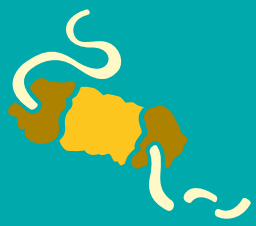
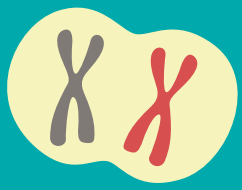
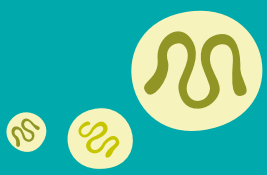
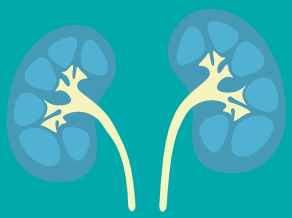
Mendel Lectures
2016—2017









2016 — 2017

Wolfgang Baumeister

*1946

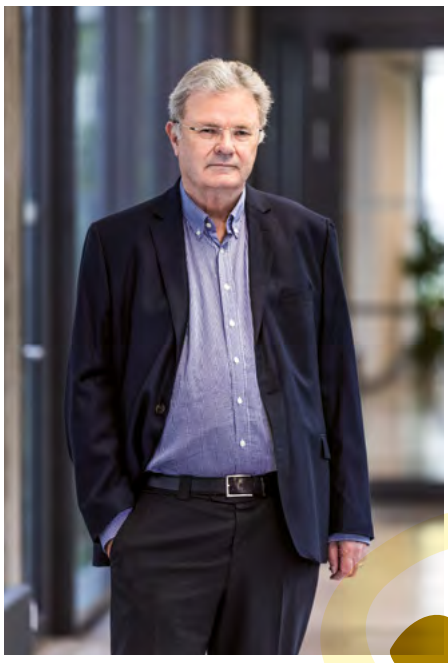
Department of Molecular Structural Biology, Max Planck Institute of Biochemistry, Martinsried, Germany

