DK-MCD Virtual Guest Lecture Series (summer term 2021)

Friday, 26.02.2021, 2:30 pm **Bridges, Tunnels, and Ferries: How bacteria move lipids between membranes** by Prof. **Damian Ekiert** Department of Cell Biology and Department of Microbiology, Skirball Institute; NY, USA http://bhabhaekiertlab.org/ https://med.nyu.edu/faculty/damian-c-ekiert You gain access by an invitation shortly before the presentation. Please register by email to docfund.mobiles@uni-graz.at subject: "**Guest lecture Ekiert**"	2 Units
Metabolism Month - Online conference about energy control & metabolism 02./09./16./23.03.2021 https://cbmr.ku.dk/metabolismmonth2021/ Registration is required but free of charge.	2 Units per day
ÖGMBT Life Science Tuesday https://oegmbt.at/jahrestagung/life-science-tuesdays (registration required) 09.03.2021 Daniela Thommen (Netherlands Cancer Institute, The Netherlands): Dissecting immune reactivity in human cancers using patient-derived tumor fragments 23.03.2021 Stephane Guillouet (INSA, Toulouse, France): Metabolic pathway and bioreactor engineering for biofuel and chemical production from CO2 in Cupriavidus necator	2 Units per day
Innovations in Fetal Therapy 15.04.2021, 15.30 - 18.00 LUMC Global and Leiden University Medical Center's Fetal Therapy department Registration is for free but required. For more information, please see below or visit the event page.	2 Units
Wednesday, 21.04. 2021, 2-5 pm **Unsuck your Science** ***How a culture of care improves our lives as scientists, as well as those of our animals*** This event is free of charge, will be held in English, and is organised by the German non-profit Pro-Test Deutschland e.V. More information and a detailed programme at http://unsuck.science	2 Units
Cell Adhesion, Signaling and Cancer **Mary Beckerle** (University of Utah) Adhesion, Signaling and Cancer (36 min) https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-1 Discovery and Characterization of a Focal Adhesion Protein Implicated in Tumor Progression (51 min) https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-2 Focal Adhesions as Stress Sensors (31 min) https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-3	2 Units
Mitochondria, Metabolism, and Cell Behavior **Jared Rutter** (University of Utah, Howard Hughes Medical Institute) Mitochondria: The Mysterious Cellular Parasite (31 min) https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-1 Mitochondrial Metabolism and Cell Decisions (25 min) https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-2 Mitochondria: The Fuel and the Fire (26 min) https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-3	2 Units
Protein Sorting and its Role in Organelle Function and Shape **Tom Rapaport** (Harvard Medical School and Howard Hughes Medical Institute, National Academy of SciencesGerman Academy of Sciences Leopoldina) Organelle Biosynthesis and Protein Sorting (35 min) https://www.ibiology.org/cell-biology/protein-sorting/#part-1 How are cellular organelles shaped? (33 min)	2 Units

https://www.ibiology.org/cell-biology/protein-sorting/#part-2	
Protein Localization Inside Cells **Ramanujan Hegde** (MRC Laboratory of Molecular Biology, Royal Society) Compartmentalization of Proteins Inside Cells (43 min) https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-1 Quality Control of Protein Localization (34 min) https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-2 Recognition of Protein Localization Signals (47 min) https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-3	2 Units
Protein Folding, Prions, and Disease **Susan Lindquist** (Whitehead and Massachusetts Institute of Technology, National Academy of SciencesNational Medal of Science) Protein Folding in Infectious Disease and Cancer (21 min) https://www.ibiology.org/biochemistry/prions/#part-1 Protein Folding in Neurodegenerative Disease (27 min) https://www.ibiology.org/biochemistry/prions/#part-2 Hsp 90: a Driver of Novelty in Evolution (59 min) https://www.ibiology.org/biochemistry/prions/#part-3 Prions: Protein Elements of Genetic Diversity (47 min) https://www.ibiology.org/biochemistry/prions/#part-4	2 Units
The Evolutionary Design of Proteins: How does Protein Design Happen? **Rama Ranganathan** (University of Texas Southwestern Medical Center) What is Protein Design? (27 min) https://www.ibiology.org/biophysics/protein-design-happen/#part-1 Model for Protein Design (32 min) https://www.ibiology.org/biophysics/protein-design-happen/#part-2 Protein Function and Adaptability (45 min) https://www.ibiology.org/biophysics/protein-design-happen/#part-3	2 Units
Metalloproteins in Action **Catherine Drennan** (Massachusetts Institute of Technology & Howard Hughes Medical Institute) Introduction to Metalloproteins (43 min) https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-1 Metalloproteins and Medicine (32 min) https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-2 Metalloproteins and the Environment (33 min) https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-3	2 Units
Neurodegenerative disease: The Coming Epidemic **Gregory Petsko** (Weill Cornell Medical College, National Academy of Sciences) Neurodegenerative disease: The Coming Epidemic (21 min) https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-1 Parkinson's disease: How might it be stopped? (25 min) https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-2 A potential gene therapy for ALS (25 min) https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-3	2 Units

Rules

- Only lectures from this list will be acknowledged.
- If we become aware of additional, suitable guest lectures, we will announce them by e-mail after approval by the program speakers.
- For each of these online lectures, the respective number of units as indicated in the list can be accredited.
- Please note that the units are accredited for the entire topic, not for each/an individual lecture therein, e.g. Obesity: all 3 lectures must be watched to gain 2 units.
- Attendance must be approved by signature of your PI in the attendance list for Journal Clubs and Guest lectures.
- At least 4 but not more than 8 units per attendance list can be covered by these virtual guest lectures. The remaining 22-26 units must be covered by Journal Clubs (4 units for attendance/6 units for the presentation per Journal Club session).
- When you have filled the attendance list with 30 units, send a scan to Karin. She will compare it with our list and forward it to the Office of Doctoral Studies if all is correct.

