast, we recently showed that specific suppression of this pathway results in CIN. However, the link of Wnt signalling and CIN is unknown. To investigate whether Wnt signalling in general, or specific ligands suppress mitotic errors, we screened the ability of most Wnt ligands to rescue elevated microtubule dynamics and identified one main ligand - Wnt10b – as the main regulator of microtubule dynamics and CIN and confirmed these findings in other cell lines. Furthermore, we were able to show that knock-out of WNT10b specifically results in aneuploidy. To gain more mechanistic insight, we investigated which cell cycle phase links loss of Wnt signalling and the occurrence of mitotic aberrations. To our surprise, we observed defects only after loss of Wnt(10b) signalling during S-phase but not after loss during mitosis. This suggests that mitotic errors after loss of Wnt signalling result as side effect from dysregulated replication.

**P16**

**Characterization of a humanized CYP21A2 mouse model for congenital adrenal hyperplasia (CAH)**

Shamini Ramkumar Thirumalasetty[1], Tina Schubert[1], Nicole Reisch[2], Ronald Naumann[3], Ilka Reichardt[4], Dana Landgraf[1], Mirko Peitzsch[6], Katrin Koehler[1], Angela Huebner[1]

[1]Children's Hospital, Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany
[2]Medizinische Klinik und Poliklinik IV, Ludwig-Maximilians-Universität München, Ziemssenstrasse 1, 80336 Munich, Germany
[3]Transgenic Core Facility, Max Planck Institute of Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, 01307 Dresden, Germany
[4]Genome Engineering Facility, Max Planck Institute of Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, 01307 Dresden, Germany
[5]University Cancer Center (UCC) Dresden, Medical Systems Biology, Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany
[6]Institute of Clinical Chemistry and Laboratory Medicine, Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, 01307 Dresden, Germany

Congenital adrenal hyperplasia (CAH) is a genetic disorder of autosomal recessive inheritance that is characterized by impaired steroidogenesis of the adrenal glands. It causes a wide array of symptoms in both children and adults. CAH due to 21-hydroxylase deficiency (21-OHD) is its most common form and is caused by mutations in the *CYP21A2* gene. Patients with 21-OHD present with low levels of cortisol and high levels of adrenal androgens driven by an unsuppressed hypothalamo-pituitary-adrenal feedback loop. Main clinical symptoms include virilized genitalia in newborn females, accelerated growth and precocious puberty. With challenges in current treatment options, an animal model integrated with mutations relevant to CAH will be useful to test novel therapeutic options *in vivo*. In this study, humanized mice, where the human orthologue *CYP21A2* replaces the mouse gene *Cyp21a1*, integrated with the human point mutation R484Q is used to investigate the phenotypes of CAH. Preliminary results from the tandem mass spectrometry measurements of the mice plasma at 20 weeks show decreased corticosterone and increased ACTH levels in both male and female homozygous animals. Progesterone levels in the homozygotes was higher than its wild type littermates. Histologically, enlarged adrenals were seen in the homozygous animals in comparison to its wild type littermates. Blood pressure measurements at 8 weeks using the cuff-tail method revealed by trend lower values of mean blood pressure in homozygotes than in wild type animals. In conclusion, we show that the humanized mutant *CYP21A2* mice represent an excellent animal CAH model to test novel treatment strategies for CAH patients. This model will support the transition from basic research to clinical application.

**P17**

**Liquid-liquid phase separation of Tau**

Zheng Shen [1], Markus Zweckstetter [1,2]

[1]German Center for Neurodegenerative Diseases (DZNE), Von Siebold Str. 3a, 37075 Goettingen, Germany
[2]Max Planck Institute for Multidisciplinary Sciences, Am Fassberg 11, 37077 Goettingen, Germany

Emerging research presents that liquid-liquid phase separation (LLPS) is a crucial phenomenon underlying the biomolecular condensation of intrinsically disordered proteins (IDPs) and nucleic acids. LLPS has attracted widespread interest as it is involved in various cellular activities and human diseases. Tau, a microtubule-associated IDP, is widely expressed in neurons and plays a vital role in microtubule stabilization and axonal transport. A growing body of recent studies suggests that LLPS drives Tau to form liquid-like biomolecular condensates via multivalent inter- and intramolecular interactions among Tau and its binding partners, facilitating Tau to perform its physiological functions. However, the aberrant LLPS induces the formation of solid-like neurofibrillary tangles of Tau, which is a pathological hallmark of several neurodegenerative disorders including Alzheimer's disease. Here, we applied biochemical reconstitution approaches and quantitative biophysical measurements, such as high-resolution NMR spectroscopy, to gain novel and broad insights into the molecular mechanism of Tau LLPS in both physiological and pathological conditions, paving the way for the development of medical treatment targeting Tau in neurodegenerative disorders.

**P18**

**MiR-34a suppresses stemness and enhances T cell function through modulating PTEN/PI3K/AKT signaling pathway and targeting PD-L1 in breast cancer**

Vahid Tavakolpour[1], Hamid Reza Soleimanpour-lichaei[1], Mossa Gardaneh[1], Fatemeh Kouhkan[2]

[1]Department of Stem Cells and Regenerative Medicine, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
[2]Stem Cell Technology Research Center, Tehran, Iran

Programmed death ligand 1 (PD-L1), highly expressed on breast cancer (BC) tumor cells, preserves BC stemness by activating the PI3K/AKT pathway and suppresses T-cells responses against tumors. Recently, microRNAs (miRNAs), which regulate gene expression at the post-transcriptional level, have emerged as promising therapeutic tools in cancer research. MiR-34a, a tumor-suppressor microRNA, was previously found to be downregulated in BC. It also has been shown that miR-34a targets PD-L1 in human leukemia cells. The current study examined the suppressive effect of miR-34a on PD-L1 and its consequences on the BC stemness and T-cells immune response. Our bioinformatics and qRT-PCR analysis indicated that miR-34a was significantly reduced in BC samples and MDA-MB-231 compared to adjacent normal tissues and other BC cell lines, negatively correlated with PD-L1 expression. Moreover, the luciferase assays confirmed that miR-34a binds the PD-L1 3′-UTR specific region. The subsequent investigation revealed that transduced MDA-MB-231 cells with lentiviruses containing miR-34a significantly decreased both mRNA and protein levels of PD-L1. Notably, upon transduction of miR-34a, the western blotting experiment on MDA-MB-231 cells showed a reduction of PI3K and AKT and upregulation of PTEN proteins, associated with significant downregulation of cancer stem cell marker Oct4. Finally, in a co-culture system, we found that suppression of PD-L1 via miR-34a could modulate pro-inflammatory cytokines interleukin (IL)-2, TNF-α, and anti-inflammatory cytokines IL-10 and TGF-β. Given the involvement of miR-34a in effectively targeting PD-L1 in BC cells resulting in a remarkable reduction in BC stemness and enhancing antitumor properties of T-cells, our findings suggest that this miRNA could be considered a promising therapeutic strategy for improving BC treatment outcomes.