September 22, 2016

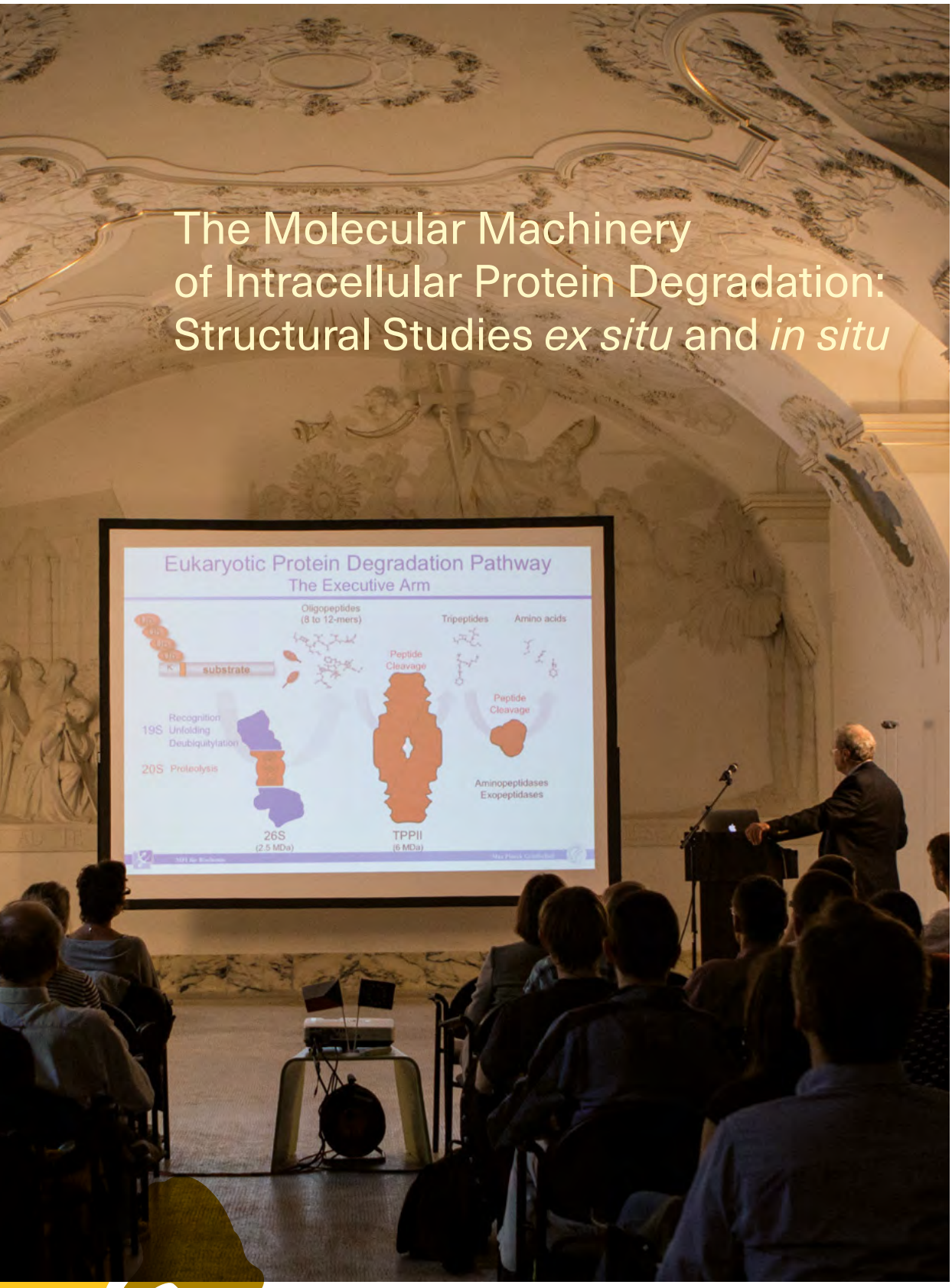
Wolfgang Baumeister studied biology, chemistry and physics at the Universities of Münster and Bonn, Germany, and obtained his PhD from the University of Düsseldorf in 1973. From 1973–1980 he was a research associate in the Department of Biophysics at the University of Düsseldorf. From 1980 to 1981 he spent time as a postdoc at the Cavendish Laboratory in Cambridge, England. In 1982 he became a Group Leader at the Max Planck Institute of Biochemistry in Martinsried, Germany, and in 1988 Director and head of its Department of Structural Biology. In 2000 he was named Moore Distinguished Scholar at the California Institute of Technology in Pasadena, USA.

Wolfgang Baumeister made seminal contributions to our understanding of the structure and function of the cellular machinery of protein degradation, in particular the proteasome, ribosomal supercomplexes such as polysomes, the cytoskeleton, and synaptic structures. Moreover, Baumeister's department has developed cryo-electron tomography, a method enabling the visualization of the macromolecular structures in a functional context and true-to-life state in shock-frozen cells. Images from different projection angles are recorded in the microscope and mathematically combined into 3D image cubes (tomograms). The method is widely used now to study cellular architectures of prokaryotes and eukaryotes at subnanometer resolutions.

Baumeister's contributions to science were recognized by numerous awards including the 1998 Otto Warburg Medal, the 2003 Louis-Jeantet Prize for Medicine, the 2004 Stein and Moore Award, the 2005 Schleiden Medal and the Harvey Prize in Science and Technology, the 2006 Ernst Schering Prize, the 2018 Ernst Jung Medal for Medicine in Gold, the 2019 Science Award by the Stifterverband für die Deutsche Wissenschaft, and the Van Deenen Medal. He has been a member of the Bavarian Academy of Sciences since 2000, the Academy of German Natural Scientists Leopoldina since 2001, the American Academy of Arts and Sciences since 2003, and the National Academy of Sciences since 2010.



The Molecular Machinery of Intracellular Protein Degradation: Structural Studies *ex situ* and *in situ*



Austin Smith

*1960

Department of Biochemistry, University of Cambridge /Wellcome Trust/ MRC Cambridge Stem Cell Institute, UK

