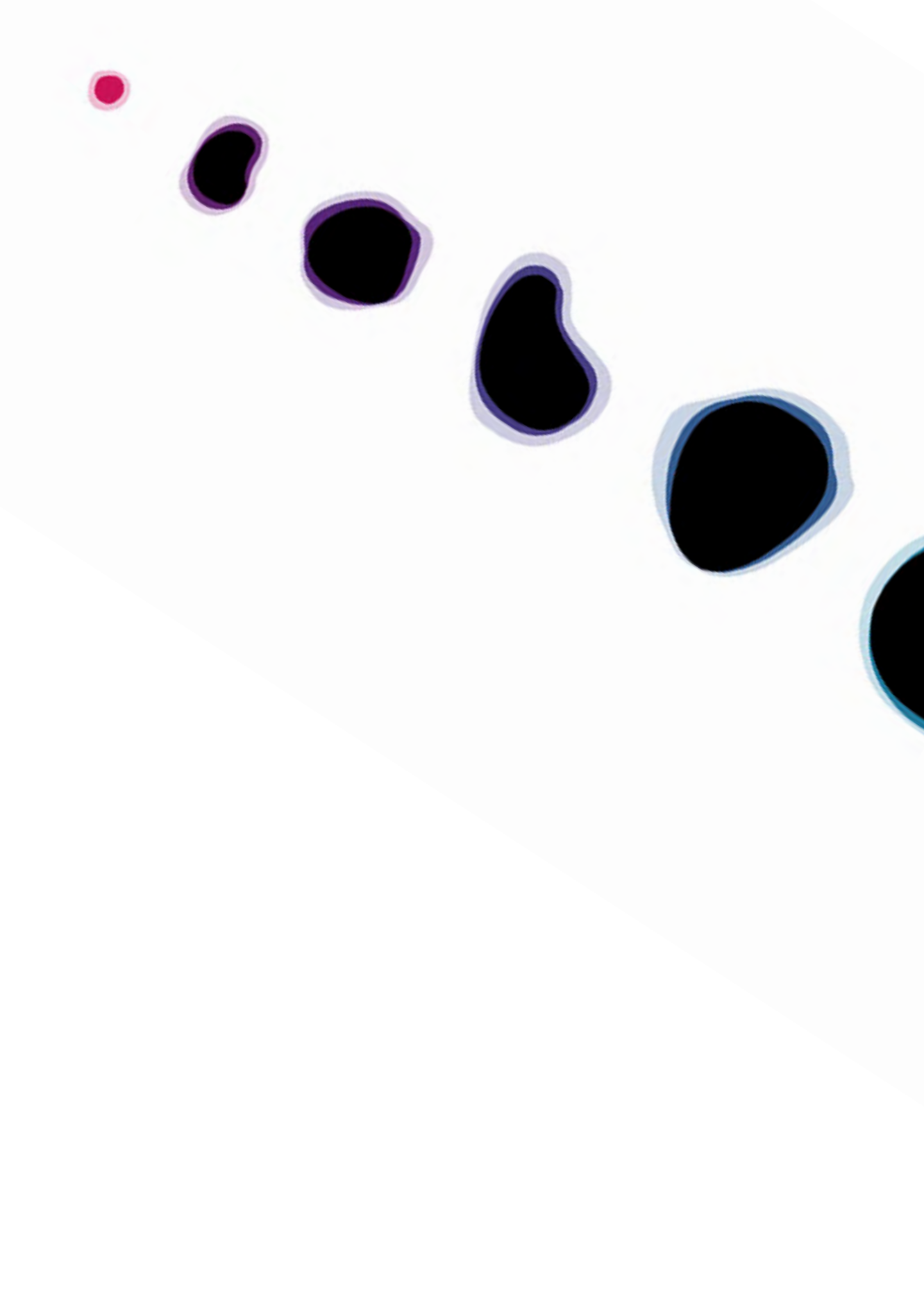
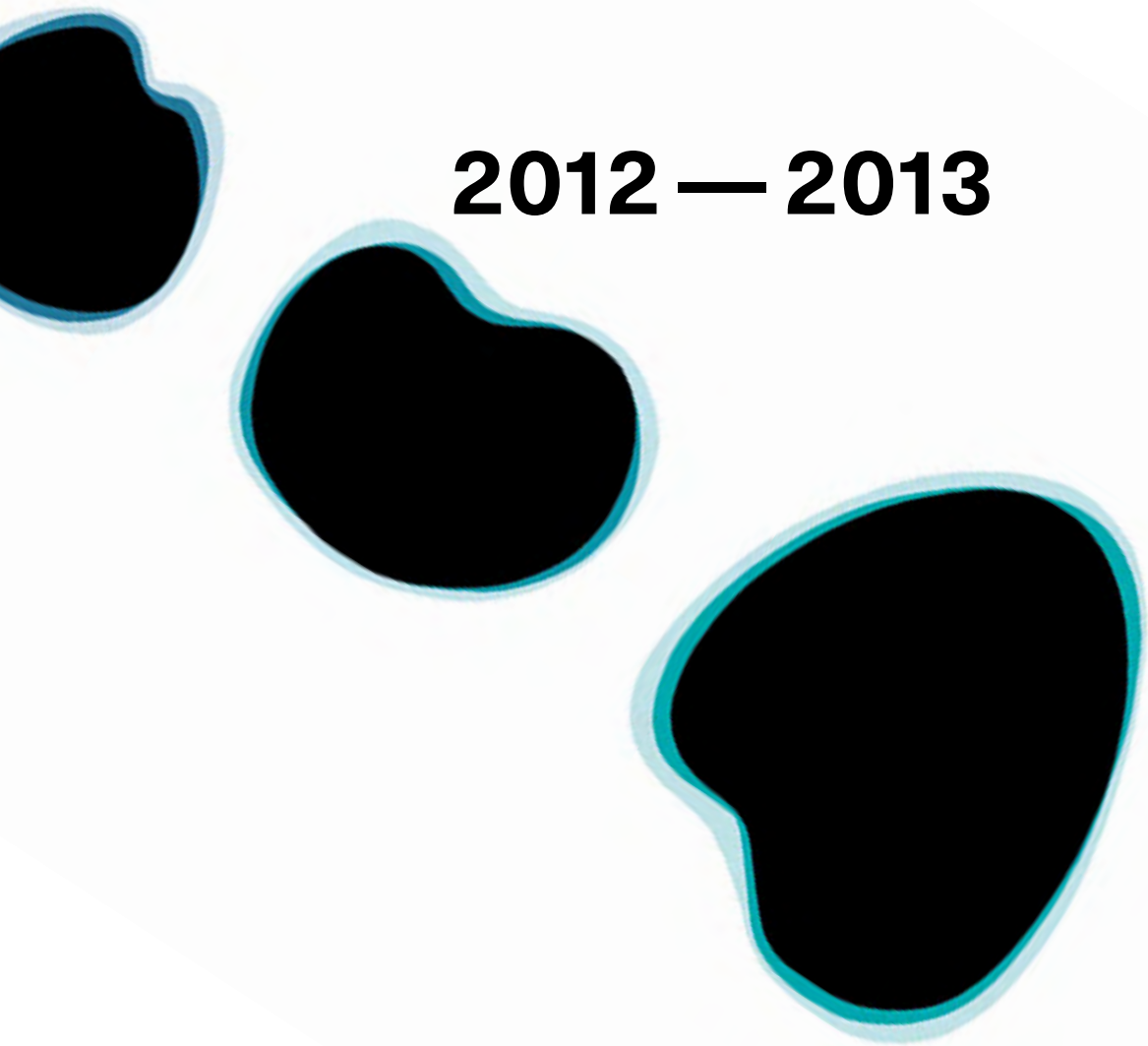
Mendel Lectures
2012—2013





