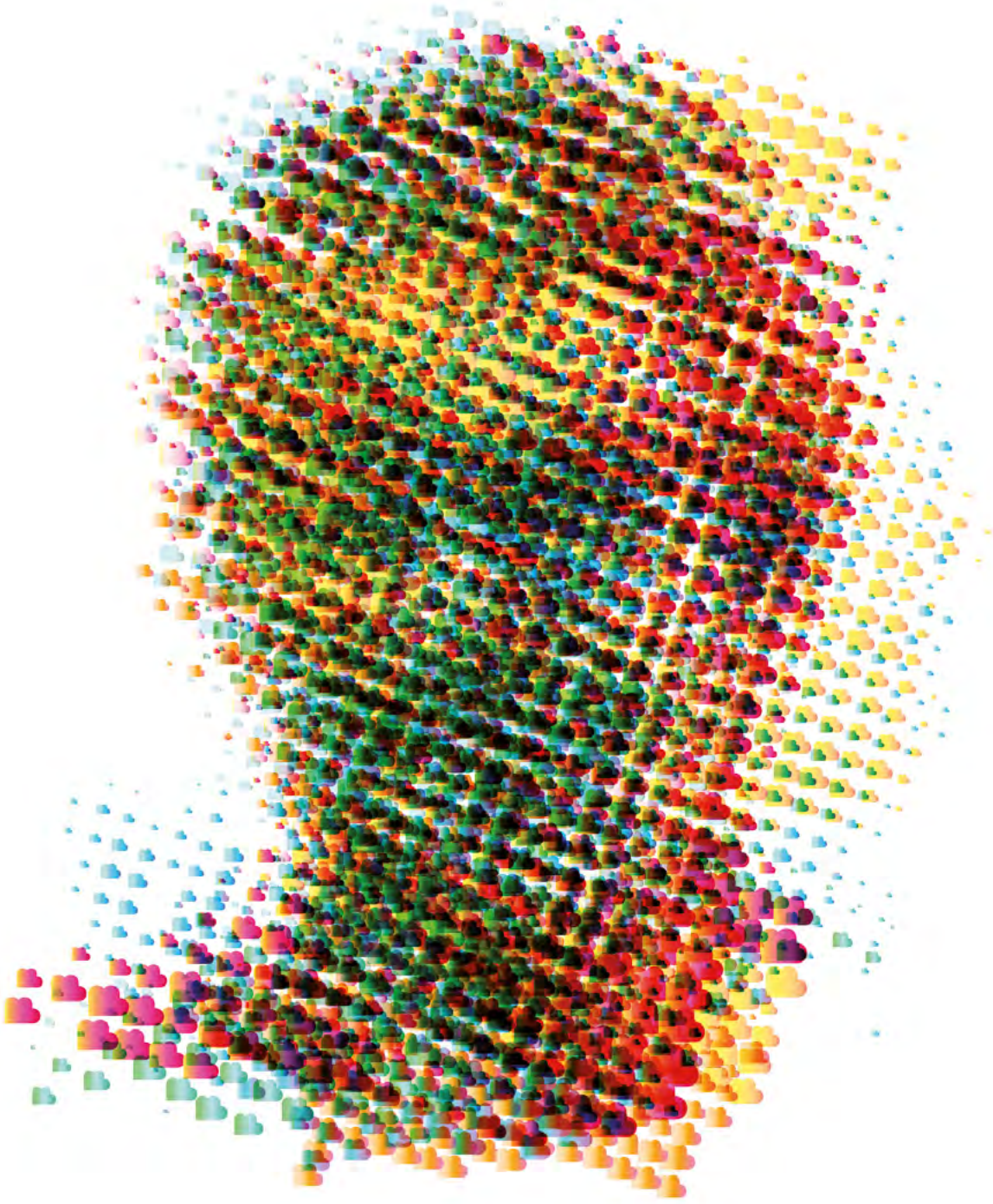
# Mendel Lectures
2018—2019



# 2018 — 2019

# Eric F. Wieschaus

*1947

*Howard Hughes Medical Institute / Department of Molecular Biology, Princeton University, USA*