November 10, 2016

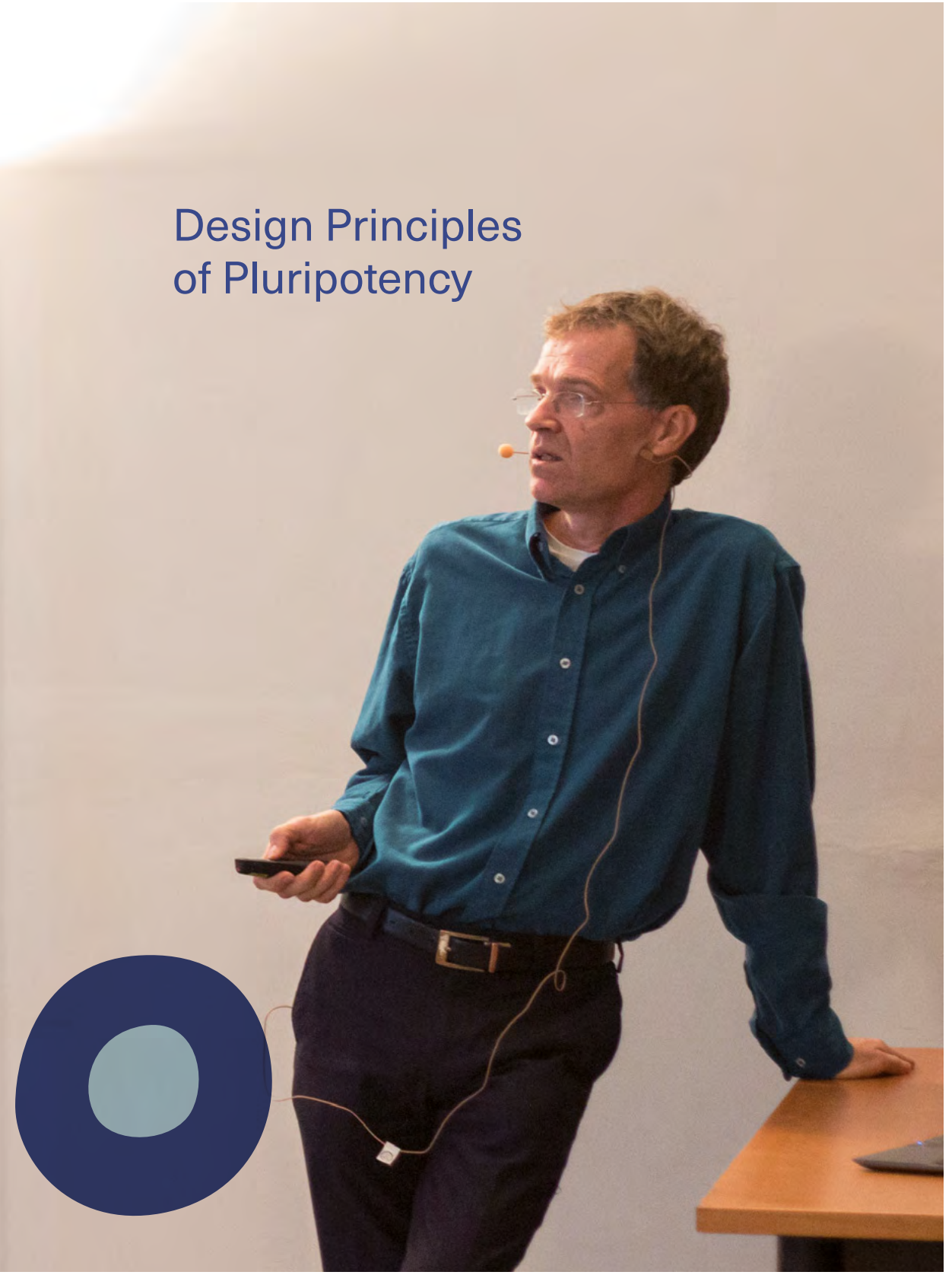
Austin Gerard Smith is a British biologist, notable for his pioneering work on the biology of embryonic stem cells.

Smith studied biochemistry at the University of Oxford where he became captivated by pluripotency. He pursued this interest in his doctoral studies at the University of Edinburgh (PhD in 1986) and in postdoctoral research at the University of Oxford, before joining the Centre for Genome Research at the University of Edinburgh as a group leader in 1990. He returned to Edinburgh as a Group Leader in 1990. In 1996, he was appointed director of the Centre, which became the Institute for Stem Cell Research under his leadership. In 2006 he moved to Cambridge where he was the founding Director of the Wellcome Trust Centre for Stem Cell Research and in 2012 became the director of the new Wellcome Trust-MRC Cambridge Stem Cell Institute at the University of Cambridge. In 2019 he took up the post of Director of the Living Systems Institute at the University of Exeter.