**P19**

**Quantitative evaluation of sulfate-reducing bacteria *Desulfovibrio oryzae* forming biofilm on poly(ethylene terephthalate) under *Bacillus velezensis* culture fluid treatment**

Liubov Zelena[1,2], Nataliia Tkachuk[3]

[1]Danylo Zabolotny Institute of Microbiology and Virology of National Academy of Sciences of Ukraine, Kyiv, Ukraine
[2]Kyiv National University of Technologies and Design, Kyiv, Ukraine, zelenalyubov@gmail.com
[3]T.H. Shevchenko National University "Chernihiv Colehium", Chernihiv, Ukraine, nataliia.smykun@gmail.com

Sulfate-reducing bacteria (SRB) are part of sulfidogenic community that plays an important role in biodamage/biodegradation of materials. The purpose of this study was to investigate the number of *Desulfovibrio oryzae* strains NUChC SRB1 and NUChC SRB2 in the biofilm formed on the PET surface *in vitro* under the influence of the culture liquid of strains *Bacillus velezensis* NUChC C1 and NUChC C2b using the qPCR with primers to the sulfite reductase genes. Samples of PET (10×10 mm) were cultured in the presence of SRB and *B. velezensis* culture fluid 50 days. The moderate adherence of the studied SRB strains was observed although the same amount of the biofilm biomass was composed of 2 times higher number of NUChC SRB2 cells as compared to NUChC SRB1. It was proposed that the strain specificity of biofilm matrix production could explain the difference in cell number. Treatment of SRB biofilms with *B. velezensis* NUChC C1 and NUChC C2b culture fluids resulted in the decreasing of both adhesive properties and the cell number of NUChC SRB1. The strain demonstrated the weak adherence: the mass of the biofilm was 2 times less in comparison with the NUChC SRB1 monoculture, and the cell number has decreased by 1.4 times (NUChC C1) and 4.8 times (NUChC C2b). Effects of *B.velezensis* on biofilm formation by SRB could be caused by the secondary metabolites in its culture fluid and their antagonistic/antimicrobial properties. It makes *B.velezensis* species useful as a promising agent for biocontrol of biological damages, in particular those associated with sulfate-reducing bacteria.

**P20**

**The influence of genotypic variability in the Stearoyl-coenzyme A Desaturase 1 gene with milk yield performance in crossbreed anglo-nubian dairy goats.**

Eloise Ann Kristine B, Makasiar*, Carlo Stephen O. Moneva

MIndanao State University- Iligan Institute of Technology, Iligan City
Email: eloiseannkristine.makasiar@g.msuiit.edu.ph

In ruminants, the *Stearoyl-CoA desaturase* gene has been extensively studied, mostly through association studies between the gene's SNP and the fatty acid spectrum. However, only few studies linking the SCD gene to milk output have been undertaken. The present study was carried out to assess the polymorphism in the SCD1 gene (G931T) and investigate whether these polymorphisms have something to do with milk yield production in the 101 crossbred Anglo-Nubian dairy goats from Awang, Opol Misamis Oriental and Talay, Dumaguete City, Negros Oriental, Philippines. Data on milk yield performance of the 101 goats was adjusted to 90 and 140 days of milking. Hair follicles from goats were collected to obtain genomic DNA. The genotyping of the 101 gDNA was carried out using Polymerase chain reaction– restriction fragment length polymorphism (PCR-RFLP) with *Rsa*I as the restriction enzyme (RE). Association analysis was conducted following the two-way factorial (2 x 4) in a randomized complete block design (RCBD), where SCD1 genotypes and parity were used as main factors and farm as the blocking factor. Only two genotypes (TT and GT) were obtained.GT genotype (0.71) showed dominance over TT genotype (0.29) and TC (0.50). However, allele T (0.64) occurred more frequently than allele G (0.36) in the total population studied. All farms did not deviate Hardy-Weinberg Equilibrium ($p > 0.05$). Milk yield traits at both 140 d milking period in crossbred Anglo-Nubian dairy goats were significantly influenced by SCD1 genotypes. Goats with GT genotype were observed to have noticeably higher milk yield performance ( 90d ADMY: 0.94± 0.047 L, 90d ATMP: 82.70± 4.12 L, 140dADMY: 0.98± 0.058 L, 140ATMP: 135.78± 8.33 L ) than goats with TT genotype ( 90d ADMY: 0.52± 0.025 L, 90d ATMP: 45.92± 2.26 L, 140dADMY: 0.54± 0.027 L, 140ATMP: 75.32± 3.88 L ) Furthermore, the author suggests for future studies with the same field of interest to use spectrophotometer during DNA extraction to check purity of the gDNA, to ensure good reads after PCR-RFLP. DNA sequencing of the PCR amplicons and digested RFLP product should also be considered to make sure that the PCR amplicons being amplified is the gene of interest and its target polymorphisms. The present study also wish to conduct the same research with a much larger number of sampled goats to validate the results of the present research in the association of the polymorphisms in SCD1 with milk yield performance of the crossbred Anglo-Nubian dairy goats. It would be interesting to have this research using Philippine native goats or other goat breeds found in the Philippines and assess milk quality and milk yield, the results will surely be very helpful in designing gene-assisted selection program that will help boost small-scale farmers in the country. Lastly, future research should consider conducting full assessment on the association of *SCD1* gene with milk yield, protein yield, and milk quality on crossbred Anglo-Nubian dairy goats.
Keywords: Anglo-Nubian, *Stearoyl-Coenzyme A desaturase* , milk yield, PCR-RFLP, polymorphisms.