Guest lecture

PhD program
Molecular Metabolism

Invitation to an interesting talk given by…

Prof. Damian Ekiert

Assistant Professor, Department of Cell Biology and Department of Microbiology, Skirball Institute; NY, USA

Title: **Bridges, Tunnels, and Ferries: How bacteria move lipids between membranes**

Date: Friday, February 26th 2021, 2:30 p.m.

Venue: Via WebEx;
If you are interested please send an email to doc.fund.mobiles@uni-graz.at with the subject: "Guest lecture Ekiert" for registration. You will get an invitation lnk a day before the presentation.

host: DocFund MOBILES

Abstract

Gram-negative bacteria are surrounded by an outer membrane composed of phospholipids and lipopolysaccharide, which acts as a barrier and contributes to antibiotic resistance. The transport systems that drive phospholipid translocation across the periplasm, such as the MCE (Mammalian Cell Entry) systems, have not been well characterized at the molecular level. Using Cryo-EM and other approaches, we have begun to unravel some of the mechanisms of lipid transport across the bacterial envelope by MCE systems, particularly focused on the Mla, Pqi, and Let transporters from E. coli. Our lab is interested in understanding how these systems drive the insertion/extraction of lipids from membranes, facilitate transport across the envelope, and how this entire process is regulated. I will present our latest work on this intriguing family of transporters, and discuss our working model for how they facilitate the maintenance of the Gram-negative outer membrane.

Metabolism Month – An online conference about energy control and metabolism

Metabolism Month brings together researchers within the field of metabolism to discuss the latest science in metabolic diseases and energy control. It is hosted and organised by the Novo Nordisk Foundation Center for Basic Metabolic Research (CBMR) at the University of Copenhagen.

We have organised eight internationally-recognised speakers, three poster sessions and a debate, which will be held on **March 2, 9, 16 and 23**. The format is the same for each day: Two speakers with a poster session or debate in between, from 16:00 to 18:00 CET.

Registration is required

Metabolism Month is open to everyone, but to attend the lectures and poster sessions, registration is required.

March 2 - Integrative Metabolism and Environmental Influences

16:00-16:45
Joseph Bass, Department of Medicine and Neurobiology, Northwestern University, USA
16:45-17:15
Poster Session 1 – Integrative Metabolism and Environmental Influences
17:15-18:00
Philipp Scherer, Touchstone Diabetes Center, University of Texas Southwestern, USA

March 9 - Human Genomics and Metagenomics in Metabolism

16:00-16:45
Ruth Loos, Charles R. Bronfman Institute of Personalized Medicine, Icahn School of Medicine at Mount Sinai, USA
16:45-17:15
Poster Session 2 – Human Genomics and Metagenomics in Metabolism
17:15-18:00
Molly S. Bray, Department of Nutritional Sciences, University of Texas at Austin, USA

March 16 - Nutrient and Metabolite Sensing

16:00-16:45
Susan Ozanne, Institute of Metabolic Science Metabolic Research Laboratories, University of Cambridge, United Kingdom
16:45-17:15
Poster Session 3 – Nutrient and Metabolite Sensing
17:15-18:00
Martin Myers, Department of Internal Medicine and Molecular & Integrative Physiology, University of Michigan, USA