Smith's group studies pluripotent stem cells. These are cell lines derived from early embryos that retain the potential to generate all somatic cell types. Having identified the intrinsic and extrinsic factors that support pluripotency, he developed a culture medium for mouse stem cells that allows them to renew themselves indefinitely. This allows him to understand how they maintain this broad potency and how they transition into lineage specification and commitment. The group compares pluripotent cells from different mammals to elucidate common principles and species-specific adaptations.

In 2000, Dr. Smith was awarded the Pfizer Academic Award, in 2002 the Ellison-Cliffe Medal, and in 2003 the MRC Research Professorship and was elected to the Royal Society of Edinburgh. In 2004, Smith was elected a Member of the European Molecular Biology Organization, and in 2006 a Fellow of the Royal Society. In 2010, he was co-recipient of the Louis-Jeantet Prize for Medicine along with French cardiologist Michel Haissaguerre. In 2016, he received the ISSCR McEwen Award for Innovation.

Design Principles of Pluripotency



Ada Yonath

*1939

Department of Structural Biology, Weizmann Institute of Science, Rehovot, Israel

March 2, 2017

Ada E. Yonath is an Israeli crystallographer best known for her pioneering work on the structure and function of the ribosome.

Yonath graduated from the Hebrew University of Jerusalem with a bachelor's degree in chemistry in 1962, and a master's degree in biochemistry in 1964. In 1968, she obtained her PhD from the Weizmann Institute of Science for x-ray crystallographic studies on the structure of collagen. After her postdoctoral studies at Carnegie Mellon University (1969) and MIT (1970), she returned to Israel and established the protein crystallography laboratory. From 1979 to 1984 she was a group leader with Heinz-Günter Wittmann at the Max Planck Institute for Molecular Genetics in Berlin. In the years 1986–2004 she headed a Max Planck Institute Research Unit at DESY in Hamburg, Germany, in parallel to her research activities at the Weizmann Institute.

Yonath focuses on the mechanisms underlying protein biosynthesis by crystallography, using a research line she pioneered from 1980 despite considerable scepticism in the international scientific community. In 1986 she discovered the tunnel through which nascent proteins exit the ribosom, and in 2000 and 2001, she determined the complete high-resolution structures of both ribosomal subunits and discovered within the otherwise asymmetric ribosome, the universal symmetrical region that provides the framework and navigates the process of polypeptide polymerization. Consequently, she showed that the ribosome is a ribozyme that places its substrates in stereochemistry suitable for peptide bond formation and for substrate-mediated catalysis. She also re-visualized the path taken by nascent proteins and revealed the dynamic elements enabling its involvement in various steps of protein synthesis. Her work has also led to the elucidation of the modes of action of many different antibiotics targeting the ribosome, illuminated the mechanism of drug resistance and synergism, and demonstrated the structural basis for antibiotic selectivity, paving the way for structure-based next generation antibiotics.

Among others, Yonath is a member of the United States National Academy of Sciences; the American Academy of Arts and Sciences; the Israel Academy of Sciences and Humanities; the European Academy of Sciences and Art; the European Molecular Biology Organization; the Pontifical Academy of Sciences at the Vatican; and is a Foreign Member of the Royal Society.

Her awards and honours include the Israel Prize (2002), the Harvey Prize (2002), the Paul Karrer Gold Medal (2004), the Louisa Gross Horwitz Prize (2005), the Wolf Prize in Chemistry and the EMET Prize for Art, Science and Culture in Life Sciences (2006), and the Albert Einstein World Award of Science (2008). In 2009, she received the Nobel Prize in Chemistry along with Venkatraman Ramakrishnan and Thomas A. Steitz for revealing the structure and function of the ribosome, becoming the first Israeli woman to win the Nobel Prize and the first woman in 45 years to win the Nobel Prize for Chemistry.

The Genetic Apparatus, from Mendel to Critical Issues in Contemporary Medicine

It is my great honour to be invited to deliver the Mendel Lecture. I am most grateful for this, since it gave me an opportunity to be impressed by Mendel's actual environment alongside discussing his points of view.