**P21**

**Structural basis of TIRAP assembly revealed by cryo-EM**

Jan-Hannes Schäfer, Arne Moeller

Structural Biology Division, Osnabrueck University, Osnabrueck, Germany

Toll-like receptors (TLRs) activate the innate immune response during pathogen infection. Upon ligand-induced receptor dimerization, intracellular adapter proteins, like TIRAP (TIR-domain containing adaptor protein), initiate the assembly of large signaling complexes. In resting TLR-positive cells, TIRAP multimerizes into filaments at the plasma membrane and is subsequently converted into dimers during TLR signaling. However, the exact process of TIRAP filament formation and interaction with TLR dimers remains unknown.
Here, we utilize negative-stain and cryo-EM to investigate the mechanism of TIRAP multimerization. We demonstrate that the full-length human TIRAP forms filaments in a temperature-dependent and reversible manner in the absence of TLRs. Our 3.2 Å cryo-EM structure, together with the negative-stain analysis, indicates a sequential filament formation, starting from stable dimers that polymerize into thin filamentous intermediates and tubes with a diameter of about 30 nm. Together, our data support the presence of TIRAP filaments in resting TLR-positive cells. Furthermore, filamentous TIRAP may provide a pool of required adapter proteins to stimulate TLR-based signal transduction.

**P22**

**Design and deployment of a High-Performance Computing system for cryo-EM**

Kilian Schnelle, Arne Moeller

Structural Biology Division, Osnabrueck University, Osnabrueck, Germany

The constant development of faster electron detectors and microscope software and the analysis of flexible and dynamic macromolecular complexes demand powerful computing resources. While the microscope operation and image processing are getting increasingly automated and require less manual input, the design and deployment of an HPC system, suitable to fulfill such demands, is still very tedious and can quickly become overwhelming, especially for not professional system administrators.
Here we describe the design choices for our recent cryo-EM HPC system and explain how we automated its installation and deployment with a combination of Metal-As-A-Service (MAAS) and Ansible. The cluster incorporates multi-GPU nodes, highspeed Interconnection (InfiniBand HDR) and a parallel file system (BeeGFS). Our approach can be easily adapted to different storage and hardware systems and enables inexperienced personnel to set up an HPC with little time.

**P23**

**Bacillus Calmette–Guérin Immunotherapy restores the impaired antiviral immunity in Recurrent Respiratory Papillomatosis**

Evelina Vetskova, Maria Nikolova

National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria

Recurrent respiratory papillomatosis (RRP) is characterized by recurrent proliferation of benign squamous papillomas within the respiratory tract causing severe airway obstruction. More than 90% of RRP cases are caused by human papillomavirus (HPV) type 6 and 11. The current therapeutic strategy - classical surgery does not prevent relapses, and its combination with antiviral drugs or IFN alpha therapy has no significant success and does not completely prevent recurrence of the papillomas. *BCG (Bacillus Calmette–Guérin*) is a potent modulator of the immune response and has been successfully applied for treatment of superficial bladder cancer and malignant melanoma. The present study investigates the effects of BCG on antiviral immune response in RRP patients subjected to combined surgery / BCG immunotherapy. Blood samples from RRP patients subjected to combined surgery / BCG-immunotherapy on approved scheme were studied before (0), 6, 12 and 20 months after the start of immunomodulation. The percentage and absolute count of peripheral blood lymphocyte subsets and the *in vitro* stimulated secretion of Th1/Th2/Th17 cytokines were studied by multicolor flow cytometry. Significantly increased levels of IFN gamma-secreting CD4 (Th1) and CD8 (Tc1) cells were established in RRP patients in response to non-specific stimulation as compared to healthy controls. Th1 cells were normalized to control reference value after 20 months of BCG immunotherapy. In addition, the share of the regulatory T-cells was increased as compared to untreated RRP patients and healthy controls and Th17 cells was decreased. BCG immunotherapy significantly increased level of mature and plasmocytoid dendritic cells. These results indicate that BCG restores the impaired *antiviral response.*

**P24**

**Deregulated origin firing as a driver of whole chromosomal instability**

Nicolas Böhly[1], Benjamin O. Slusarenko[1], Holger Bastians[1]

[1]University of Göttingen, UMG, GZMB, Institute of Molecular Oncology, Section of Cellular Oncology, 37077 Göttingen, DE

A common feature among solid tumors is chromosomal instability (CIN) which has been described as a major driver of tumorigenesis and tumor progression. CIN can be divided into two subtypes differentiating between whole chromosomal (*i.e.* loss/gain of whole chromosomes) and structural chromosomal (*i.e.* structural aberrations) instability. Interestingly, both types seem to occur concomitantly and replication stress (RS), defined as slowed or stalled replication fork progression, during DNA synthesis might act as a link. Our lab showed that RS leads to an increase in microtubule plus end polymerization rates in mitosis which in turn causes an increase in the occurrence of lagging chromosomes and ultimately causes whole chromosomal missegregation and aneuploidy in colorectal cancer cells (CRC). Furthermore, we were able to specifically link this phenotype to deregulated DNA replication initiation independent of the more general aspect of RS. Overexpression of key origin firing factors, such as *CDC45* and *GINS1*, increases the rate of origin firing while replication fork speed remains unchanged. Moreover, this causes an increase in microtubule dynamics and lagging chromosomes culminating in W-CIN and aneuploidy. Notably, inhibition of the Cdc7 kinase reduces origin firing and rescues this CIN phenotype both in a RS dependent and independent context. Thus, we identified increased origin firing in S phase as a novel trigger for whole chromosomal instability in human cancer cells.

**P25**

**Direct-PCR based detection method for mislabeled Fish meat samples from local markets of Lahore, Pakistan**

Tamkeen Zaman & Fouzia Qamar

Lahore Garrison University, Lahore, Pakistan

Direct -PCR based analysis has been carried out for the fish meat identification to check the fraudulence and authenticity of the type sold at the local market. For this purpose an in house developed assay was performed for DNA extraction(PCR kit KCl buffer). A Polymerse Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) method has been developed for the detection of four majorly consumed local species of fish in Punjab, Pakistan. The Universal primers designed targeted the mitochondrial gene (16S rRNA) and amplified the product. The results obtained from enzymes digestion could be used to distinguish the four fish species of fish *i.e*. Rohu (*Labeo rohita*) , Malli (*Wallago attu*), Singharra (*Sperata seenghala*), Chirra (*Oreochronis niloticus*).This direct PCR based amplification and quick developed RFLP method will address a technically challenging issue of fish meat speciation and will help especially to identify the misrepresentation of meat of four local fish species of Pakistan, suspected to be mislabeled in the local market.