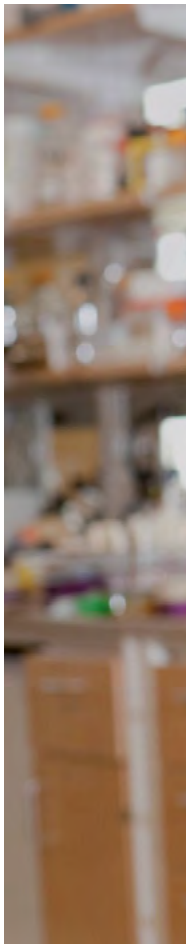
2012 — 2013

Nancy Kleckner

*1947

Harvard University, Cambridge, USA

October 25, 2012



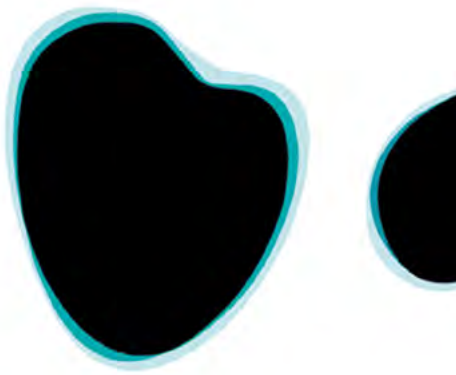
Nancy Kleckner graduated from Harvard, where she studied the reciprocity of recombination genetically in bacteriophage lambda with Matthew Meselson. She earned a PhD at the Massachusetts Institute of Technology in 1974 and remained for a postdoctoral fellowship with geneticist David Botstein, with whom she described the first transposable drug resistance element, Tn10.