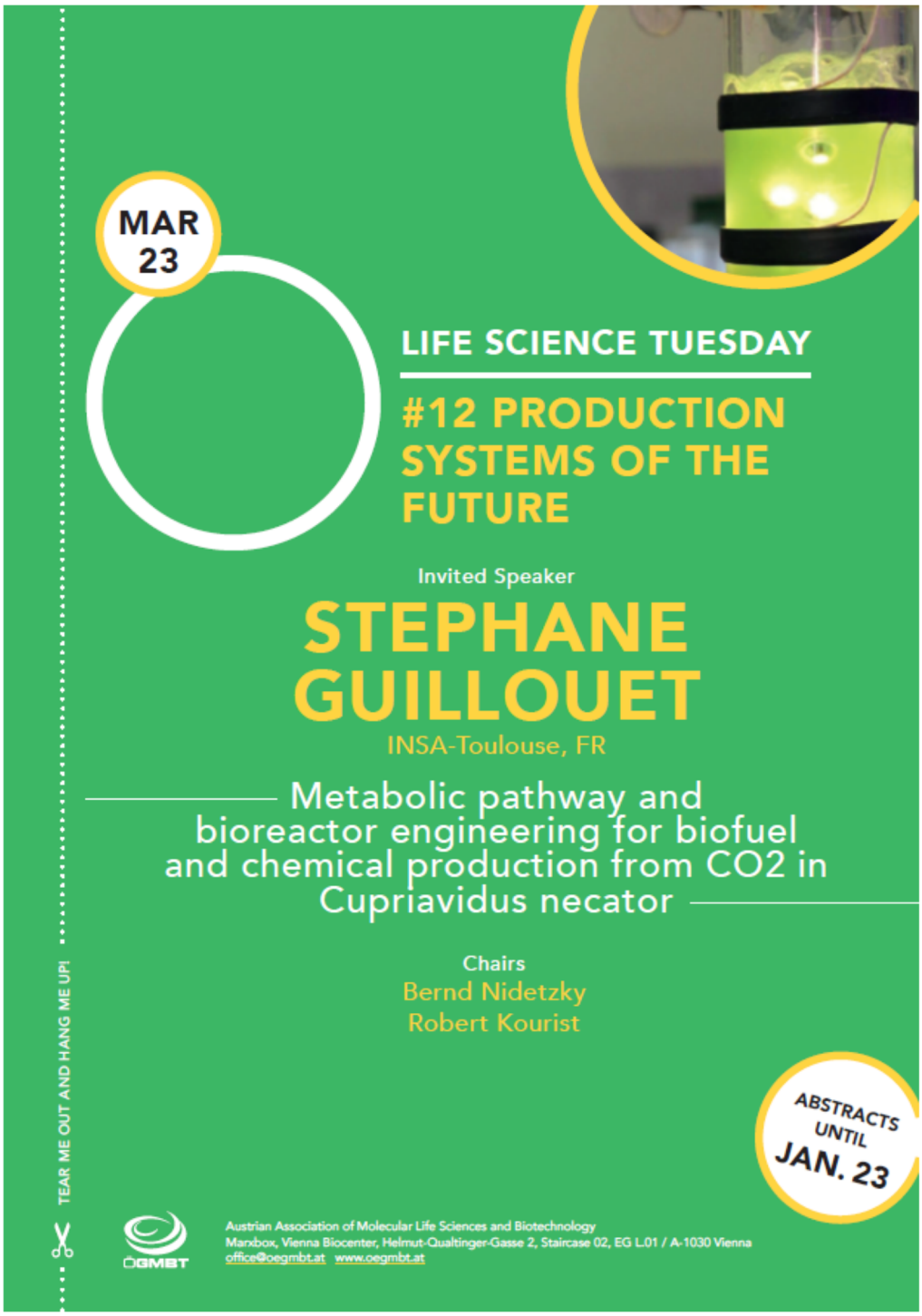
March 23 – Metabolic Science in Culture

16:00-16:45
Michael Snyder, Department of Genetics, Stanford University, USA
16:45-17:15
Debate – Metabolic Science in Culture
17:15-18:00
Hannah Landecker, Institute for Society and Genetics, University of California, USA

Life Science Tuesday #11/12: TRANSLATIONAL ONCOLOGY

Daniela S. Thommen, Netherlands Cancer Institute, NL

Daniela Thommen is a Junior Group Leader at the Netherlands Cancer Institute. She received her MD and PhD from the University of Basel, Switzerland. She then specialized in Medical Oncology in Switzerland. In parallel to her clinical training, she worked as a research fellow in tumor immunology at the Department of Biomedicine in Basel. In 2016, she joined the lab of Prof. Ton Schumacher at the Netherlands Cancer Institute, and started her own lab as a Junior group leader in 2020. Her research focuses on understanding the role of intratumoral immune cell heterogeneity for immunotherapy response and on the development of novel biomarkers and personalized immunotherapy strategies using patient-derived organotypic models. Daniela Thommen is the recipient of the 2019 Swiss Pfizer Research Prize in Oncology.



Life Science Tuesday #12/12: PRODUCTION SYSTEMS OF THE FUTURE

Stéphane Guillouet, Toulouse Biotechnology Institute, Bio & Chemical Engineering, FR

Innovations in Fetal Therapy

Dear partner,

On the 15th of April, LUMC Global and Leiden University Medical Center's Fetal Therapy department will host an online expert event on **Innovations in Fetal Therapy**. This event will be in the afternoon, between 15.30 and 18.00 o'clock.
This expert event will showcase the latest innovations and zoom in on several themes in the field of Fetal Therapy. It will also emphasize the importance of international collaborations. We hope to not only give insight into the latest developments in the field, but also spur you on to connect with us, to build a community to improve the care for the tiniest of patients even further.

Program
15.30 Welcome
15.35 Prof. Roland Devlieger, (UZ Leuven) - Fetoscopic treatment of fetal spina bifida
16.00 Dr. Monique Haak, (LUMC) - Fetal Cardiac Interventions
16.25 Prof. Dick Oepkes, (LUMC) - Monoclonal FcRN-blocker to prevent allo-immune hemolytic disease of the fetus.

10 min break

17.05 Prof. Anna David, (University College London) - Fetal stem cell treatment for Osteogenesis Imperfecta
17.30 Prof. Tippi MacKenzie, (University of California San Francisco) - In utero stem cell & enzyme replacement therapy
17.55 End discussion

Registration is for free, and we ask you to forward this information to your interested master or Phd students, as well as interested researchers. Register for free here!
For more information, please Visit our event page.

We hope to (virtually) see you there!

Best wishes,

Evelien Hack

Drs. E. Hack (MA), Advisor Internationalisation
Leiden University Medical Center
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Leids Universitair Medisch Centrum

Pro-Test Deutschland e.V.

Event announcement

Unsuck your Science

How a culture of care improves our lives as scientists, as well as those of our animals

As students and postdocs, we're the actual crew of this ship called Science. Some of us get to stand on deck and enjoy the public applause. But more often than not, we're just busy working deep down in the engine room. And that can be a privilege, because few other jobs are as interesting and rewarding as ours!

We want to do our job well. We care about our research. And though almost everyone around is well-intentioned, we can see much we don't like – a flawed analysis here, a missing control experiment there, wishful thinking by our boss. Because we're often the only ones to see that something's broken, we're also the only ones who can fix it. This holds especially true when performing animal experiments. We care about our lab animals. Taking responsibility for the life and death of another creature is never easy, but if done correctly, animal experiments can be both ethically sound and scientifically valid. So how do you know you're doing it right? And how can you do even better in the future?

Join us online on Wednesday 21 April 2021, 2-5 pm.