**P26**

**Structural Characterization of the Human Pyruvate Dehydrogenase E2 Core by Cryo-Electron Microscopy**

Eduardo Cienfuegos-Pecina[1], Sabin Prajapati[2], Rahul Shaha[2], Kai Tittmann[2], Holger Stark[1]

[1]Department of Structural Dynamics, Max Planck Institute for Multidisciplinary Sciences
[2]Department of Molecular Enzymology, Göttingen Center for Molecular Biosciences, University of Göttingen

The pyruvate dehydrogenase (PDH) complex is one of the most important crossroads in metabolism, linking the anaerobic glycolysis with the aerobic metabolism, the synthesis of fatty acids, and the production of ketone bodies. It is a ~10 MDa multienzyme complex, with three catalytic activities: pyruvate dehydrogenase (E1p), dihydrolipoyl transacetylase (E2p), and dihydrolipoyl dehydrogenase (E3). However, the structure of this complex remains elusive, and current efforts have been focused in elucidate the structures of its isolated components. In this study, the structure of the truncated E2p (tE2p) core (containing only the core-forming domain) was obtained at a resolution of 3.4 Å by cryo-electron microscopy. In addition, tE2p was evaluated in the presence of CoA, acetyl-CoA, decanoyl-CoA, DMSO, and two drug candidates. This is the first structural study showing the interaction of the human tE2p with its substrate. The CoA, acetyl-CoA, and decanoyl-CoA molecules bound the active site in an extended conformation, stabilizing the flexible loop formed by the residues Ala$^{519}$, Gly$^{520}$, and Leu$^{521}$. These residues act as gatekeepers of the substrate channel, locking the substrate inside the active site. In addition, this study suggests the binding of the two drug candidates to the region of the active site that interacts with the lipoyl groups. These results give a new insight into the structural dynamics and mechanistic details of the human tE2p and represent a starting point in the development of new strategies to understand the structural characteristics of the PDH complex.

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**P27**

**The SH2 domain-containing inositol 5-phosphatase 2 controls the survival of Burkitt's lymphoma by regulating ATP production**

Florian Mayr[1], Vanessa Kruse[1], Dominik Fuhrmann[2], Sebastian Wolf[2], Jens Löber[3], Björn Chapuy[3], Thomas Oellerich[2], Michael Engelke[1]

[1]Institut für zelluläre und molekulare Immunologie, Universitätsmedizin Göttingen
[2]Hämatologie/Onkologie, AG Oellerich, Universitätsklinikum Frankfurt
[3]Klinik für Hämatologie und medizinische Onkologie Universitätsmedizin Göttingen, Klinik m.S. Hämatologie, Onkologie und Tumorimmunologie, Charité, Campus Benjamin Franklin

The survival of a substantial proportion of Burkitt's lymphoma (BL) relies on aberrant tonic BCR signals. The survival signaling downstream of the phosphatidylinositol 3-kinase (PI3K) is important, the details of BL-specific tonic BCR signaling remains unclear. By Phosphoproteomics of tonic BCR signaling and drop-out screening we identified the SH2-containing inositol phosphatase SHIP2 as a novel effector in this pathway.
SHIP2 inhibition and interfering with SHIP2 expression markedly reduced the proliferation and survival of several BL cell lines that have been shown to rely on aberrant tonic BCR signaling. Since SHIP2 is a functional antagonist of PI3K, we assessed the efficiency of tonic BCR survival signals in the absence of SHIP2. However, activity of the survival kinase AKT remains unaffected by SHIP2 deficiency. Contrary, SHIP2-deficient BL cells exhibit higher sensitivity to PI3K inhibition than parental or reconstituted cells. Proteomic analyses confirmed that PI3K signaling is unaffected by SHIP2 deficiency but indicate a shift in metabolism affiliated proteins. Consistently, a seahorse assay revealed significantly reduced ATP production in the absence of SHIP2, while the surface abundance of glucose transporters and glucose uptake are not altered. These data prompted us to asses, if the SHIP2 product PI(3,4)P2 accounts for the effect on metabolism. For this purpose we down regulated the expression of SHIP1, which should further reduce the amount of PI(3,4)P2 in the plasma membrane. This approach revealed further attenuation of BL cell proliferation, survival and an increased sensitivity of BL cells to PI3K inhibition.

Our findings suggest that targeting the 5'-inositol phosphatases, thereby reducing PI(3,4)P2, affects the energy resources of this aggressively proliferating lymphoma by compromising ATP production. Hence, inhibition of SHIP2 may be an efficient option for combinatorial therapies to treat BL.

**P28**

**Identification and characterization of novel crosstalk among cadherins and nectins that mediate cell-to-cell adhesion**

Sagarika Dash, Dibyendu Samanta

School of Bioscience, Indian Institute of Technology Kharagpur, Kharagpur, West Bengal, 721302, India

Cell-to-cell adhesion is fundamental for the initiation and regulation of various physiological processes and any alterations in the adhesion process can lead to disruption of cellular function and disease progression. Cadherins and nectins are cell-surface proteins that organize and assemble to form adherens junction at the sites of cellular contacts of different cell types to form higher-ordered multicellular structures. Cadherins engage in calcium-dependent homophilic and nectins engage in calcium-independent homophilic as well as heterophilic interactions respectively. Intracellular crosstalk among the cytosolic adaptor proteins of nectins and cadherins has been well elucidated with respect to their assembly and formation of the adherens junction. However, only a few studies suggest direct crosstalk between these cadherins and nectins through their ectodomains, and this area of research needs thorough investigation. We have recently characterized the recognition between N-cadherin and E-cadherin followed by structure-guided mutagenesis and complementary biophysical experiments to elucidate the binding interface. Furthermore, using SPR-based protein-protein interactions, we have identified a novel crosstalk between E-cadherin and nectin-4 mediated through their membrane distal ectodomains. In conclusion, our biophysical, biochemical and cell-based studies reveal the direct crosstalk among cadherins, and nectins mediated through their N-terminal ectodomains required for physiologically relevant cell-to-cell adhesion.