**October 4, 2018**

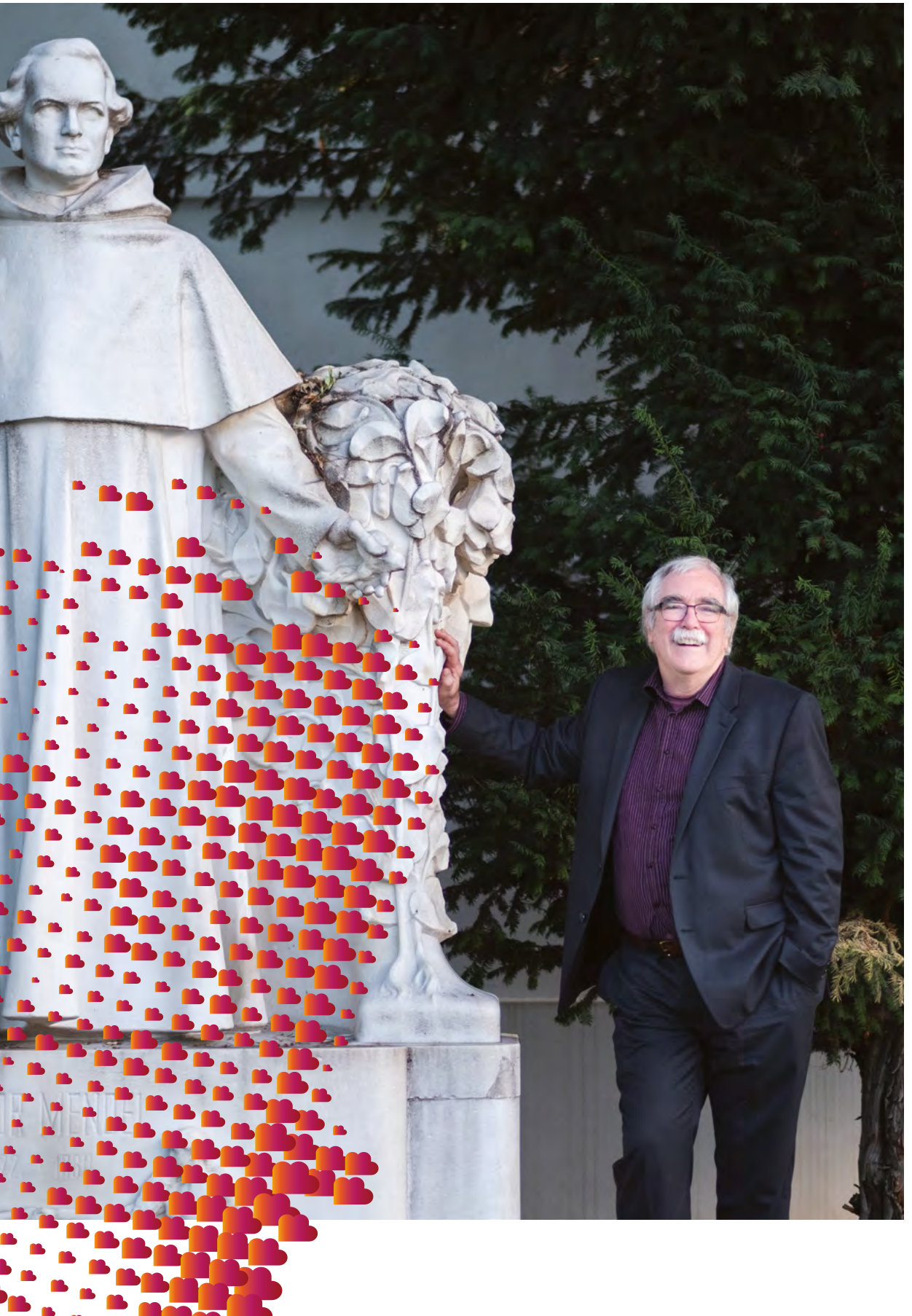
Eric Francis Wieschaus is an American evolutionary developmental biologist and 1995 Nobel Prize winner.

Wieschaus obtained his BS in Biology from the University of Notre Dame in Indiana in 1969 and continued his studies at Yale University, obtaining his PhD in 1974. He pursued postdoctoral work at the University of Zurich, Switzerland, in 1975–1978. In 1978, he moved to his first independent job, at the European Molecular Biology Laboratory in Heidelberg, Germany, and in 1981 he moved to Princeton University in the United States where he became a Professor in 1997. The same year he became an HHMI Investigator.

Much of his research has focused on embryogenesis in the fruit fly *Drosophila melanogaster*, specifically in the patterning that occurs in the early *Drosophila* embryo. Together with Nüsslein-Volhard, he discovered that about 5000 fruit fly genes are important for embryonic development, with 140 being essential. Their widely accepted model defined three sets of genes controlling subdivision in the developing embryo. Most of the gene products used by the embryo at these stages are already present in the unfertilized egg and were produced by maternal transcription during oogenesis. A small number of gene products, however, are supplied by transcription in the embryo itself. He has focused on these "zygotically" active genes because he believes the temporal and spatial pattern of their transcription may provide the triggers controlling the normal sequence of embryonic development.