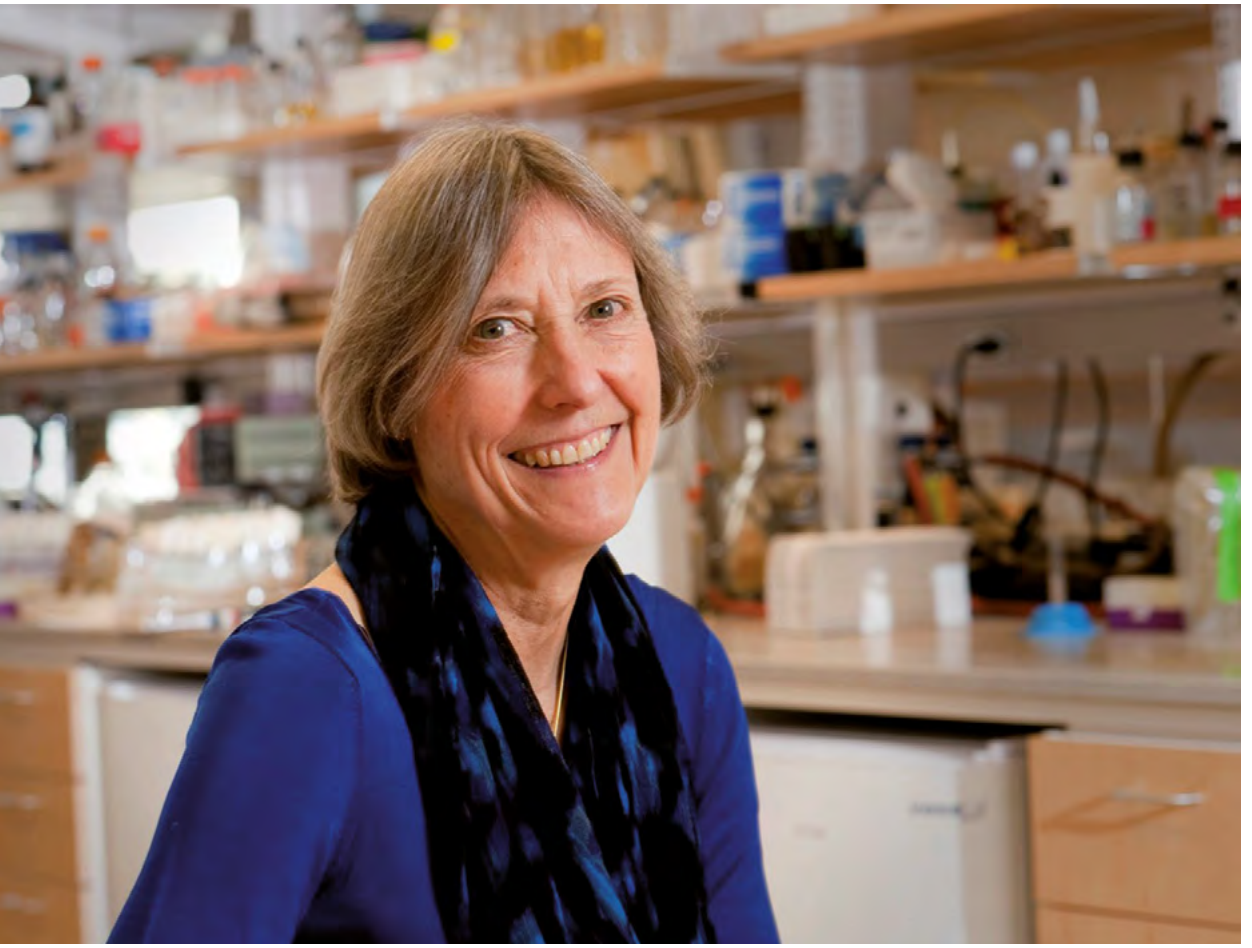
In 1977, Harvard hired Kleckner as an assistant professor. Her continued studies on transposons led to identification of the first anti-sense RNA to control gene expression and genetic proof that Tn10 moves by a cut-and-paste mechanism. She also became a leading expert in the biochemistry of tranposons. In 1985 she was the nineteenth woman awarded tenure at Harvard. She then added two new lines of research: *E. coli* replication and cell cycle, and meiosis.