In our online seminar, 8 researchers will share their own solutions to 8 common issues. In addition to these practical fixes, we will highlight how better communications within your lab (and with the outside world) can enable such improvements in the first place. Joined by a panel of experts, we will then discuss what still makes it hard for YOU to make a difference, and what you need to overcome those hurdles. After the core event you may engage in open discussion with some of our speakers and members of our organisation in virtual break-out rooms.

This event is free of charge, will be held in English, and is organised by the German non-profit Pro-Test Deutschland e.V. (http://www.pro-test-deutschland.de/ueber-uns/mission/). More information and a detailed programme at http://unsuck.science *[website soon to be activated].*

Preliminary schedule

2.00 pm	introductory talk	*What is this "Culture of Care"?*
2.20 pm	brief presentations	*Solutions that work I (four examples)*
3.00 pm	roundtable discussion	*How can junior researchers make a change?*
4.10 pm	brief presentations	*Solutions that work II (four examples)*
5.00 pm	end of programme; transition to optional break-out rooms with speakers for open discussion	

Confirmed contributions

brief presentations:
- André Bleich, MHH Hannover
- Sabine Bischoff, Jena University Hospital
- Fabienne Ferrara, ConScienceTrain
- Katharina Hohlbaum, FU Berlin
- Sarah Jeuthe, Lise Meitner School of Science Berlin
- Vanessa von Kortzfleisch, U Muenster
- Annemarie Lang, Charité 3R Berlin
- Lars Lewejohann, BfR Berlin

roundtable:
- Stephanie Krämer, JLU Giessen
- Emily Sena, U Edinburgh
- Christa Thöne-Reineke, FU Berlin

Florian Dehmelt of Pro-Test will host the event and moderate the roundtable discussion.

Core audience

- English-speaking junior researchers across disciplines (MSc students to postdocs), especially those with hands-on experience working with lab animals, or with plans to experience such work in the future
- No explicit geographic focus, but in case specificity is required (e.g., with respect to regulations and other legal aspects), the situation in Germany will be emphasised.
- Despite this general focus, positively anyone is welcome to register.

Event registration

- free of charge, with an online ticketing system to keep track of participants: http://unsuck.science *[website soon to be activated]*

Accreditation

- Pro-Test is currently in touch with a number of institutions to allow participants to earn credit points where possible. These institutions will be listed in the final event programme and on the event website (unless otherwise requested by their representatives).
- Suggestions regarding additional institutions are most welcome (event@pro-test-deutschland.de).

Organisers

Pro-Test Deutschland e.V. is a non-profit, non-governmental organisation run entirely by about 85 volunteers across Germany. As researchers, animal caretakers, veterinarians, and graduate students, our volunteers speak their own minds in advocating a more open and honest debate on animal experiments. This includes pointing out actual problems and seeking solutions. Far beyond our little group, we want to encourage as many individual scientists as possible – especially junior ones – to make a difference in their own diverse environments.

Cell Adhesion, Signaling and Cancer

Mary Beckerle (University of Utah)

Mary Beckerle is Professor of Biology and Oncological Sciences at the University of Utah. Dr. Beckerle serves as the Executive Director of Huntsman Cancer Institute and holds the Ralph E. and Willia T. Main Presidential Endowed Chair.

She obtained her undergraduate training at Wells College and earned a PhD in Molecular, Cellular, and Developmental Biology at the University of Colorado at Boulder where she provided the initial evidence for a cytoplasmic dynein in microtubule-based intracellular transport. While a post-doctoral fellow at the University of North Carolina at Chapel Hill, Beckerle demonstrated the presence of a protease at cell-substratum adhesion sites, providing some of the earliest evidence that focal adhesions are dynamic, regulatory structures.

She subsequently identified zinc finger proteins, such as zyxin, as focal adhesion constituents and demonstrated shuttling of focal adhesion proteins to the nucleus. In recent work, Beckerle's research team has elucidated novel pathways for the control of cell motility and has defined the mechanism by which cells reinforce their actin cytoskeltons in response to mechanical stress. Dr. Beckerle's honors include receipt of a Guggenheim Fellowship, the American Cancer Society Sword of Hope Award, and the Utah Governor's Medal for Science and Technology. In 2006, Beckerle served as President of the American Society for Cell Biology.

Mary Beckerle describes advances in our understanding of cancer as a genetic disease, and the influence of cell adhesion on control of cell growth. (Talk recorded in July 2007)

Adhesion, Signaling and Cancer (36 min)
https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-1
Cell-substratum adhesion is mediated by integrins, a family of transmembrane, heterodimeric, extracellular matrix receptors that are concentrated at focal adhesions. Integin engagement influences a variety of signaling pathways and regulates cell behaviors including motility, proliferation, and survival. Disturbance of normal integrin function is associated with a variety of pathologic conditions including cancer. In the first segment of my seminar, I provide a broad overview of the cancer problem for a lay audience. Advances in our understanding of cancer as a genetic disease are discussed. The influence of cell adhesion on control of cell growth is reviewed.

Discovery and Characterization of a Focal Adhesion Protein Implicated in Tumor Progression (51 min)
https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-2
In the second segment, I describe the identification of the focal adhesion protein, zyxin, by my lab. Recent work revealed that zyxin is down-regulated upon expression of the Ewing sarcoma oncoprotein, EWS-FLI. Loss of zyxin expression results in enhanced cell motility and is also associated with failed apoptotic signaling. Evidence that zyxin shuttles between focal adhesions and the nucleus is presented. The impact of reduced zyxin expression on tumor progression is discussed.