Wieschaus is a Fellow of the American Academy of Arts and Sciences (1993) and a Member of the National Academy of Sciences (1994). In 1995, he was awarded the Nobel Prize in Physiology or Medicine with Edward B. Lewis and Christiane Nüsslein-Volhard "for their discoveries concerning the genetic control of early embryonic development". In 1998 he was elected a Member of the American Philosophical Society and a Member of EMBO, and in 2003 he was inducted into the NICHD Hall of Honor.

## Genes and the Mechanics of Cell Shape



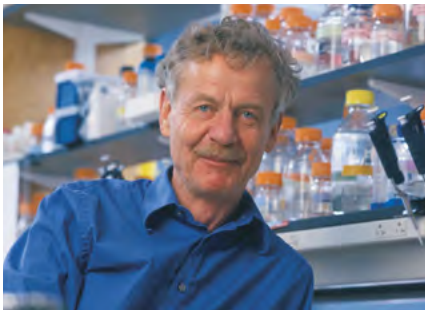
# Rudolf Jaenisch

*1942

*Whitehead Institute for Biomedical Research, MIT, Cambridge, USA*

**October 11, 2018**

Rudolf Jaenisch is a founding member of the Whitehead Institute for Biomedical Research. He is a pioneer of transgenic science, in which an animal's genetic makeup is altered.



Jaenisch completed his MD at the University of Munich in 1967 and studied for another two years at Munich and the Max Planck Institute before moving to the United States in 1970 to carry out postdoctoral research at Princeton University, the Fox Chase Institute for Cancer Research, and subsequently at the Salk Institute. He returned to Germany in 1977 to become the head of the Department of Tumour Virology at the Heinrich Pette Institute at the University of Hamburg. After seven years in Germany, Jaenisch moved to the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts.

His first breakthrough showed that foreign DNA could be integrated into the DNA of early mouse embryos, generating the first transgenic mammals in history. His current research focuses on the epigenetic regulation of gene expression, which has led to major advances in creating embryonic stem cells and "induced pluripotent stem" (IPS) cells, and their use in therapeutic applications. In 2007, the Jaenisch laboratory was one of the first three laboratories worldwide to report reprogramming cells taken from a mouse's tail into IPS cells. He has since shown therapeutic benefits of IPS cell-based treatment for sickle-cell anaemia and Parkinson's disease in mice. Additional research focuses on the epigenetic mechanisms involved in cancer and brain development.

Jaenisch received various awards during his career, including the Inaugural Genetics Prize of the Gruber Foundation (2001), the Robert Koch Prize (2003), the Max Delbrück Medal (2006), the Vilcek Prize (2007), the National Medal of Science (2010), the Wolf Prize in Medicine (2011), and the Otto Warburg Medal (2014). He is a fellow of the American Academy of Arts and Sciences (from 1992) and an elected member of the US National Academy of Sciences (from 2003). He also served as president of the International Society for Stem Cell Research (2014–15).

# Epigenetic Regulation in Development, Aging and Disease States

# Patrick Sung

*1959

*Department of Molecular Biophysics and Biochemistry, Yale University / University of Texas, USA*

**October 18, 2018**

Patrick Sung obtained his BSc degree from the University of Liverpool in 1981 and his DPhil degree from Oxford University in 1985. He received his training as a postdoctoral fellow with Louise Prakash and Satya Prakash at the University of Rochester before joining the faculty at the University of Texas Medical Branch at Galveston in 1993. He moved to the University of Texas Health Sciences Center at San Antonio in 1997, where he became full professor in 2001. In 2003, he joined Yale University as a professor of molecular biophysics and biochemistry, where he also served two three-year terms as department chair between 2009 and 2015. He returned to the University of Texas Health Sciences Center at San Antonio in 2019 as a professor of biochemistry and structural biology, Associate Dean for Research in the Long School of Medicine, and the Robert A. Welch Distinguished Chair in Chemistry. He also serves as co-leader of the Cancer Development and Progression Program in the National Cancer Institute-designated Mays Cancer Center.

Sung's research focuses on DNA double-strand break repair by homologous recombination in yeast and humans. In 1994, he showed that the yeast RAD51 protein, a key member of the RAD52 epistasis group, mediates the homologous DNA pairing and strand exchange reaction central to all recombination-dependent processes, including the repair of DNA double-strand breaks. This finding marked the beginning of studies on homologous recombination enzymology in eukaryotic organisms and has created a much-needed experimental framework for dissecting the role of the other proteins, including the tumour suppressors BRCA1 and BRCA2, in the recombination reaction.