Her lab is particularly interested in higher order processes involving the integration of spatial, temporal and functional elements and in viewing chromosomes as physical objects for which mechanical forces (stresses) play important roles. They study meiotic chromosomes in budding yeast and other organisms, thereby elucidating the several steps of homolog recognition and juxtaposition, the functional interplay between chromatin and structural axes along and between chromosomes, and the programmed spatial patterning of interhomolog crossovers. They also study the global chromosome dynamics of both *E. coli* and mammalian chromosomes, including investigating a general "stress hypothesis". They have also developed new tools for chromosome imaging and for monitoring forces within chromosomes *in vivo*.

Dr. Kleckner was awarded the GSA Medal of the Genetics Society of America in 1990 and the GSA Thomas Hunt Morgan Medal for Lifetime Achievement in 2016. She was elected to the American Academy of Arts and Sciences in 1991, to the US National Academy of Sciences in 1993, and as a Foreign Associate member of the European Molecular Biology Organization in 2004. At Harvard, she founded the PhD track in Engineering and Physical Biology. She is also a Fellow of the American Association for the Advancement of Science and the American Academy of Microbiology.

Meiotic Recombination: The Exception to, and the Executor of, Mendel's Laws





Visiting the site of Mendel's experiments and being immersed in his life and surroundings was memorable and meaningful and it was an honour to have the opportunity to give a Mendel Lecture.

Brenda Schulman

*1967

St. Jude Children's Research Hospital, Memphis, USA

March 14, 2013

Brenda Schulman received her bachelor's degree in biology from Johns Hopkins University in 1989 and her PhD in biology from the Massachusetts Institute of Technology in 1996. She then worked as a postdoctoral fellow at the Massachusetts General Hospital Cancer Center (1996–1998) and later at the Memorial Sloan Kettering Cancer Center (1998–2001). Schulman joined the faculty at the St. Jude Children's Research Hospital in 2001. She became a Howard Hughes Medical Institute Investigator in 2005.