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**P29**

**Mitigating endoplasmic reticulum stress, astrogliosis, microgliosis by empagliflozin improves motor function in rotenone-induced Parkinson's disease rat model.**

Tarek K. Motawi [1], Rawan H. Al-Kady [2], Sahar M. Abdelraouf [2], Mahmoud A. Senousy [1]

[1]Biochemistry department, Faculty of Pharmacy, Cairo University, Cairo, Egypt.
[2]Biochemistry department, Faculty of Pharmacy, Misr International University, Cairo, Egypt

Empagliflozin (Empa), a selective sodium-glucoseco-transporter-2 inhibitor, has been highlighted as a promising therapeutic agent for motor impairment neurodegenerative diseases such as Alzheimer's. Endoplasmic reticulum (ER) stress is a major participant in neurodegeneration and occurs at the intersections of various pathologic pathways, yet its role in Parkinson's disease (PD) pathology remains poorly elucidated. miR-211-5p is known to promote neuronal development and viability and is thought to target CHOP, an ER stress pathway downstream effector. This study aims to uncover the potentiality of empa to have a neuroprotective impact in an induced rat model of PD from the perspective of ER stress. Wistar male rats were randomly assigned into 4 groups; group 1 received the vehicle, while group 2 received empa (10mg/kg/day p.o), group 3 were given rotenone (1.5mg/kg/48hr s.c) and group 4 received rotenone (1.5mg/kg/48hr s.c) for 21 days, concomitantly with empa (10mg/kg/day p.o) for 15 days. During the histopathological assessment, rotenone did induce SNpc neuronal degeneration and state of neuroinflammation evidenced by the upsurge in immune reactivity of glial fibrillary acidic protein (GFAP) and ionized calcium-binding adaptor protein 1 (Iba1). On the molecular level, the striatal levels of the ER stress inducers were upregulated in the rotenone intoxicated rats, as GRP78, total and P-PERK, eIF2α, and CHOP. Empa abated the rotenone-induced neurobehavioral deficits (open field, grip strength, and footprint gait), neuroinflammation, and histopathological abnormalities. Empa suppressed striatal miR-211-5p levels and enhanced both beclin1 and catalase activity. Finally, these findings highlight empagliflozin's neurotherapeutic potential in PD by modulating the ER stress protein effectors, downregulating miR-211-5p, resolving oxidative stress, reducing astrocyte/microglial activation and neuroinflammation, and enhancing autophagy.

**P30**

**Mechanism of molnupiravir-induced SARS-CoV-2 mutagenesis**

Florian Kabinger, Carina Stiller, Jana Schmitzová, Christian Dienemann, Goran Kokic, Hauke S. Hillen, Claudia Höbartner & Patrick Cramer

Molnupiravir is an orally available antiviral drug candidate currently in phase III/ IV trials for the treatment of patients with COVID-19. Molnupiravir increases the frequency of viral RNA mutations and impairs SARS-CoV-2 replication in animal models and in humans. We establish the molecular mechanisms underlying molnupiravir-induced RNA mutagenesis by the viral RNA-dependent RNA polymerase (RdRp). Biochemical assays show that the RdRp uses the active form of molnupiravir, β-D-$N^4$-hydroxycytidine (NHC) triphosphate, as a substrate instead of cytidine triphosphate or uridine triphosphate. When the RdRp uses the resulting RNA as a template, NHC directs incorporation of either G or A, leading to mutated RNA products. Structural analysis of RdRp–RNA complexes that contain mutagenesis products shows that NHC can form stable base pairs with either G or A in the RdRp active center, explaining how the polymerase escapes proofreading and synthesizes mutated RNA. This two-step mutagenesis mechanism probably applies to various viral polymerases and can explain the broad-spectrum antiviral activity of molnupiravir.

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**P31**

**Structural and functional studies of Bestrhodopsins – a novel protein family found in unicellular algae**

Igor Kaczmarczyk[1,2], Donna Matzov[1], Andrey Rozenberg[3], Ishita Das[4], Johannes Vierock[5], Mordechai Sheves[4], Peter Hegemann[5], Oded Béjà[3], Moran Shalev-Benami[1]

[1]Department of Chemical and Structural Biology, Weizmann Institute of Science, Rehovot, Israel
[2]Max Planck Research Group, Malopolska Centre of Biotechnology, Jagiellonian University, Krakow, Poland
[3]Faculty of Biology, Technion – Israel Institute of Technology, Haifa, Israel
[4]Department of Molecular Chemistry and Materials Science, Weizmann Institute of Science, Rehovot, Israel
[5]Institute for Biology, Experimental Biophysics, Humboldt-Universität zu Berlin, Berlin, Germany

Rhodopsins, a family of evolutionary conserved light-harvesting membrane proteins are extensively utilized in nature for a variety of cellular applications. Over the years, hundreds of rhodopsin species have been identified, demonstrating that despite all share common structural and mechanistic features, the family members are rather diverse, with functions that range from light-driven activation of ion pumps and light-gated ion channels to light-sensors that activate transducer proteins for intracellular signaling. Through a collaborative work between nine groups across the globe, we discovered and characterized a novel family of rhodopsins derived from unicellular algae – the bestrhodopsins. Bestrhodopsins, are composed of one (or two) rhodopsin domains, linked in tandem, that are C-terminally fused to a bestrophin-like channel domain. We solved 3.2 Å cryoEM structure of the bestrhodopsin complex and revealed that they assemble as pentameric megacomplexes (~700 kDa), where five (or five-pairs of) rhodopsins surround a central ion channel and act to mediate light-depended ion permealization. We then showed that heterologously expressed bestrhodopsins behave as a light-modulated anion channels. Altogether, this work sheds light on the structure and function of a novel family of rhodopsins – the bestrhodopsins, providing new insights regarding the evolution, structure, and mechanisms of light-sensing in nature. In addition, it has important applicative aspects, especially in the emerging field of optogenetics, that utilizes engineered rhodopsins to deepen our understanding of the brain and brain circuits function.