Sir Peter Donnelly

*1959

Nuffield Dept. of Medicine, Dept. of Statistics, University of Oxford / Wellcome Centre for Human Genetics, UK

March 16, 2017

Sir Peter James Donnelly is an Australian who trained in mathematics and statistics but has gone on to make substantial contributions in population, statistical, and human genetics, and in meiosis.

Donnelly graduated from the University of Queensland and studied for a doctorate at Oxford. When elected to a chair at Queen Mary College, London, in 1988, Donnelly was only 29, and possibly the youngest Professor in Great Britain. He held a chair at the University of Chicago (1994–96) and was head of the Department of Statistics at the University of Oxford from 1996 to 2001. From 2007 to 2017 he was Director of the Wellcome Centre for Human Genetics (WCHG) in Oxford.

Donnelly was one of the global leaders in what has been called the "genetic revolution", the explosion in knowledge of genetic variation associated with common human diseases. He had a leading role in the International HapMap project and chaired the Wellcome Trust Case Control Consortium (WTCCC), which was named by *Scientific American* as the top scientific achievement of 2007, and its successor WTCCC2 looking at the genetics of more than 20 common diseases across 60,000 individuals.

Donnelly has also made major contributions to coalescent theory, and through large-scale genetic analyses, to our understanding of the history of human populations, especially in Europe. His group has been responsible for a number of breakthroughs in our understanding of meiosis and meiotic recombination, including the identification of the protein which localizes recombination hotspots, its additional roles downstream of double strand breaks, and the mechanism which underpins its role as the first speciation gene identified in vertebrates.

With colleagues, Donnelly founded Genomics PLC in 2014, and became its CEO in 2017. The company uses large-scale genetic data to identify novel drug targets and understand individual risk for common human diseases in order to drive a prevention-first approach to healthcare.

Donnelly was elected a Fellow of the Royal Society in 2006 and a Fellow of the Academy of Medical Sciences in 2008. Other significant awards have included the 2004 Guy Medal in Silver from the Royal Statistical Society, the 2009 Weldon Memorial Prize, the Genetics Society Medal 2020, and the Royal Society's 2021 Gabor Medal. He was knighted by Her Majesty the Queen in 2019 for services to the understanding of human genetics in disease.

Meiosis, Recombination and the Origin of a Species


It was a huge honour to be asked to deliver one of the Mendel Lectures, and a great personal and scientific thrill to be able to visit the home of Mendel, and his profoundly important work, in Brno. I will cherish the memories for a long time.

Friedhelm Hildebrandt

*1957

Harvard Medical School / Boston Children's Hospital / Howard Hughes Medical Institute, USA

March 23, 2017

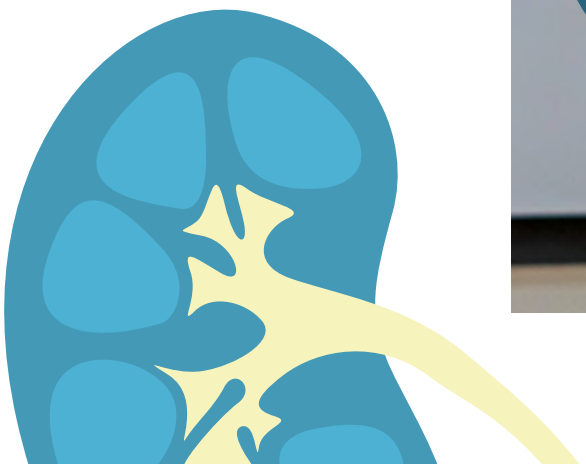
Dr. Hildebrandt received his MD degree from Heidelberg University, Germany, in 1982, obtained his paediatrics and nephrology subspecialty training at Marburg University Children's Hospital, and was a postdoctoral research fellow in nephrology at the Yale School of Medicine in 1988–1989. After his return to Germany he worked at the University of Freiburg where he obtained tenure in 1995. In 2001, he became the Frederick G.L. Huetwell Professor of Pediatrics and Human Genetics at the University of Michigan. Since 2008 he has been an Investigator at the Howard Hughes Medical Institute and the chief of nephrology at the Boston Children's Hospital. In 2013 he became the William E. Harmon Professor of Pediatrics at the Harvard Medical School.

syndrome and congenital malformations of the kidney and urinary tract. His lab studies the function of newly identified disease genes in disease models of mice and zebrafish.