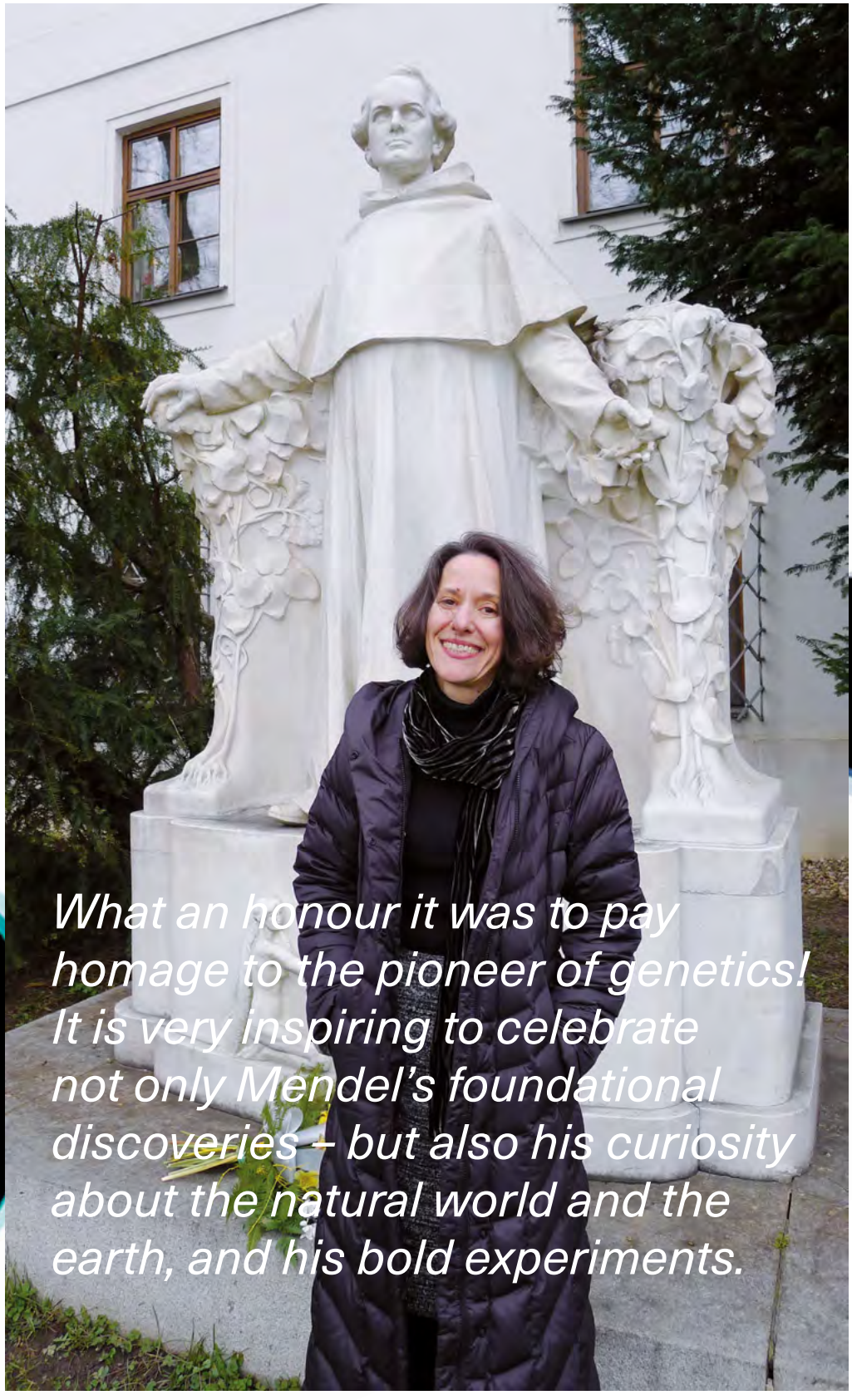
She is broadly interested in how ubiquitin and ubiquitin-like proteins are matched with specific substrates, and how they alter the functions of their targets to regulate the cell cycle, autophagy, metabolic signalling, differentiation and other biological processes. Her lab structurally visualizes transient ubiquitylation complexes trapped as if in action, biochemically reconstitutes signalling pathways, develops chemical tools to probe ubiquitin signalling, and employs cell biology to investigate how ubiquitylation mediates regulation. Knowledge of this regulation has contributed to our understanding of how defects caused by mutations contribute to diseases including cancers and neurodegeneration, and how viruses hijack ubiquitin pathways during infections.

Brenda Schulman received the 2004 Presidential Early Career Award for Scientists and Engineers, the 2011 Dorothy Crowfoot Hodgkin Award from the Protein Society, and was elected to the American Academy of Arts and Sciences in 2012. Dr. Schulman was elected to the National Academy of Sciences in 2014 and received a MERIT Award from the National Institute of General Medical Sciences the same year.

After sixteen years at St. Jude's, Schulman moved to the Max Planck Institute of Biochemistry in Germany in 2017, becoming a Director and Scientific Member. In 2019, she was awarded the Ernst Jung Prize for Medicine, the Gottfried Wilhelm Leibniz Prize and was elected to the Leopoldina.

She continues working on ubiquitin and protein degradation.

Twists and Turns in Ubiquitin Conjugation Cascades


What an honour it was to pay homage to the pioneer of genetics! It is very inspiring to celebrate not only Mendel's foundational discoveries – but also his curiosity about the natural world and the earth, and his bold experiments.

Tom Rapoport

*1947

Harvard Medical School, Boston, USA

April 11, 2013

Tom Abraham Rapoport is a German-American cell biologist who studies protein transport in cells. He received his PhD in 1972 from the Humboldt University in East Berlin (then in the German Democratic Republic) for work in enzymology. He then focused on mathematical modelling of metabolism, for which he received his second degree (*habilitation*) from the same institution. In 1979 he moved to the Zentralinstitut

für Molekularbiologie der Akademie der Wissenschaften der DDR, later called the Max Delbrück Center for Molecular Medicine, where he became a professor in 1985. After the reunification of Germany, he moved to the United States in 1995. He has been a professor at the Harvard Medical School since 1995, and an HHMI investigator since 1997.

The Rapoport lab is interested in the mechanisms by which proteins are transported across membranes, how misfolded proteins are degraded, and how organelles form and maintain their characteristic shapes. Most of the projects centre around the endoplasmic reticulum (ER).

