Mendel Lectures
2007—2008


2007—2008

Titia de Lange

*1955

Rockefeller University, New York, USA

October 2, 2007

Titia de Lange is a Dutch cell biologist and a leading expert on telomeres. She is the Director of the Anderson Center for Cancer Research, the Leon Hess Professor and the head of Laboratory Cell Biology and Genetics at Rockefeller University.

Titia de Lange studied biochemistry at the University of Amsterdam and received a PhD in biochemistry from the University of Amsterdam for her work at the Netherlands Cancer Institute. In 1985, she accepted a postdoctoral position with Harold Varmus (the 1989 Nobel prize laureate) at the University of California, San Francisco. There, she isolated human telomeric DNA and was the first to show that tumour telomeres are shortened. De Lange joined Rockefeller University as an assistant professor in 1990.

The goal of de Lange's research is to understand how telomeres protect chromosome ends and what happens when telomere function is lost during the early stages of tumorigenesis before telomerase is activated. De Lange's group was instrumental in the discovery of shelterin, the protein complex that binds to telomeres and prevents DNA damage signalling and inappropriate DNA damage repair at chromosome ends. In 1995 she identified TRF1 and found that it is crucial in the regulation of telomere length. She next discovered TRF2, which she showed protects telomeres from DNA damage signalling and end-to-end fusions. Using electron microscopy with Jack Griffith she discovered that t-telomeres are in a lariat configuration, termed the t-loop. T-loops hide the end of the telomere, thereby safeguarding telomeres from the DNA damage response. More recently, de Lange showed that telomere shortening has a dual role in cancer development: on one hand, telomere shortening limits cancer development; on the other, telomere loss can drive genome instability in checkpoint deficient cancer cells.

For her scientific contributions, de Lange was elected a member of the Royal Dutch Academy of Sciences, the European Molecular Biology Organization, the American Academy of Arts and Sciences, and is a foreign associate of the National Academy of Sciences, and a member of the National Academy of Science Institute of Medicine. She received the first Paul Marks Prize for Cancer Research in 2000.

Titia de Lange is the recipient of the 2011 Vilcek Prize in Biomedical Science, the 2012 Heineken Prize, the inaugural 2013 Breakthrough Prize in Life Sciences, and the 2014 Canada Gairdner International Award.

How Telomeres Deal with the DNA Damage Response


My grandmother was a graduate student with Hugo de Vries, who rediscovered the Mendel laws. It was therefore a special privilege to be invited for a Mendel Lecture and see where he did his monumental work.

Walter Jakob Gehring

*1939
Biozentrum, University of Basel, Switzerland

November 8, 2007

Walter Gehring was a Swiss developmental biologist. He trained as a classical zoologist, gaining his first research experience with radar studies of bird migration. He studied zoology at the University of Zurich, where he obtained his PhD in 1965. His model organism of choice from the time of his PhD work onward was the fruit fly *Drosophila melanogaster*. Gehring also found a gain-of-function allele of Antennapedia, which transformed fruit fly antennae into legs. The realization that tissues can be transformed from one into another through transplantation or mutation defined Gehring's research path and inspired his quest to identify the molecular basis of tissue identity. After earning his PhD, he moved to Yale University in 1965, first as a postdoctoral fellow, then being quickly promoted to assistant and then associate professor of developmental biology. In 1972, he returned to Switzerland as a founding member of the Biozentrum of the University of Basel.

Gehring was probably best known for the discovery of the Homeobox in 1984, a gene segment coding for the evolutionarily conserved DNA binding Homeodomain, which is present in many related transcription factors such as the homeotic or Hox proteins that specify different regions along the anterior-posterior body axis in animals throughout the animal kingdom. His second major impact was the discovery of the conserved function of the Eyeless/Pax6 gene family in eye development, leading to the pioneering concept that corresponding organs in different animals are specified by conserved transcription factors. Both these discoveries had immense impacts in biology and changed how developmental biology was approached, both at the experimental level, where suddenly interesting genes were easily cloned through their homology to other patterning genes, and at the level of perception as developmental studies in model organisms immediately became paradigmatic for human organogenesis and disease.