**P32**

**Structures of Importin 7 bound to RanGTP and in complex with Importin b and histone H1°**

Zhenglin Fu, Bernard Freytag, Trevor Huyton, and Dirk Görlich[1]*

[1]Department of Cellular Logistics, Max Planck Institute for Multidisciplinary Natural Sciences, am Fassberg 11, 37077 Göttingen, Germany

Importins are responsible for transporting a wide range of proteins into the cell nuclei. For the import of highly positively charged proteins, they not only act as transport receptors but also operate as chaperones to shield the positively charged regions from undesired ionic interactions. H1° is a prime example of such basic cargo, and its transport requires two Impβ-superfamily proteins, Importin 7 and Importin β. In this study, we now report the cryo-EM structures of the Imp7-Impβ-H1° and the Imp7-RanGTP complexes. The H1° import complex revealed that Importin 7 interacts with Importin β via three surfaces, and that the heterodimerization results in a large negatively charged cavity. This acidic cavity, together with the long acidic loop of Importin7, is in transient non-specific interactions with H1° positively charged tails while Importin 7 wraps around the H1° globular domain alone with its inner surface. This explains why the heterodimer of Importin 7 and Importin β is necessary for safe transport and how the importins can protect the massive positive charge of this cargo. The structure of Importin 7 bound to RanGTP shows how H1° is released in the nucleus.

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**P33**

**iBench & inSPIRE: Getting peptide sequences right**

John A. Cormican[1], Yehor Horokhovskyi[1], Wai Tuck Soh[1], Michele Mishto[2,3], Juliane Liepe[1]

[1]Max-Planck-Institute for Multidisciplinary Sciences (MPI-NAT), 37077 Göttingen, Germany
[2]Centre for Inflammation Biology and Cancer Immunology (CIBCI) & Peter Gorer Department of Immunobiology, King's College London, SE1 UL London, United Kingdom
[3]The Francis Crick Institute, WC2A 3LY London, United Kingdom

Large scale peptide and protein identification via mass spectrometry (MS) has allowed deeper insight into cellular function. From proteogenomics to HLA-I immunopeptidomics, MS has a wide-reaching impact on our understanding of cellular processes. Despite these successes, obtaining high sensitivity in peptide identification can be very challenging in certain cases, particularly if there is a large search space of possible peptides present in the sample. Such complex samples present a challenge to achieve high sensitivity - detecting the correct peptide as often as possible, while maintaining high specificity – avoiding false identifications of incorrect peptides. In recent years, large scale machine learning based efforts in MS enable the prediction of many experimentally observable peptide properties, which can be used to inform MS peptide identification algorithms via rescoring of peptide candidates. Newly developed approaches should be carefully benchmarked in terms of their performance before application, to determine the method's precision, recall, and to elucidate potential biases in the pool of identifiable peptides. Here we propose a novel MS benchmarking platform, iBench, which was applied to compare the performance of existing MS identification methods, with and without rescoring approaches. Furthermore, using the iBench platform, we developed a novel rescoring approach for peptide identification - inSPIRE, which outperforms current state of the art tools, both in terms of precision and recall. Finally, we demonstrate how inSPIRE can overcome large sequence space problems on the example of identification of proteasome generated spliced peptides. The combination iBench and inSPIRE allows modern research to push the boundaries of MS identification with highly sensitive tools, while maintaining a firm eye on the accuracy and specificity of the method. This will enable the robust and confident identification of non-canonical peptides and proteins.

**P34**

**Onkopus – A Decision Support Framework for Evidence-Based Interpretation and Selection of Actionable Genetic Alterations in Cancer Research and Precision Medicine**

Nadine S. Kurz[1,2], Kevin Kornrumpf[1], Klara Drofenik[1], Tim Tucholski[1], Vera Gnaß[1], Jürgen Dönitz[1,2,3]

[1]Dept. of Med. Bioinformatics, University Medical Center Göttingen (UMG), Germany
[2]Comprehensive Cancer Center Lower Saxony (CCC-N), Germany
[3]Inst. of Computational Biology (ICB), Helmholtz Zentrum München, Germany

Precision oncology offers new methods for identifying relevant genetic alterations in cancer patients, distinguishing benign from pathogenic variants as well as identifying actionable variants.

This requires the identification and interpretation of genetic variants in terms of estimating the pathogenicity of each variant for a particular tumor type. As the manual annotation of variants is a very extensive task, there is a high need for computational support systems that offer a solution for variant annotation and interpretation. Here we present Onkopus, a framework focusing on variant interpretation for precision medicine and cancer research. Onkopus is based on a large number of separate modules, offering functionality for SNP frequency, variant pathogenicity estimation, variant impact scoring and machine learning approaches. For interpreting variants of unknown significance (VUS), we have developed a new method. We will further work on modules for copy number variation analysis, protein docking and 3D structure prediction of proteins and their impact on loss of function (LoF) proteins. Finally, all the gathered variant information will be employed in a newly developed machine learning based method for functional and clinical variant interpretation that will result in direct treatment recommendations to clinicians on an individual basis. Onkopus will be available in two ways, on the one hand as a web front-end for clinicians, on the other hand as a command line client targeting big data analyses. In cooperation projects, we will develop and evaluate our framework. In lymphoma projects, we will identify new targets and drug combinations. In a molecular tumor board (MTB), we will evaluate Onkopus on real patient data and compare our final treatment recommendations to clinicians' decisions to test the performance of our algorithm.

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**P35**

**Gene polymorphism of Melanocortin-4 Receptor (MC4R) and its association with milk yield performance in crossbred anglo-nubian dairy goats**

Jessah P. Trillo*, Carlo Stephen O. Moneva

Mindanao State University-Iligan Institute of Technology, Iligan City
Email: jessah.trillo@g.msuiit.edu.ph