He was a member of the Akademie der Wissenschaften der DDR from 1988 until 1992, when it was dissolved. He has been a member of the German Academy of Sciences Leopoldina since 2003, a member of the US National Academy of Sciences since 2005, and he is a fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science. His pioneering research has been recognized with many awards including the Max-Delbrück Medal in 2005, the Sir Hans Krebs Medal in 2007, and the Schleiden Medal in 2011, among many others.

Tom Rapoport is still working at the Harvard Medical School. Recently, the Rapoport lab has started to study how proteins are imported into peroxisomes, and how lung surfactant proteins generate lamellar bodies.

How the ER Gets into Shape

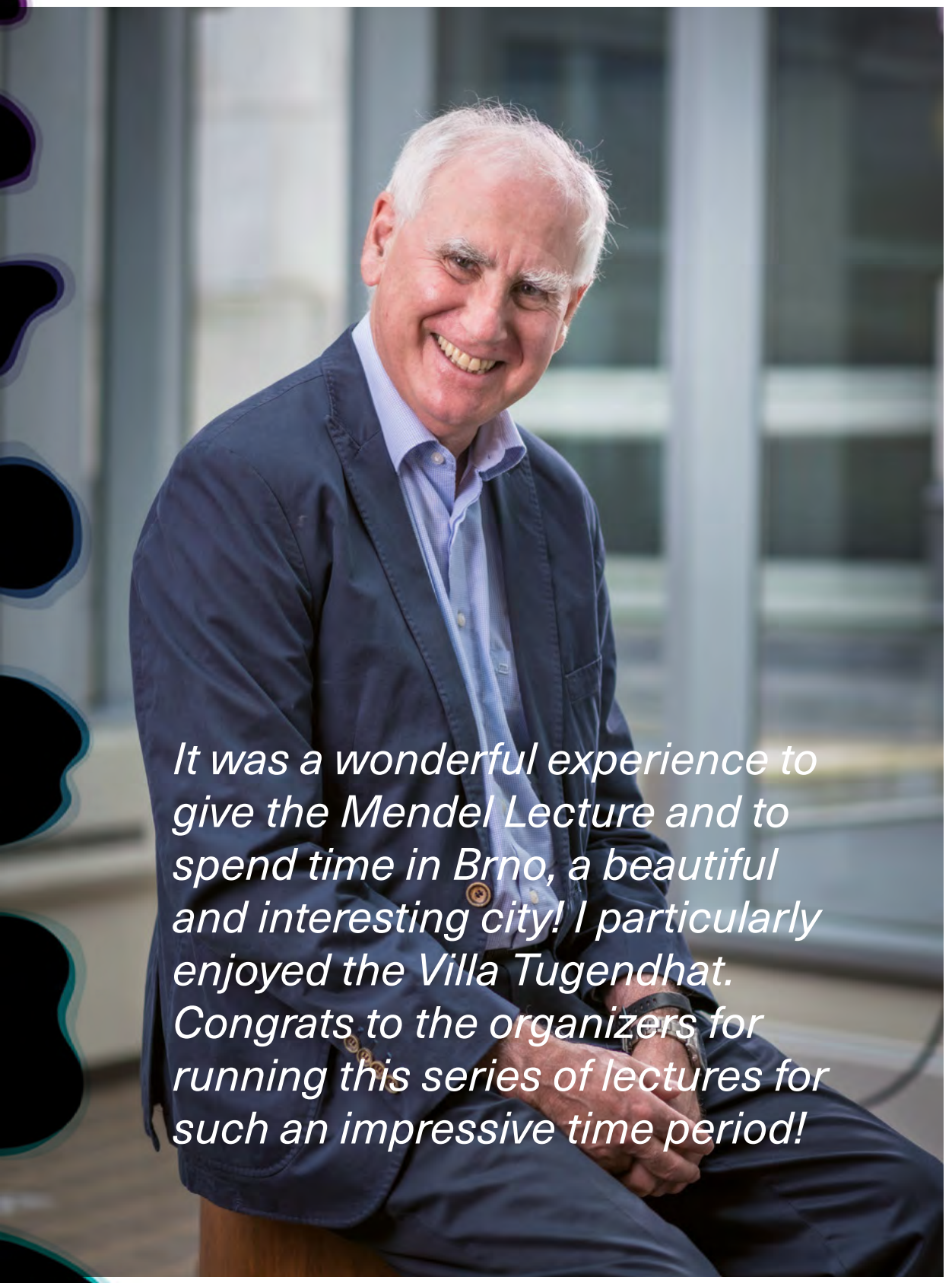


Photo: Sam Ogden

Torben Heick Jensen

*1965

Department of Molecular Biology and Genetics, Aarhus University, Denmark

April 18, 2013

Torben Heick Jensen (THJ) studied at Aarhus University, Denmark, receiving his MSc in Molecular Biology in 1993 and his PhD in 1997. He then spent three years as a postdoctoral scholar at the Howard Hughes Medical Institute, Brandeis University (USA) under the mentorship of Nobel laureate Michael Rosbash. Upon returning to Denmark in 2001, THJ was appointed assistant professor, and subsequently associate professor at Aarhus University. In 2010, he was appointed full professor at what was then the Department of Molecular Biology.