He has received multiple awards for his research, including the E. Mead Johnson Award for Pediatric Research in 2004 from the Society for Pediatric Research, the highest research award given in paediatrics. He is a recipient of the 2014 Homer Smith Award and the 2017 Alfred R. Newton Award of the International Society of Nephrology. Hildebrandt was elected as member of the Association of American Physicians in 2005, the Leopoldina in 2007, and the American National Academy of Medicine in 2015.

Chronic Kidney Disease: The Mendelian Surprise

Hildebrandt's clinical interests include hereditary renal disease. His laboratory focuses on the identification and functional characterization of recessive single-gene causes of kidney diseases in children. His group has identified over 80 novel causative genes among the 240 genes that are currently known to cause chronic kidney disease, if mutated. Gene identification extends to nephrotic



Mendel's work has exemplified the universality of the laws of nature. When visiting Brno to give the Mendel Lecture, I was reminded how the mission of science is a universal, international one.

David Tollervey

*1955

Wellcome Trust Centre for Cell Biology, University of Edinburgh, UK

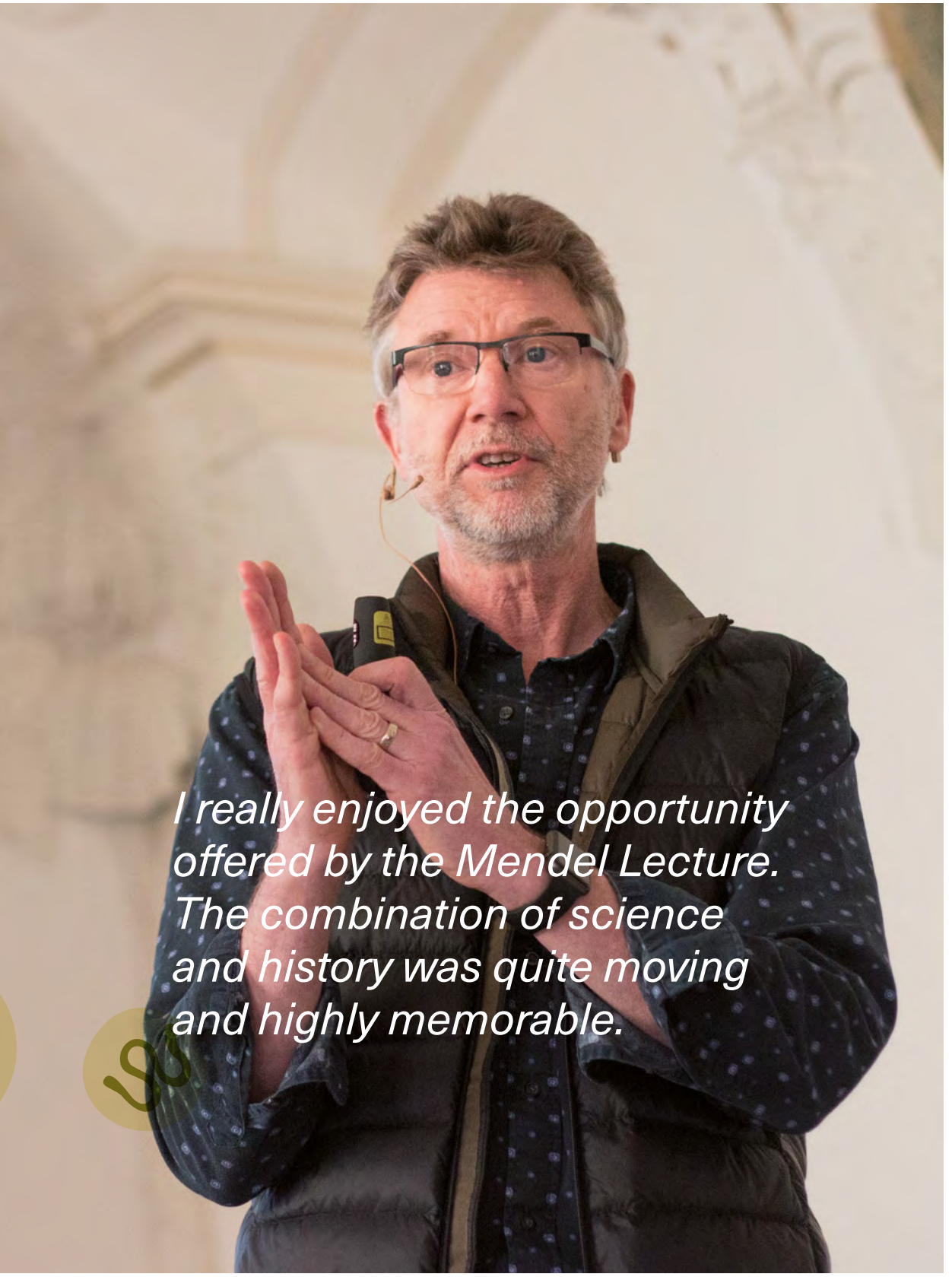
April 20, 2017

David Tollervey studied for his BSc in microbiology in Edinburgh and then for a PhD in genetics at Cambridge. As a postdoctoral fellow, he moved to the University of California and in 1983 he relocated to a permanent position at the Institut Pasteur in Paris, France. In 1988 he became a group leader