Focal Adhesions as Stress Sensors (31 min)
https://www.ibiology.org/cell-biology/cell-adhesion-signaling-cancer/#part-3
In the third segment of my seminar, I address a new frontier in cell biology, that is how cells respond to mechanical information. Cells and tissues are exposed to physical forces in vivo and excessive mechanical stress leads to a variety of pathological consequences. I describe a system for exposing cells to controlled mechanical stress and discuss the stretch response. We have discovered that the focal adhesion protein, zyxin, is exquisitely sensitive to mechanical stimulation and is required for the ability of cells to reinforce the actin cytoskeleton when challenged by exposure to cyclic stretch.

Mitochondria, Metabolism, and Cell Behavior

Jared Rutter (University of Utah, Howard Hughes Medical Institute)

Jared Rutter is a Professor of Biochemistry and holds the Dee Glen and Ida Smith Endowed Chair for Cancer Research at the University of Utah. Dr. Rutter received his PhD from the University of Texas Southwestern Medical Center in 2001, working with Dr. Steve McKnight. After receiving his PhD, he spent 18 months as the Sara and Frank McKnight Independent Fellow of Biochemistry before joining the faculty at the University of Utah. As of September 2015, Dr. Rutter is an Investigator of the Howard Hughes Medical Institute. In addition to leading his laboratory at the University of Utah, Dr. Rutter is also actively involved in translating these academic discoveries into therapies as a founder, consultant and board member of several companies and venture firms. Dr. Rutter also serves as co-Director of the Diabetes and Metabolism Center at the University of Utah and co-Leader of the Nuclear Control of Cell Growth and Differentiation at Huntsman Cancer Institute. https://rutter.biochem.utah.edu/

Dr. Jared Rutter shares new insights into the interplay between mitochondria, metabolism, and cellular behavior. (Talk recorded in August 2019)

Mitochondria: The Mysterious Cellular Parasite (31 min)
https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-1
Mitochondria are integral to the metabolism of eukaryotic cells, yet many of their properties are not fully understood. In Part 1 of this iBioSeminar, Dr. Jared Rutter lays out the foundational knowledge of mitochondrial structure and origin, and shares what is currently known about mitochondrial roles in metabolism, protein homeostasis, and signaling. He ends by highlighting a focus of his research group: to unravel the functions of uncharacterized mitochondrial proteins.

Mitochondrial Metabolism and Cell Decisions (25 min)
https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-2
In Part 2 of his talk, Rutter describes his group's work to unravel the relationship between the activity of the Mitochondrial Pyruvate Carrier (MPC) and the behavior of numerous cell types, including cancer and stem cells. His group found that forced expression of the MPC in multiple stem cell models led to reduced "stemness" and proliferative capacity, and that MPC inhibition could promote organoid formation in culture and tumor formation in vivo. These data indicate an important link between mitochondria, metabolism, and cell behavior.

Mitochondria: The Fuel and the Fire (26 min)
https://www.ibiology.org/cell-biology/mitochondria-metabolism/#part-3
In his Part 3, Rutter emphasizes the challenge of mitochondrial protein synthesis. How do the components of the electron transport chain (ETC) assemble in the right stoichiometry at the right time? Rutter introduces the LYR family of proteins, which aid assembly of ETC components. LYR proteins interact with a common binding partner, the acyl carrier protein (ACP), via a unique fatty acyl moiety on ACP. Rutter's group showed that ACP acylation is necessary for assembly of the ETC and activation of oxidative phosphorylation.

Protein Sorting and its Role in Organelle Function and Shape

Tom Rapaport (Harvard Medical School and Howard Hughes Medical Institute, National Academy of SciencesGerman Academy of Sciences Leopoldina)

Dr. Tom Rapoport has been a Professor of Cell Biology at Harvard Medical School since 1995 and a Howard Hughes Medical Institute Investigator since 1997. Prior to joining Harvard, Rapoport was a Professor at the Institute for Molecular Biology in East Berlin, which later became the Max-Delbrück Institute for Molecular Medicine. Rapoport received his PhD from Humboldt University of Berlin.
Rapoport's research focuses on the understanding how organelles, in particular the endoplasmic reticulum (ER), derives its characteristic shape and performs its specific functions. He has had a long standing interest in how proteins are translocated across organelle membranes. His pioneering research has been recognized with many awards including the Max-Delbrück Medal in 2005, the Sir Hans Kreb Medal in 2007, and the Schleiden Medal in 2011, among many others. Rapoport is a member of the National Academy of Sciences, USA and the German Academy of Sciences, Leopoldina. He is also a Fellow of the American Association for the Advancement of Science (AAAS).
Learn more about Rapoport's research here and here.

Eukaryotic cells have many different membrane-bound organelles with distinct functions and characteristic shapes. How does this happen? Dr. Tom Rapoport explains the important role of protein sorting in determining organelle shape and function. (Talk recorded in February 2019)

Organelle Biosynthesis and Protein Sorting (35 min)
https://www.ibiology.org/cell-biology/protein-sorting/#part-1
In his first talk, Dr. Tom Rapoport explains that eukaryotic cells contain many membrane-bound organelles each of which has a characteristic shape and distinctive functions that are determined by specific proteins. Most proteins are made in the cytosol but must move to different cellular destinations. Signal sequences on the proteins act as "zip codes" and direct protein sorting. Many proteins sort first to the endoplasmic reticulum (ER) before moving to other intracellular organelles or the plasma membrane. Rapoport explains that the Sec 61 channel in the ER membrane is key to protein sorting. Solving the structure of Sec 61 allowed Rapoport's lab to understand how proteins are transported across the ER membrane and directed to their final destination.