Sung is a member of the Connecticut Academy of Science and Engineering and a recipient of the Recruitment of Established Investigators Award from the Cancer Prevention and Research Institute of Texas, and the Outstanding Investigator Award from the National Cancer Institute. He has served as an associate editor of the *Journal of Biological Chemistry* since 2014, being in charge of the DNA and Chromosomes section of the journal.

## Mechanism of Homology-directed Chromosome Damage Repair in Eukaryotes


*The Mendel Lectures honour the Father of Genetics and also serve as a fabulous tool to encourage students to pursue advanced biological research.*

# Richard J. Davidson

*1951

*Center for Healthy Minds, University of Wisconsin–Madison, USA*

**March 14, 2019**

Richard Davidson is a professor of psychology and psychiatry known for his ground-breaking work studying emotion and the brain.

Davidson received his BA in psychology from New York University in 1972 and his PhD at Harvard University in personality, psychopathology, and psychophysiology in 1976. After that he took a teaching post at the State University of New York at Purchase where he subsequently held several posts including research consultancies at the Department of Pediatrics and Infant Laboratory at Roosevelt Hospital in New York, and the Laboratory of Neurosciences in the National Institute on Aging at the NIH. In 1984 he joined the faculty of the University of Wisconsin at Madison where he has worked since. He previously served as the director of the Laboratory for Affective Neuroscience and of the Waisman Laboratory for Brain Imaging and Behavior. He is founder and director of the Center for Healthy Minds.

Davidson's research is broadly focused on the neural bases of emotion and emotional style as well as methods to promote human flourishing, including meditation and related contemplative practices. He has been popularizing the idea of the plasticity of brain, such that one can learn happiness and compassion as skills like sports or playing a music instrument. His studies have centred on people across the lifespan, from birth through old age. In addition, he has conducted studies involving individuals with emotional disorders such as mood and anxiety disorders and autism, as well as expert meditation practitioners with tens of thousands of hours of experience. Davidson has been a long-time friend of the 14th Dalai Lama, and some of his work involves research on the brain as it relates to meditation.

Davidson was nominated to the National Academy of Medicine and received the Distinguished Scientific Contribution Award for lifetime achievement from the American Psychological Association; the William James Fellow Award from the American Psychological Society; the Mani Bhaumik Award for advancing the understanding of the brain and conscious mind in healing; and the Paul D. MacLean Award for Outstanding Neuroscience Research in Psychosomatic Medicine.


# Well-being Is a Skill: Perspectives From Affective and Contemplative Neuroscience

# Emanuelle Charpentier

*1968

*Max Planck Institute for Infection Biology, Berlin, Germany*

**March 21, 2019**

Emmanuelle Marie Charpentier is a French biologist known for her role in the discovery and characterization of the CRISPR/Cas9 system and winner of the 2020 Nobel Prize in Chemistry.

Charpentier studied biochemistry, microbiology and genetics at the Pierre and Marie Curie University (today the Faculty of Science of Sorbonne University) in Paris. She was a graduate student at the Institut Pasteur from 1992 to 1995, where she continued after graduation as a postdoctoral fellow (1995–1996) before moving to the United States for further postdoctoral research at the Rockefeller University in New York (1996–1997). She worked as an assistant research scientist at the New York University Medical Center from 1997 to 1999 and held the position of Research Associate at the St. Jude Children's Research Hospital and at the Skirball Institute of Biomolecular Medicine in New York (1999–2002). She returned to Europe and spent 2002–2009 at several departments of the University of Vienna. In 2009, Charpentier moved to Sweden to the Laboratory for Molecular Infection Medicine Sweden (MIMS) at Umeå University (till 2014). Then she moved to Germany as a department head and Professor at the Helmholtz Centre for Infection Research in Braunschweig and the Hannover Medical School from 2013 until 2015. In 2015 she became a director at the Max Planck Institute for Infection Biology in Berlin. In 2018, she founded an independent research institute, the Max Planck Unit for the Science of Pathogens.

Charpentier is best known for her role in deciphering the molecular mechanisms of the bacterial CRISPR/Cas9 immune system and repurposing it into a tool for genome editing. In particular, she uncovered a novel mechanism for the maturation of a non-coding RNA which is pivotal in the function of CRISPR/Cas9. In collaboration with Jennifer Doudna's laboratory, Charpentier's laboratory showed that Cas9 could be used to make cuts in any DNA sequence desired. The method they developed involved the combination of Cas9 with easily created synthetic "guide RNA" molecules. Researchers worldwide have employed this method successfully to edit the DNA sequences of plants, animals, and laboratory cell lines.