at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. He returned to Edinburgh in 1997 as a Professor of RNA Biology and Wellcome Trust Principle Research Fellow. Since 2011 he has served as Director of the Wellcome Centre for Cell Biology.

Lighting up RNA Interactions in Living Cells

The aim of the Tollervey group is to understand the nuclear pathways that process newly transcribed RNAs and assemble RNA-protein complexes, the mechanisms that regulate these pathways, and the surveillance activities that monitor their fidelity. His current research combines genetics, biochemistry, transcriptomics, bioinformatics, *in vivo* UV crosslinking and high-throughput sequencing to precisely identify sites of RNA-protein interaction and RNA-RNA base pairing. He has long been a world leader in ribosome synthesis and RNA quality control, having characterized the remarkable protein complex known as the exosome, which can break down RNA molecules. The technology and tools that the Tollervey laboratory has developed have considerable potential for enhancing our understanding of disease states, including infection with viruses and bacteria.

Professor Tollervey is a Fellow of the Royal Society (2004) and of the Royal Society Edinburg (2004), a Member of EMBO (1999), and past President of the International RNA Society.


I really enjoyed the opportunity offered by the Mendel Lecture. The combination of science and history was quite moving and highly memorable.

Paul Modrich

*1946

Department of Biochemistry, Duke University Medical Center / Howard Hughes Medical Institute, Durham, USA