THJ's research covers the biogenesis and turnover of RNA in eukaryotic cells and its contribution to gene expression regulation at the post-transcriptional level. For the past decade, his research group has contributed to identifying the molecular mechanisms that help to sort newly transcribed RNA between a productive pathway, involving RNA packaging with proteins and cellular transport, and a destructive pathway, involving RNA degradation complexes identified by the THJ group.

In 2004, THJ was awarded the prestigious five-year Hallas Møller Fellowship from the Novo Nordisk Foundation. In 2005, the Danish National Research Foundation awarded him a five-year grant to establish a Centre of Excellence – the Centre for mRNP Biogenesis and Metabolism, which was extended for another five years to 2015. In 2012, he was elected as a member of the European Molecular Biology Organization (EMBO), and he was the recipient of an Advanced ERC Grant in 2014–2019.

The focus of THJ's laboratory continues to be to understand the molecular principles dictating the sorting of newly transcribed RNA.

Making and Breaking RNA in Human Nuclei

Simon Boulton

*1972

The Francis Crick Institute, London, UK

May 2, 2013

Simon Boulton received his MSc from the University of Edinburgh in 1994 and completed his PhD at the University of Cambridge in 1998 under the supervision of Steve Jackson of the Gurdon Institute. From 1998–2002 he worked as an HFSP and EMBO Postdoctoral Research Fellow at Harvard Medical School in Boston, USA, in the labs of Nicholas Dyson and Marc Vidal. Following his return to the UK in 2002 he established his own lab at Clare Hall Laboratories, London Research Institute, and was subsequently promoted to senior scientist in 2007. In 2015, his lab moved to become part of the Francis Crick Institute in London.

Boulton's career has focused on the discovery of DNA repair genes and providing molecular insights into genome instability disorders and cancer. His team exploits the experimental strengths of *C. elegans* and mouse genetics, human cell culture, biochemistry and biophysical approaches. Most notably, Boulton's work has played an instrumental role in shaping our understanding of the regulation and execution of homologous recombination (HR), a key DSB repair pathway frequently inactivated in cancer. Boulton was the first to establish the existence of error-prone micro-homology mediate end joining, which operates as a backup DNA repair pathway to NHEJ. He also identified RTEL1 as the first negative regulator of HR in metazoan, which controls meiotic recombination, ensures accurate genome duplication and maintains telomere integrity. He has also provided insights into the mechanisms that protect chromosome ends in pluripotent and somatic cells, and how cancer cells use Alternative Lengthening of Telomeres to achieve replicative immortality.

Boulton's academic achievements have been acknowledged with several prestigious accolades. In 2006 he was awarded the Colworth Medal, and in 2007 he received the European Molecular Biology Organization (EMBO) Young Investigators Programme Prize. In 2008, he was awarded the European Association for Cancer Research (EACR) Young Researcher Award and the Eppendorf/Nature Award for Young European Investigators. In 2009, he became an EMBO member. In 2010, he was awarded a Royal Society Wolfson Research Merit Award, and in 2011 he received the prestigious EMBO Gold Medal award and gave the Royal Society Francis Crick Prize Lecture. In 2012, he was elected as a Fellow of the Academy of Medical Sciences. In 2013, Boulton received the Paul Marks Prize for Cancer Research, which recognizes a new generation of leaders in cancer research.

Since 2015 Boulton has been a senior group leader and Ambassador for Translation at the Francis Crick Institute, London. He is also co-founder and Vice President of Science Strategy of Artios Pharma Ltd. (2016), a biotech company that is developing small molecule DNA repair inhibitors to selectively kill cancer cells either as monotherapies or in combination with existing treatments. Most recently, Boulton was appointed the director of RadNet City of London, a Cancer Research UK initiative to accelerate our understanding of radiobiology to improve radiation treatments for cancer patients.