Charpentier has been awarded numerous international prizes, awards, and acknowledgements, including the Breakthrough Prize in Life Sciences (2015), the Louis-Jeantet Prize for Medicine (2015), the Gruber Foundation International Prize in Genetics (2015), the Leibniz Prize (2016), the Canada Gairdner International Award (2016), the Tang Prize (2016), the Japan Prize (2017), and the Kavli Prize in Nanoscience. She also received the BBVA Foundation Frontiers of

Knowledge Award jointly with Jennifer Doudna and Francisco Mojica, whose pioneering work has ignited "the revolution in biology permitted by CRISPR/Cas9 techniques". In 2020, Charpentier, together with Jennifer Doudna of the University of California, Berkeley, was awarded the Nobel Prize in Chemistry "for the development of a method for genome editing".

In 2013, Charpentier co-founded CRISPR Therapeutics and ERS Genomics along with Shaun Foy and Rodger Novak.

## CRISPR/Cas9: A Bacterial Immune System Repurposed as a Transformative Genome Engineering Technology

# Manolis Kellis

*1977

*Computer Science & Artificial Intelligence Lab and the Broad Institute of MIT and Harvard, USA*

**May 2, 2019**

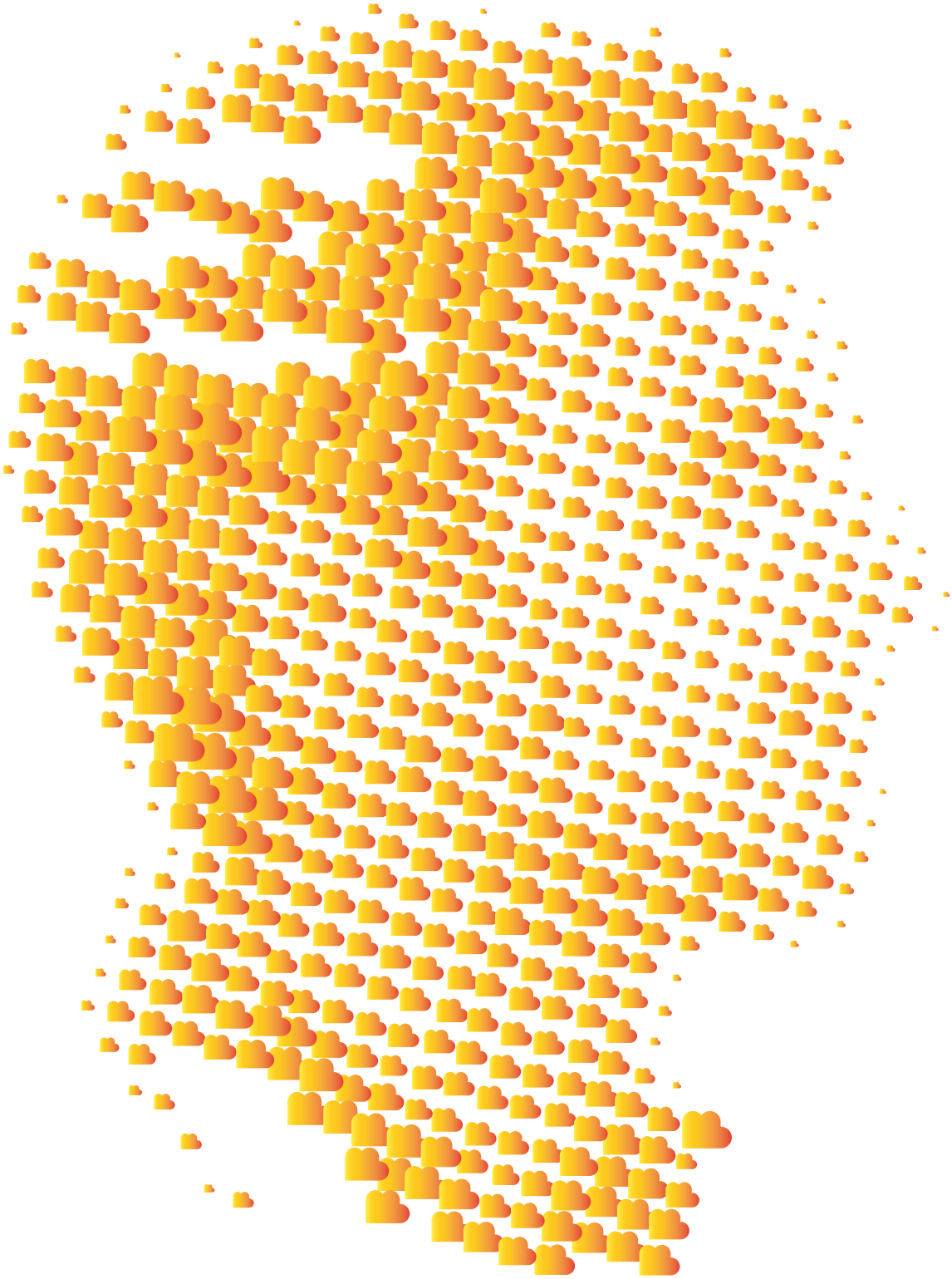
Dr. Kellis lived in Greece and France before moving to the USA, where he studied and conducted research at MIT, the Xerox Palo Alto Research Center, and the Cold Spring Harbor Lab.