May 18, 2017

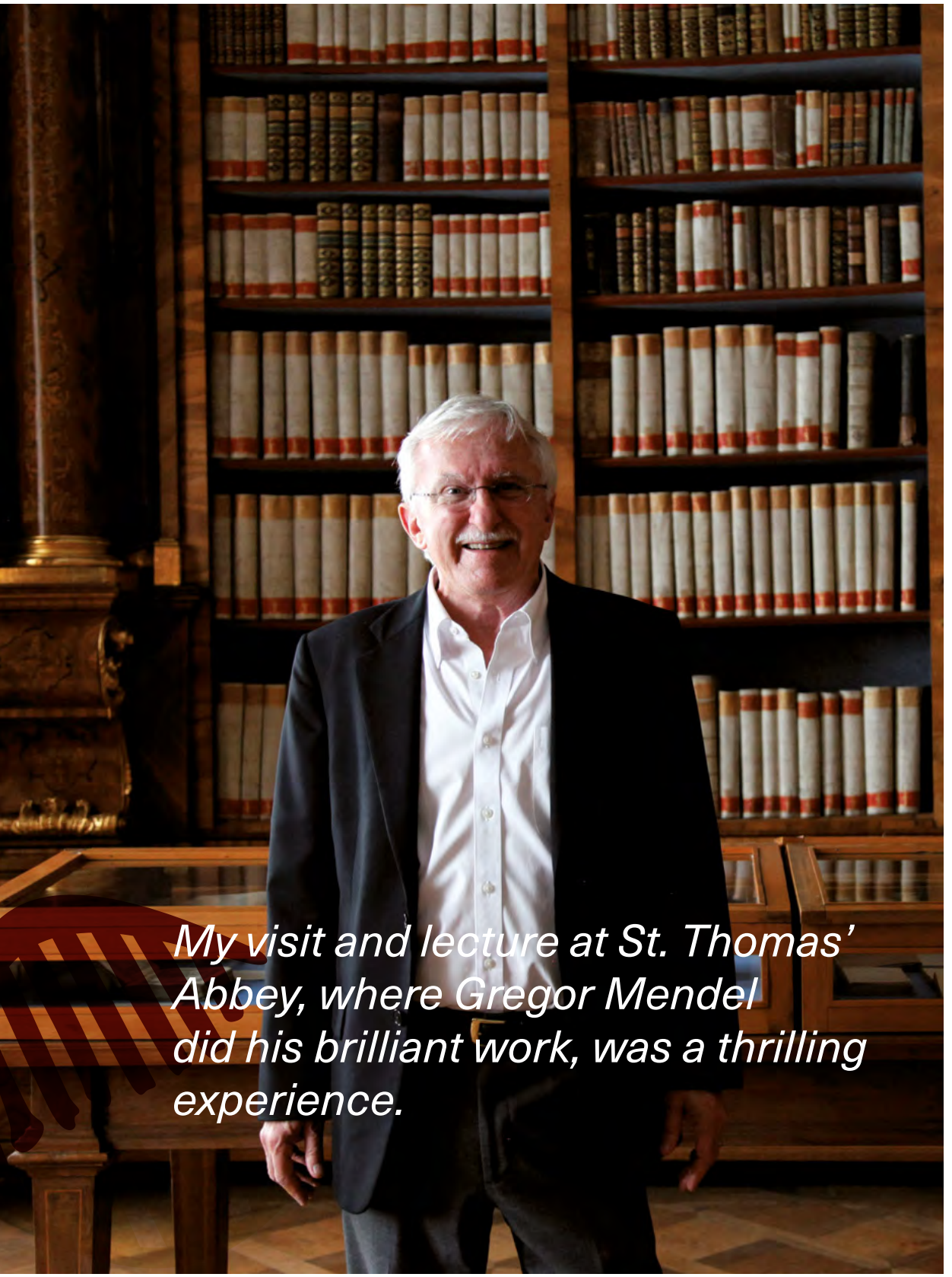
Paul Lawrence Modrich is an American biochemist and 2015 laureate of the Nobel Prize in Chemistry. He is known for his research on DNA mismatch repair.

Modrich obtained a BS degree from the Massachusetts Institute of Technology in 1968 and his PhD in biochemistry from Stanford University in 1973. After postdoctoral work at the Harvard Medical School (1973–1974), he was appointed Assistant Professor in the Chemistry Department at the University of California, Berkeley. He joined Duke University's faculty in 1976 and was a Howard Hughes Investigator from 1994–2019.

Modrich studies mismatch repair, a pathway that corrects base-pairing errors in the DNA helix and plays an important role in the control of mutation production. His laboratory identified multiple proteins and enzymes responsible for mismatch repair in *E. coli* and human cells and established basic features of the pathway in both organisms. During the course of this work, Modrich and colleagues demonstrated that Lynch syndrome cancers and certain sporadic tumours are defective in mismatch repair and identified the components of the repair system that are lacking in these cancer cells. They also showed that mismatch repair-defective cells are resistant to certain anti-cancer drugs.

For his scientific achievements, he received the 1983 Pfizer Award in Enzyme Chemistry, the 1996 Charles S. Mott Prize in Cancer Research, the 1998 Robert J. and Claire Pasarow Foundation Medical Research Award, and the 2005 American Cancer Society Medal of Honor. In 2015 he was awarded the Nobel Prize in Chemistry, jointly with Tomas Lindahl and Aziz Sancar, "for mechanistic studies of DNA repair". In 2016 he received the Arthur Kornberg and Paul Berg Lifetime Achievement Award in Biomedical Sciences. Modrich was elected to the US National Academy of Sciences in 1993 and the following year became a Howard Hughes Medical Institute Investigator. He is also an elected member of the US National Academy of Medicine and a fellow of the American Academy of Arts and Sciences.

Mechanisms in DNA Mismatch Repair



My visit and lecture at St. Thomas' Abbey, where Gregor Mendel did his brilliant work, was a thrilling experience.