Genome Stability and the Control of Recombination

As a trained geneticist, it was a huge honour to give the Mendel Lecture and to visit the location where the great man conducted his transformative work.

Peter Walter

*1954

Howard Hughes Medical Institute, Department of Biochemistry and Biophysics, University of California, San Francisco, USA

May 9, 2013

After obtaining his BS in chemistry at the Freie Universität Berlin in 1973, Peter Walter completed his MS degree in organic chemistry at Vanderbilt University. In 1976, he enrolled in a PhD programme at Rockefeller University, where he worked with Günter Blobel. During his dissertation work, he purified proteinaceous members of a complex essential for protein translocation and showed that it selectively recognizes secretory proteins in the cytoplasm and targets them to the endoplasmatic reticulum (ER). He remained in Blobel's group for two additional years, first as a postdoctoral fellow and then as an assistant professor, during which time he identified a 7S RNA component of the signal recognition particle. Since 1983 Walter has worked in the Department of Biochemistry and Biophysics at the University of California, San Francisco (UCSF), where he became a professor in 1991 and served as department chair from 2001 until 2008.

Walter's laboratory explores the signalling pathway by which cells alter their quantities of ER. Working with yeast as a model, he has pioneered studies to gain a mechanistic understanding of protein sorting/targeting to the ER. The same principles also apply in higher organisms, including humans. This communication process is so crucial to cells that imbalances can lead to a number of diseases including cancer, diabetes, cystic fibrosis, and vascular and neurodegenerative diseases.

Walter is an elected member of several scientific societies such as the German Academy of Natural Scientists Leopoldina, the National Academy of Sciences, the National Academy of Medicine, the American Association for Arts and Science, and the European Molecular Biology Organization. He is a co-author of the textbooks *Molecular Biology of the Cell* and *Essential Cell Biology*, two of the world's most widely used standards in the field of molecular cell biology. Among the many awards he has received are the Eli Lilly Award, the Wiley Prize, the Stein and Moore Award from the Protein Society, the Gairdner Award, the E. B. Wilson Medal, and the Jung Prize.

Walter received the 2012 Paul Ehrlich and Ludwig Darmstaedter Prize, the 2014 Shaw Prize and Lasker Award, the 2015 Vilcek Prize, and the 2018 Breakthrough Prize. In 2016 Walter was the president of the American Society of Cell Biology.

The Unfolded Protein Response in Health and Disease

Stanislas Leibler

*1957

The Rockefeller University, New York, USA

May 16, 2013

Stanislas Leibler completed his undergraduate studies in physics at the University of Warsaw. He received an MS in theoretical physics in 1979, a PhD in theoretical physics in 1981 and a second PhD in physics in 1984, all from the University of Paris. He spent a year at the École Normale Supérieure and then from 1984 to 1992 he was a research fellow at the Saclay Nuclear Research Centre. Leibler spent two years at Cornell University (1985–1987) and another two years at the École Supérieure de Physique et Chimie Industrielles (1989–1991). In 1992, he moved to Princeton University as a professor in the Department of Physics, becoming a professor in the Department of Molecular Biology in 1993. From 1997 to 1998 he was a visiting scientist at the European Molecular Biological Laboratories in Heidelberg, Germany, and moved to the Rockefeller University in 2001. Leibler was a tri-institutional professor at Weill Cornell Medical College and the Sloan-Kettering Institute from 2003 to 2010. Since April 2009 he has been sharing his time between Rockefeller and the Institute for Advanced Study at Princeton.

Leibler's laboratory is developing both the theoretical and experimental methods necessary for conducting studies on the collective behaviour of biomolecules, cells and organisms. By selecting a number of basic questions on how simple genetic and biochemical networks function in bacteria, his lab is beginning to understand how individual components can give rise to complex, collective phenomena. They have developed simple genetic networks in bacteria that act like clocks or logic circuits. Together with Michael Elowitz, Leibler's group built a synthetic network to implement a negative feedback system of gene regulation in *E. coli*, representing one of the key results of synthetic biology. Currently his laboratory is focusing on how microbial populations survive in varying environments.

Leibler is a fellow of the American Physical Society. He was a 1997–1998 Humboldt Research Award winner at the European Molecular Biology Laboratory (EMBL) in Heidelberg.

In 2015 Leibler won the Max Delbruck Prize awarded by the American Physical Society and in 2016 he was elected to the National Academy of Sciences.

Following in Mendel's Footsteps: Statistical Analysis of Microbial Behavioural Phenotypes