The *melanocortin 4-receptor* (*MC4R)* is a promising candidate gene for studies on the genetic regulation of body composition and growth. Association studies have been conducted on its polymorphisms in several domestic animals, but to date, no conclusive evidence on the influence of its polymorphism on milk production traits has been reported. In this study, the association of the genetic polymorphisms of the *MC4R* with milk yield performance in 101 crossbred dairy goats was investigated using the PCR-RFLP method from the farms in the Philippines namely, Awang, Opol, Misamis Oriental and Talay, Dumaguete City, Negros Oriental in the Philippines. Milk yield performance data were standardized to 9- and 140 d milking periods. The goat's hair follicles were subjected to extract genomic DNA. Oligonucleotide primers standardized for goats F (5') TCGGGCGTCTTGTTCATCAT (3') and R (5') CAAGACTGGGCACTGCTTCA (3') amplified the 642 bp fragment of the *MC4R* gene. Using the *KpnI* restriction enzyme, three genotypes (CC, CT, TT) were detected. The CT genotype had three bands at 642 bp, 447 bp, and 165 bp, the CC genotype had at 642 bp, and TT yielded two fragments at 447 bp and 165 bp positions. Statistical analysis was performed following the two-way factorial (2 x 4) in a randomized complete block design (RCBD), where *MC4R* genotypes and parity were used as the main factors, whereas farm as the blocking factor. CT genotype (0.63) and both C (0.50) and T (0.50) allele frequencies were found predominant in the studied population. The observed heterozygosity value was higher than the expected heterozygosity value. The studied population has a significant variation in Hardy-Weinberg equilibrium ($p<0.05$) based on the chi-squared test using the Pop Gene 32.1 software. It is highest in Opol A and lowest in Opol B. Meanwhile, the TT genotype significantly increases the milk yield performance at 90 days' average milk yield and total milk production (90dADMY: 1.22±0.053, 90dTMP: 105.77±4.16) The results demonstrated that *MC4R* (C1079T) could be used as a potential marker for future selection breeding programs.

Keywords: Anglo-Nubian, *melanocortin 4-receptor*, milk yield, PCR-RFLP, polymorphisms

**P36**

**An intruder-targeting system eliminates paternal mitochondria after fertilization in *Drosophila***

Sharon Ben-Hur, Sara Afar, Yoav Politi, Liron Gal, Ofra Golani, Keren Yacobi-Sharon and Eli Arama

Department of Molecular Genetics, Weizmann institute of Science, Rehovot, Israel
Sharon.benhur@weizmann.ac.il

Maternal inheritance of mitochondria occurs in almost all organisms, spanning from fungi and plants to humans. Upon fertilization, a sperm penetrates the egg together with its mitochondria, resulting in a short period where mitochondria from both gametes populate the early embryo. Within a few cell cycles, however, paternal mitochondria (**PM**) are eliminated, and propagating maternal mitochondria take over the mitochondrial network. Several reports illustrate PM elimination as an outcome of passive dilution by the vast maternal mitochondrial pool. Yet, recent studies, performed on different organisms, suggest active elimination of PM by egg-derived mechanisms. In particular, our group previously demonstrated that in *Drosophila*, PM is eliminated soon after fertilization. Moreover, we showed that egg-derived multi-vesicular bodies (**MVBs**) associate with PM immediately after fertilization to promote PM degradation. However, the mechanisms by which MVBs mediate paternal mitochondrial destruction remain unknown[1].
Here, I will present our recent findings aiming to identify the mechanisms by which egg-derived MVBs target and destroy PM in *Drosophila*. Specifically, MVBs isolation and subsequent proteomic analysis uncover possible involvement of proteins related to innate immunity. Furthermore, we identify a cell intruder-targeting pathway, called LC3-associated phagocytosis (LAP), which is a common endocytic, autophagic and phagocytic pathway, as the main executer of PM elimination. Our model indicates that MVBs loaded with LAP-specific components engage with PM to mediate its elimination. LAP-specific phosphatidylinositol 3-phosphate kinase (PI3K) complex is recruited to PM for PI3P production. The presence of PI3P, together with ROS production, promotes Atg8 (LC3) conjugation to PM, facilitating sequestration of PM to lysosomes. Finally, I will also present initial evidence for possible conservation of some of these mechanisms during corresponding processes in mammalian eggs.

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**P37**

**Proline/Arginine dipeptide repeat polymers derail protein folding in amyotrophic lateral sclerosis and frontotemporal dementia.**

Maria Babu[1] , Filippo Favretto[1] , Alain Ibáñez de Opakua[1] , Marija Rankovic[2], Stefan Becker [2] & Markus Zweckstetter [1,2]

[1]German Center for Neurodegenerative Diseases (DZNE), Göttingen, Germany
[2]Department for NMR-based Structural Biology, Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

Amyotrophic lateral sclerosis(ALS) and frontotemporal dementia(FTD) are two neurodegenerative diseases with clinical and pathological overlaps. The most common cause of familial ALS and FTD is a hexanucleotide repeat expansion(HRE) mutation in the non-coding region of C9orf72 gene. The toxicity of this mutation is associated with dipeptide repeat polymers (DPRs) that are unconventionally translated from the expanded region of C9orf72 gene. Five different dipeptide repeat species are translated from the expanded region which includes Pro/Arg, Gly/Arg, Gly/Pro, Pro/Ala and Gly/Ala repeats. Among these five, the Pro/Arg and Gly/Arg repeats, that are rich in arginine, are the most toxic species. In our work, we identified a novel toxic pathway in C9orf72 mutated ALS and FTD, that is based on the inhibition of molecular chaperones. Using protein folding assay, we demonstrated that Pro/Arg repeat polymers inhibit the activity of the folding chaperone PPIA. PPIA is an abundant chaperone in the cell, that enhances the rate of folding of nascent amino acid chains by enhancing the cis-trans interconversion of prolyl peptide bonds. NMR spectroscopy and X-Ray crystallography provided the structural basis of the inhibition of PPIA by Pro/Arg repeats. Pro/Arg repeats bind to the catalytic pocket of PPIA thus inhibiting its activity. Our data establish a toxic mechanism that is specific for Pro/Arg dipeptide repeats and leads to disrupted protein homeostasis in *C9orf72*-ALS and FTD.

**P38**

**Monitor and manipulate nuclear envelope formation - Lamin-B-receptor and atlastin specific nanobodies**

L. Gräser, D. Görlich

Nanobodies (Nb) are antigen-binding domains derived from camelid heavy-chain only antibodies. They can be selected to high specificity and affinity, are easy to produce in *E. coli*, straightforward to label with fluorescent dyes, and, due to their small size (~15 kDa), can access epitopes that are inaccessible to traditional antibodies.

We employed nanobodies here to study nuclear envelope (NE) disassembly and re-formation after mitosis. To obtain such nanobodies, we immunized alpacas with the respective target, generated immune libraries, and isolated binders by phage display. Nbs binding different epitopes would allow to either monitor the target´s fate during assembly and disassembly without sterically interfering or to block protein-protein interactions by masking binding sites.