How are cellular organelles shaped? (33 min)
https://www.ibiology.org/cell-biology/protein-sorting/#part-2
The ER is a vast network that includes different domains with different functions. The rough ER is made of ribosome covered membrane sheets and is involved in protein translation. The smooth ER consists of tubules and is important for lipid synthesis and Ca2+ transport. In his second talk, Rapoport explains how his lab identified several families of proteins needed to generate and maintain a tubular ER network. Using ultra-thin section microscopy, Rapoport and others also showed that stacked ER sheets are held together by helicoidal membrane connections that form a "parking-garage" like structure.

Protein Localization Inside Cells

Ramanujan Hegde (MRC Laboratory of Molecular Biology, Royal Society)

As an undergraduate, Ramanujan (Manu) Hegde studied biology at the University of Chicago with the thought that he would become a doctor. His summers and spare time were spent working in a lab, where he came to love the problem-solving of basic research. Hegde then fled Chicago winters for the sunshine of The University of California, San Francisco, where he completed an MD-PhD combined degree program. By then, he had decided to pursue basic research as a career, and moved to the National Institutes of Health where he was an investigator for 11 years. In 2011, Hegde moved to the Laboratory of Molecular Biology in Cambridge, England, where his research focuses on the mechanisms of protein biosynthesis and quality control.
Hegde's research contributions have been recognized with his election as a member of the European Molecular Biology Organization in 2013 and as a Fellow of the Royal Society in 2016.
Learn more about Manu Hegde's research here and here.

How does the cell regulate protein localization to be sure that proteins end up where they should? Manu Hegde reviews experiments that answer this question. (Talk recorded in April 2017)

Compartmentalization of Proteins Inside Cells (43 min)
https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-1
Cells are organized into many different compartments such as the cytosol, nucleus, endoplasmic reticulum (ER), and mitochondria. Almost all proteins are made in the cytosol, yet each cellular compartment requires a specific set of proteins. How does the cell regulate protein localization to be sure that proteins end up where they should? In his first lecture, Manu Hegde reviews the history of this field and highlights key experiments that have led to our current understanding of how protein localization occurs.

Quality Control of Protein Localization (34 min)
https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-2
In his second lecture, Hegde explains that although the protein localization system usually operates accurately, it does sometimes fail. This can be due to genetic mutations, stress within an organelle, or just intrinsic inefficiencies that accompany any complex process. As a graduate student, Hegde used a cell-free in vitro system to study the translocation of prion protein into the ER. He found that a small amount of prion protein did not completely cross the ER membrane as expected, but remained in a transmembrane form. Worried that this was an artifact of the in vitro system, he designed experiments in mice to see what the effect of an increase in mislocalized, transmembrane prion protein would be. He found a striking result – even a small increase in the amount of transmembrane prion protein caused increased neurodegeneration in mice. It turns out that incomplete translocation is not unique to prion protein. Hegde tells us how, as an independent investigator, his lab went on to investigate why this happens and how the cell monitors and degrades proteins that are not properly localized.

Recognition of Protein Localization Signals (47 min)
https://www.ibiology.org/cell-biology/protein-localization-inside-cells/#part-3
Proteins that are secreted from the cell or localized to the plasma membrane need first to be translocated into the lumen of the ER or inserted into the ER membrane. Thousands of proteins, each with a unique signal sequence, move through this pathway. How does the protein translocation machinery recognize these diverse signals and correctly localize the protein? In his third talk, Hegde describes studies from his lab using cryo-electron microscopy to visualize the translocation machinery at different stages in the recognition and engagement of a secreted or membrane inserted protein. The structural information gleaned from these experiments helps to explain how the protein translocation machinery works with high fidelity even when it needs to recognize diverse signal sequences.

Protein Folding, Prions, and Disease

Susan Lindquist (Whitehead and Massachusetts Institute of Technology, National Academy of SciencesNational Medal of Science)

Susan Lindquist was a member and former Director of the Whitehead Institute for Biomedical Research. She was also a Howard Hughes Medical Institute Investigator and Professor of Biology at the Massachusetts Institute of Technology. She received her Ph.D. in biology from Harvard and was a postdoctoral fellow of the American Cancer Society. Lindquist was on the faculty of the University of Chicago for over 20 years before moving to MIT in 2001.

A pioneer in the study of protein folding, Lindquist found that the chaperone Hsp90 potentiates and buffers the effects of genetic variation, fueling evolutionary mechanisms as diverse as malignant transformation and the emergence of drug resistance. Her work established the molecular basis for protein-based mechanisms of inheritance and she demonstrated that Hsp90 and prions each provide distinct but feasible mechanisms of Lamarckian inheritance.

Dr. Lindquist was an elected member of the National Academy of Sciences, the Academy of Medicine and the Royal Society. Her honors also included the Dickson Prize in Medicine, the Otto-Warburg Prize, the Genetics Society of America Medal, the FASEB Excellence in Science Award, the E.B. Wilson Medal, the Vanderbilt Prize for Women's Excellence in Science and Mentorship and the National Medal of Science. Learn more about Susan Lindquist's research here.

Dr. Lindquist was a great scientist and a long time supporter of iBiology and we were deeply saddened to learn of her death from cancer in October 2016.

Susan Lindquist explains how prions provide a protein-based mechanism of inheritance that allows organisms to develop new traits, quickly and reversibly. (Talk recorded in July 2016)

Protein Folding in Infectious Disease and Cancer (21 min)
https://www.ibiology.org/biochemistry/prions/#part-1
In Part 1, Dr. Lindquist explains the problem of protein folding. Proteins leave the ribosome as long, linear chains of amino acids but they need to fold into complex three dimensional shapes in the extremely crowded environment of the cytoplasm. Since protein misfolding can be disastrous for cells, proteins known as heat shock proteins (HSPs) have evolved to facilitate proper protein folding. Lindquist explains that sometimes the heat shock response becomes unbalanced resulting in human disease. In the case of cancer, HSPs help cancer cells survive many stresses that would typically kill them. In contrast, many neurodegenerative diseases are a result of protein misfolding and aggregation suggesting that, in these diseases, HSPs are not activated when they should be.