He obtained his BS in 1999 and PhD in 2003 from the Massachusetts Institute of Technology. He worked as a postdoctoral fellow at Cold Spring Harbor and Harvard (2003–2004). Prior to his work on computational biology, he worked at MIT and at the Xerox Palo Alto Research Center on artificial intelligence, sketch and image recognition, robotics, and computational geometry. He is a professor of computer science at MIT, a member of the Broad Institute of MIT and Harvard, a principal investigator of the Computer Science and Artificial Intelligence Lab at MIT, and head of the MIT Computational Biology Group.

His research focuses on disease circuitry, genetics, genomics, epigenomics, coding genes, non-coding RNAs, regulatory genomics, and comparative genomics, and how they underpin disorders and diseases such as Alzheimer's disease, obesity, schizophrenia, cardiac disorders, cancer, and immune disorders. Dr. Kellis has led several large-scale genomics projects, including the Roadmap Epigenomics project, the ENCODE project, the Genotype Tissue-Expression (GTEx) project, and comparative genomics projects in mammals, flies, and yeasts.

He received the US Presidential Early Career Award for Scientists and Engineers (PECASE) from US President Barack Obama, the Mendel Medal for Outstanding Achievements in Science, the NIH Director's Transformative Research Award, the Boston Patent Law Association award, the NSF CAREER award, the Alfred P. Sloan Fellowship, the Technology Review TR35 recognition, the AIT Niki Award, and the Sprowls award for the best PhD thesis in computer science at MIT. He has authored over 245 journal publications has been cited more than 130,000 times, and obtained more than 20 multi-year grants from the NIH. His trainees hold faculty positions at Stanford, Harvard, CMU, McGill, Johns Hopkins, UCLA, and other top universities.