So far, we obtained specific Nbs against the tudor domain of the inner nuclear membrane-spanning Lamin-B-receptor (LBR). With these Nbs we were able to track the endogenous protein during nuclear assembly.

Furthermore, we raised specific Nbs against the GTPase atlastin, which was shown to drive ER membrane fusion. Nanobody-mediated inhibition of atlastin function during nuclear assembly (in the *Xenopus* egg extract system) prevented the formation of a functional NE and insertion of nuclear pore complexes (NPCs).

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**P39**

**The Mediator complex regulates enhancer-promoter interactions**

Shyam Ramasamy[1], Abrar Aljahani[1], Magdalena A. Karpinska[1], T. B. Ngoc Cao[1], J. Neos Cruz[1] & A. Marieke Oudelaar[1]

[1]Max Planck Institute for Multidisciplinary Sciences, Göttingen, 37077, Germany

Enhancer-mediated gene activation generally requires physical proximity between enhancers and their target gene promoters. However, the molecular mechanisms by which interactions between enhancers and promoters are formed remain unclear. Here, we investigate the function of the Mediator complex in the regulation of enhancer-promoter interactions, by combining rapid protein depletion and high-resolution MNase-based chromosome conformation capture approaches. We show that depletion of Mediator leads to reduced enhancer-promoter interaction frequencies, which are associated with a strong decrease in gene expression. In addition, we find increased interactions between CTCF-binding sites upon Mediator depletion. These changes in chromatin architecture are associated with a re-distribution of the Cohesin complex on chromatin and a reduction in Cohesin occupancy specifically at enhancers. Our results indicate that enhancer-promoter interactions are dependent on an interplay between the Mediator and Cohesin complexes and provide insights into the molecular mechanisms by which communication between enhancers and promoters is regulated.

**KEYWORDS**

Gene regulation, enhancers, enhancer-promoter interactions, genome organization, Mediator, Cohesin

**P42**

**Structure-function analysis and rational design of enzymes involved in cellulose biosynthesis of cotton**

Melina Shamshoon

Department of Plant and Environmental Sciences, Weizmann Institute of Science, Israel

Cellulose is the most abundant organic polymer on Earth, produced by a taxonomically diverse group of organisms. Cellulose biosynthesis is a complex process undergoing two major pathways that can also interact through an intermediate path. We recently harnessed the cellulose biosynthesis complexity in cotton by combining the chemical synthesis of building blocks that carry the desired functional and *in vitro* fertilized cotton, yielding cellulose fibers with tailored properties – material farming. These building blocks are metabolized by cellulose biosynthetic pathways, and increasing their concentration does not affect their level of incorporation, raising the question of the enzyme specificity and catalytic turnover regarding these artificial substrates.

Prior to the present work, the enzymes responsible for cotton-fiber biosynthesis had not been successfully expressed *in vitro*. Their structure is unknown, hindering our ability to understand their function and modify them to enhance their catalytic activity. Recent advances in computational power, availability of large structural databases, development of robust algorithms, and artificial DNA synthesis for experimental validation are increasingly empowering scientists and engineers to devise more effective methods for manipulating and tailoring biocatalysts. This opens a new opportunity for structural analysis and rational design of modified cellulose biosynthesis enzymes in cotton.

Using a combination of genome screening and molecular biology tools, we were able to express *in vitro* active representatives of each enzyme involved in the UDP-glucose pyrophosphorylase pathway of cellulose biosynthesis of cotton for the first time. While these are active toward their natural substrates, we found a significant catalytic activity toward unnatural glucose derivatives. Thus, we combined AI-based 3D structural predictions with rational design to create artificial “superenzymes” with enhanced catalytic activity and substrate specificity toward unnatural substrates. This will result in a deeper understanding of enzyme structure-function relations in cellulose biosynthesis in cotton while offering a novel and unique framework to create optimized biosynthetic pathways in cotton to design future sustainable cotton-based materials.

With the tequnique of predicted protein modeling we have been able to demonstrate their predicted structures, which then we will help us to implement a rational design workflow that combines theoretical and experimental approaches to establish a stable synthetic genes-based high-yield heterologous expression platform for the first time. Then, we will rationally (re)design their active sites, using theoretical and experimental approaches to enhance their catalytic activity toward artificial substrates for the first time, to express other cotton enzymes successfully and, if desired, rationally design their active sites toward enhancing their catalytic activities. Yet, this body of knowledge could pave the way for the generation of rationally designed cotton plants with tailored enzymatic functions such as new and improved fibers production.

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**P43**

***The molecular identity of the insect neural cell lineages at single-cell resolution***

Noel Cabañas[1, 2] and Gregor Bucher[1*]

[1]Department of Evolutionary Developmental Genetics, GZMB, University of Göttingen, Göttingen, Germany
[2]International Max Planck Research School for Genome Science, Göttingen, Germany
* gregor.bucher@bio.uni-goettingen.de

The brain is a complex organ that coordinates multiple vital functions and the interaction organism-environment. In insects, the fundamental brain architecture is conserved, so it is an assumption that its development is similar in all insects. Nonetheless, morphological and behavioral differences suggest evolutionary adaptations that must emerge by developmental disparities. According to *Drosophila* studies, the brain develops from neural stem cells denominated neuroblasts. They obtain different spatial identities due to the combined expression of transcription factors in the neuroectoderm before they delaminate. Subsequently, they undergo several rounds of asymmetrical divisions thereby exhibiting different temporal identities, which are inherited by the ganglion mother cells that divide once more to generate the neural and glial cells. While the number of neuroblasts is known to be different, it remains unclear in how far neuroblast identities differ between insect species. Single-cell technologies are opening new opportunities to produce genome-wide expression data at a single-cell resolution and are making possible comparisons among organisms. We focus on the red flour beetle, *Tribolium castaneum*, which exhibits an anterior development more typical of insects and has an extensive toolkit for gene function studies. We aim to use single-cell sequencing to compare the number and molecular identity of *Drosophila* and *Tribolium* neuroblasts. To achieve this goal, we set up a pipeline to analyze available *Drosophila* single-cell data, we established a transgenic line to mark neuroblasts, and we optimized a dissociation protocol that will allow us to perform single-cell mRNA sequencing. We expect to establish the *Tribolium* neuroblast lineages and their transcription expression programs, and determine the degree of conservation and divergence between the neuroblast lineage of *Tribolium* and *Drosophila*.