Protein Folding in Neurodegenerative Disease (27 min)
https://www.ibiology.org/biochemistry/prions/#part-2
Yeast have many of the same cellular processes as humans including a stress response to aid in protein folding and prevent protein aggregation. In Part 2, Lindquist describes how genetic screens in yeast helped scientists identify mutations that increased the formation of aggregates similar to those found in neurodegenerative diseases. Furthermore a screen in yeast of ~500,000 chemicals identified a number of compounds that prevented protein aggregation. Results from both experiments have since been validated in mice and human neuronal models.

Hsp 90: a Driver of Novelty in Evolution (59 min)
https://www.ibiology.org/biochemistry/prions/#part-3
When cells undergo stress, the expression of HSPs increases. In Part 3, Lindquist explains that while most HSPs are expressed only as needed, Hsp90 is expressed in excess. This "buffer" of Hsp90 facilitates the folding of some mutant proteins (such as v-src) that would usually misfold and be

degraded by the cell. Thus, Hsp90 potentiates the impact of these mutations. Interestingly, the Hsp90 "buffer" can also act to hide or suppress the impact of other mutations. These "hidden" mutations are found when cells are stressed reducing the pool of available Hsp90. Thus, Hsp90 provides a plausible mechanism for allowing genetic diversity and fluctuating environments to fuel the pace of evolutionary change.

Prions: Protein Elements of Genetic Diversity (47 min)
https://www.ibiology.org/biochemistry/prions/#part-4
In her last talk, Lindquist focuses on prion proteins. Prions are perhaps best known as the infectious agents in diseases such as mad cow disease. However, Lindquist argues that there are many great things about prions too. They provide a protein-based mechanism of inheritance that allows organisms to develop new traits, quickly and reversibly, and thereby adapt to new environments. Working in yeast, Lindquist and her colleagues were able to identify numerous prion-like proteins that are induced at different levels, depending on the temperature, pH or presence of bacteria. Expression of prions caused heritable, phenotypic changes in the yeast demonstrating that prions are another mechanism by which environmental changes can induce new traits that can be passed onto progeny.

The Evolutionary Design of Proteins: How does Protein Design Happen?

Rama Ranganathan (University of Texas Southwestern Medical Center)

Rama Ranganathan received his B.S. in Bioengineering from the University of California, Berkeley and his Ph.D. and M.D. degrees from UC San Diego where he studied signal transduction in the invertebrate visual system. He was a post-doctoral fellow at Harvard Medical School, where he studied K+ channels, and at The Salk Institute, where he learned x-ray crystallography. He joined the Department of Pharmacology at the University of Texas, Southwestern Medical Center in 1997. Currently, Ranganathan is Professor and Director of the Green Center for Systems Biology at UT Southwestern and he is affiliated with the Departments of Biophysics and Pharmacology.

Ranganathan's lab uses computational and experimental methods to study the structure, function and evolution of proteins at the atomic level. At the cellular level, his lab studies signal transduction in photoreceptor cells in the Drosophila eye. In both cases, the goal is to understand the evolutionary design of signaling systems.

How does "protein design" happen? Rama Ranganathan explains that the transformation is directed by physical interactions between small numbers of amino acids within a protein. (Talk recorded in May 2014)

What is Protein Design? (27 min)

https://www.ibiology.org/biophysics/protein-design-happen/#part-1

Proteins are synthesized as linear polymers of amino acids, yet proteins spontaneously fold into complex 3 dimensional structures, fulfill biochemical functions, and are able to adapt to a changing environment. How does this "protein design" happen? In Part 1, Ranganathan explains that the transformation is directed by physical interactions between small numbers of amino acids within a protein. Most interactions are short-range but some are surprisingly long-range and interactions between amino acids in the active sites of proteins may be co-operative. Amino acids can also cluster in modules allowing different parts of a protein to have different functions.

Model for Protein Design (32 min)

https://www.ibiology.org/biophysics/protein-design-happen/#part-2

In Part 2, Ranganathan describes a statistical approach developed by his lab to determine which amino acids in a protein drive the "design" of that protein. By studying the same protein across many species, Ranganathan and colleagues determined which amino acids were highly conserved, and thus likely important for protein function. They also tracked pairs or groups of residues where variation in one residue resulted in a change in the other residue, indicating conserved interactions. These experiments gave rise to a model in which a few, physically connected, collectively evolving groups or "sectors" of amino acids provide the "design" for natural proteins.

Protein Function and Adaptability (45 min)

https://www.ibiology.org/biophysics/protein-design-happen/#part-3

In his third lecture, Ranganathan describes experiments done in his lab to test the model proposed in Part 2. They find that a statistical matrix that predicts interactions between amino acids provides sufficient information to encode protein structure. Using saturation mutagenesis, Ranganathan's lab showed that amino acids necessary for a protein function, such as ligand binding, reside within a sector. Using a similar technique, Ranganathan was able to determine which amino acids in a protein were most likely to mutate or adapt in response to selective pressure. Again, all of the amino acids identified were in a sector position. These findings support a model in which sectors provide the necessary design parameters for protein folding, function and adaptability.