## From Genomics to Therapeutics: Uncovering and Manipulating the Genetic Circuitry of Human Disease



# Sir Fraser Stoddart

*1942

*Department of Chemistry, Northwestern University, Evanston, USA*

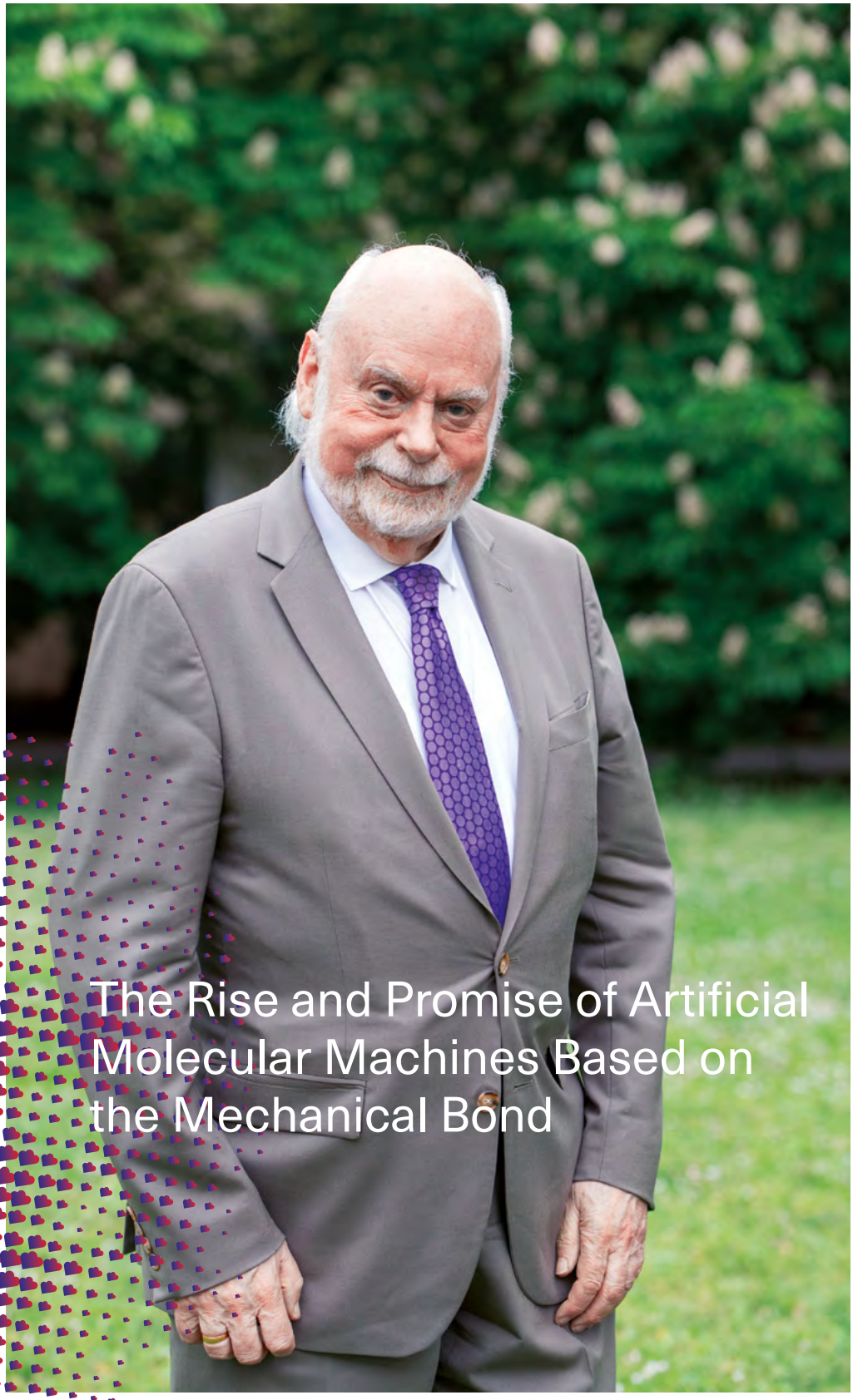
**May 16, 2019**

Sir James Fraser Stoddart is a Scottish-born chemist and laureate of the 2016 Nobel Prize in Chemistry.

Fraser Stoddart received his BSc (1964) and PhD (1966) degrees from Edinburgh University. In 1967, he went to Queen's University in Canada as a Postdoctoral Fellow, and in 1970 to Sheffield University as a Research Fellow. He was a Senior Visiting Fellow at the University of California, Los Angeles (UCLA) in 1978. After spending a sabbatical (1978–81) at the ICI Corporate Laboratory in Runcorn, he returned to Sheffield where he was promoted to a Readership in 1982. He was awarded a DSc Degree by Edinburgh in 1980 for his research into "stereochemistry beyond the molecule". In 1990, he took up the Chair of Organic Chemistry at Birmingham University and was Head of the School of Chemistry there (1993–97) before moving to UCLA as a Professor of Chemistry in 1997. In July 2002, he became Co-Director of the California NanoSystems Institute (CNSI). In 2003, he was appointed Director of the CNSI, where he stayed till 2007, and assumed the Fred Kavli Chair of NanoSystems Sciences. In 2008 he joined the faculty at Northwestern University and was appointed Emeritus Professor of Chemistry at UCLA.

Stoddart is one of the few chemists of the past several decades to have created a new field of organic chemistry – namely, one in which the mechanical bond is a pre-eminent feature of molecular compounds. He has pioneered the development of the use of molecular recognition and self-assembly processes in template-directed protocols for the syntheses of two-state mechanically interlocked molecules (MIMS) (i.e. bistable catenanes and rotaxanes). They have been employed as molecular switches that operate based on the movement of the various components with respect to each other. These molecules have potential uses in the fabrication of molecular electronic devices (MEDS) and Nano Electro Mechanical Systems (NEMS) and in the development of artificial molecular machines (AMMS).

His efforts have been recognized by numerous awards including the Carbohydrate Chemistry Award (1978), the International Izatt-Christensen Award (1993), the Cope Scholar Award (1999), the Nagoya Gold Medal (2004), the King Faisal International Prize (2007), the Albert Einstein World Award of Science (2007), the Cope Award of the American Chemical Society (2008), the Davy Medal of the Royal Society (2008), and the Science and Technology Cooperative Award of the Chinese Government (2019). In 2016 he shared the Nobel Prize in Chemistry together with Ben Feringa and Jean-Pierre Sauvage "for the design and synthesis of molecular machines".



# The Rise and Promise of Artificial Molecular Machines Based on the Mechanical Bond

# Andrew G. Myers

*1959

*Department of Chemistry and Chemical Biology, Harvard University, Cambridge, USA*

**May 23, 2019**

Andrew G. Myers graduated from MIT in 1981 with a BSc and followed with study at Harvard University from 1981–1986, both as a graduate student and then briefly as a postdoctoral researcher. Myers began his independent academic career at Caltech (1986), where he was Assistant, Associate, and then full Professor (1994). In 1998, he moved to the Department of Chemistry and Chemical Biology at Harvard University, served as Chair of the Department from 2007–2010, and is currently Amory Houghton Professor of Chemistry.

Myers' research involves the synthesis and study of complex molecules of importance in biology and human medicine. His group has developed laboratory synthetic routes to a broad array of complex natural products, including the ene-diyne antibiotics neocarzinostatin chromophore, dynemicin A, N1999A2, and kedarcidin chromophore, undertakings greatly complicated by the chemical instability of all members of the class. His laboratory developed the first practical synthetic route to the tetracycline antibiotics, allowing for the synthesis of more than three thousand fully synthetic analogues by a scalable process. Among these was the antibiotic eravacycline, approved (FDA, EMA) for the treatment of complicated intra-abdominal infections, discovered and manufactured using Myers' chemistry. Platform technology his laboratory developed for the synthesis and discovery of new macrolide antibiotics led to the commercial production of more than 2,000 novel candidates. In 2021 the Myers laboratory reported the discovery of the iboxamycin class of synthetic antibiotics, with potent activity against bacterial strains broadly resistant to virtually all current antibacterial drugs. His laboratory is dedicated to the development of highly convergent synthetic pathways that provide practical, scalable solutions for the construction of molecular classes multiplicatively expanded by incorporation of modular variations.

Myers has also discovered numerous fundamental transformations in organic chemistry, many of which bear his name. These include the Myers-Saito cyclization, the Myers deoxygenation reaction, the Myers allene synthesis, the Myers reductive coupling reaction, and the suite of extremely practical transformations collectively known as Myers asymmetric alkylation chemistry, used for the construction of optically active ketones, carboxylic acids, primary alcohols, aldehydes, and alpha-amino acids.

# Progress Toward the Discovery of New Antibiotics with Efficacy Against Multi-drug Resistant Bacterial Pathogens

# Roel Nusse

*1950

*Howard Hughes Medical Institute, Department of Developmental Biology, Stanford University, School of Medicine, Stanford, USA*

**May 30, 2019**

Dr. Roel Nusse's research was seminal in the discovery of Wnt signalling, a family of pleiotropic regulators involved in development and disease.

Nusse holds a BS and PhD from the University of Amsterdam. He did a postdoctoral fellowship under the guidance of Harold Varmus at the University of California, San Francisco, where in 1982 Nusse and Varmus discovered the Wnt1 gene. Following his postdoctoral training, he joined the Netherlands Cancer Institute and carried out much of the foundational work on Wnt signalling in fruit flies. He joined the Developmental Biology Department at Stanford University and the Howard Hughes Medical Institute in 1990.

The Nusse Laboratory at Stanford studies the function of Wnt signalling molecules during the proliferation and differentiation of stem cells, with the aim of understanding the regulation of the growth, development, and integrity of a wide variety of animal tissues. Working *in vivo* and in cell culture, the team studies multiple different organs and stem cell types, trying to identify common principles, and then extends these investigations to cancer and injury repair. They seek to understand the impacts of physiological changes, such as those occurring during hormonal stimuli, injury, or tissue degeneration, on stem cell signalling and function.

Nusse is a member of the US National Academy of Sciences, the American Academy of Arts and Sciences, the European Molecular Biology Organization, and the Royal Dutch Academy of Sciences (since 1997). He has received numerous awards including the Peter Debeye Prize from the University of Maastricht in 2000, the 2017 Breakthrough Prize in Life Sciences, the 2020 Canada Gairdner International Award "for pioneering work on the Wnt signalling pathway and its importance in development, cancer and stem cells".

## Wnt Signalling and the Generation of New Cells in the Liver

*I felt greatly honoured to deliver a Mendel Lecture in 2019 and to be able to visit the monastery where Mendel discovered the fundamental laws of genetics.*