Metalloproteins in Action

Catherine Drennan (Massachusetts Institute of Technology & Howard Hughes Medical Institute)

Cathy Drennan is a Professor of Chemistry and Biology at the Massachusetts Institute of Technology and a Professor and Investigator of the Howard Hughes Medical Institute. She studied chemistry as an undergraduate at Vassar College, received her PhD in biological chemistry from the University of Michigan, was a post-doc at the California Institute of Technology and in 1999, Drennan joined the faculty at MIT. Her lab uses X-ray crystallography and other techniques to study the structure and function of metalloproteins.
Drennan is also very involved in efforts to make chemistry education more exciting for students; perhaps due, in part, to time she spent as a high school science and drama teacher after college. Drennan helps to train graduate student teaching assistants and to develop free resources for educators. She has been recognized with several awards for excellence in undergraduate teaching, as well as outstanding research.

Catherine Drennan begins her talk by explaining what metalloproteins are and how the inclusion of a metal in the protein structure results in amazingly reactive proteins. (Talk recorded in July 2013)

Introduction to Metalloproteins (43 min)
https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-1
Dr. Drennan begins her lecture by explaining what metalloproteins are and how the inclusion of a metal in the protein structure results in amazingly reactive proteins. She describes techniques, such as X-ray crystallography and electron microscopy, which her group uses to get “snapshots” of metalloproteins in action. These “snapshots” allow them to better understand how metalloproteins function in many critical biological reactions.

Metalloproteins and Medicine (32 min)
https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-2
In Part 2, Drennan focuses on experiments her lab has done to understand the mechanism of action of ribonucleotide reductase (RNR), a key enzyme required for DNA synthesis and repair and, consequently, cell viability. By taking “snapshots” of bacterial RNR, Drennan and her colleagues deciphered how changes in the structure of RNR regulated its activity. Interestingly, the structure of bacterial RNR appears to differ from that of human RNR suggesting a possible new target for antibiotics.

Metalloproteins and the Environment (33 min)
https://www.ibiology.org/biochemistry/metalloproteins-in-action/#part-3
In the last part of her talk, Drennan explains how cobalt based metalloproteins allow acetogenic bacteria to live on CO2. This group of bacteria convert more than 1010 tons of CO2 to acetate each year and scientists are interested in understanding and using these metalloproteins to remove CO2 from the atmosphere. Structures determined by Drennan’s lab have provided information on the mechanism of action of these important enzymes.

Neurodegenerative disease: The Coming Epidemic

Gregory Petsko (Weill Cornell Medical College, National Academy of Sciences)

Gregory Petsko is Arthur J. Mahon Professor of Neuroscience in the Brain and Mind Research Institute at Weill Cornell Medical College. His lab studies protein structure and function with a particular focus on understanding and developing treatments or preventative therapies for age-related neurodegenerative diseases.

Petsko received his B.A. from Princeton University. He was awarded a Rhodes Scholarship and completed his D.Phil. from Oxford University where he studied in Sir David Chilton Phillips' lab.

Petsko is Professor Emeritus of Biochemistry and Chemistry at Brandeis University and Professor of Neurology at Weill Cornell Medical College. He is a member of the National Academy of Sciences and the Institute of Medicine and has received numerous other honors and awards. His lab studies protein structure and function with a particular focus on age-related neurodegenerative disease. Learn more about Dr. Petsko.

As the population ages, we face an epidemic of neurodegenerative disease that will take a great financial and emotional toll on family, caregivers and society. (Talk recorded in April 2016)

Neurodegenerative disease: The Coming Epidemic (21 min)

https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-1

Dr. Petsko begins his lecture by presenting the challenges associated with a growing elderly population and a shrinking work force. As the population ages, we face an epidemic of debilitating neurodegenerative disease that will take a great financial and emotional toll on family, caregivers and society. The brains of patients with Alzheimer's, Parkinson's, and ALS/Lou Gehrig's diseases are characterized by the presence of protein aggregates due to protein misfolding. While most neurodegenerative disease arises sporadically, about 10% has a direct genetic cause. Petsko explains that by studying the familiar forms, scientists have gained great insight into the cellular and molecular processes underlying these devastating diseases.

Parkinson's disease: How might it be stopped? (25 min)

https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-2

In Part 2, Petsko focuses on Parkinson's disease, the second most common neurodegenerative disease after Alzheimer's. Petsko and his colleagues studied patients with a genetic predisposition to Parkinson's disease and found a mutation in the α-synuclein gene that caused the protein to misfold and aggregate. In sporadically occurring cases of Parkinson's, they discovered that α-synuclein was cleaved and the resulting protein fragment formed aggregates. Switching to yeast as a model system and then to human cells, Petsko's lab identified caspase-1 as the protease responsible for cleaving α-synuclein. Interestingly, caspase-1 is activated during inflammation, providing a possible explanation for how head injury and brain infection may contribute to Parkinson's. The development of caspase-1 inhibitors that can penetrate the brain would present hope for an effective treatment for Parkinson's disease.

A potential gene therapy for ALS (25 min)

https://www.ibiology.org/neuroscience/neurodegenerative-disease/#part-3

Petsko and others also studied patients with familial amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease and he describes this work in Part 3. They knew that many of the genes mutated in ALS encode RNA-binding proteins and these proteins formed aggregates in neurons from ALS patients. Expression of two of these proteins, FUS and TDP43, in yeast resulted in the same phenotype. A screen for yeast genes that would suppress FUS/TDP43 toxicity identified five genes and all encoded RNA binding proteins. Excitingly, several of the human homologs of these genes also were shown to block FUS/TDP43 toxicity in human neuron and neonatal rat models. These encouraging results generate hope that targeted gene therapy may provide a future treatment for this terrible neurodegenerative disease.