Gehring's outstanding research contributions were recognized by many prestigious awards, including the Jeantet Prize for Medicine (1987), the March of Dimes Prize in Developmental Biology (1997), the Kyoto Prize for Basic Science (2000), and the Balzan Prize for Developmental Biology (2002). He was elected to several national academies, including the Royal Society of London and the US National Academy of Science. Professor Gehring acted as president of the International Society for Developmental Biologists (ISDB) and as secretary-general of the European Molecular Biology Organization (EMBO).

Walter Gehring served as professor of cell biology at the University of Basel until his retirement in 2009. He was honoured with the "Grosses Bundesverdienstkreuz" of the Federal Republic of Germany in 2010.

Walter Gehring died in 2014.

The Master Control Gene of Eye Development and the Evolution of Light Reception

Svante Pääbo

*1955

Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

November 29, 2007

Svante Pääbo is a Swedish geneticist specializing in the field of evolutionary genetics. He is one of the founders of paleogenetics, and has worked extensively on the Neanderthal genome.

Svante Pääbo studied the history of science, Egyptology and Russian at the

Faculty of Humanities, and at the Faculty of Medicine, at Uppsala University. He earned his PhD there in 1986, and after a short period at the Imperial Cancer Research Fund in London, he spent three years as a postdoc at the Department of Biochemistry, University of California at Berkeley, USA. After his return to Europe, he became a full Professor of General Biology at the University of Munich, Germany (1990–1997). In 1997 he was appointed a director of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.

Pääbo studies genomic and functional differences between humans and their closest living and extinct relatives. Over more than 30 years, he has developed methods to retrieve DNA from archaeological and paleontological remains.

In May 2010, Pääbo and his colleagues published a draft sequence of the Neanderthal genome. He and his team concluded that Neanderthals interbred with modern humans in Eurasia. Based on a genome sequence determined from a small bone from Siberia, he discovered the Denisovans, Asian relatives of Neanderthals. He has shown that genetic variants contributed to present-day humans from Neanderthals have functional consequences, for example, for the risk of falling severely ill upon infection with the SARS-CoV-2 virus.

Professor Pääbo has received numerous awards, including the Gottfried Wilhelm Leibniz Prize of the Deutsche Forschungsgemeinschaft, the Louis-Jeantet Prize for Medicine, the Gruber Prize in Genetics, the Breakthrough Prize in Life Sciences, the Lomonosov Large Gold Medal of the Russian Academy of Sciences, and the Japan Prize. Pääbo is a member of numerous academies, including the Royal Swedish Academy of Sciences, the National Academy of Sciences of the USA, and the Royal Society.

Of Humans, Neanderthals and Apes

Elliot Meyerowitz

*1951

California Institute of Technology, Pasadena, USA

March 6, 2008

Elliot Meyerowitz is an American plant scientist who has pioneered the use of the mustard plant *Arabidopsis thaliana* as a model species for plant genetics and development studies.

Meyerowitz completed his undergraduate work at Columbia University in biology (1973). He graduated with a master's degree in biology from Yale University in 1975 where he also obtained his PhD in 1977. From 1977 to 1979 he was a postdoctoral fellow in the Biochemistry Department at the Stanford University School of Medicine, developing and using methods for the molecular cloning of genes from *Drosophila* in the early days of gene cloning and genomics. Since 1980 he has been a faculty member in the Division of Biology at the California Institute of Technology, where he became the George W. Beadle Professor of Biology in 2002 and served as Division Chair from 2000 to 2010. Meyerowitz was on leave from his position at Caltech from 2011 to 2013 to serve as the inaugural Director of the Sainsbury Laboratory at the University of Cambridge, where he continues to contribute as a Distinguished Associate. Since 2013, when he returned to Caltech, he has been an Investigator at the Howard Hughes Medical Institute.

The Meyerowitz laboratory works on understanding the mechanisms of plant development using live imaging as well as computational approaches. His work is well known for its contribution to the understanding of the genetic and molecular basis of plant hormone reception. Much of his laboratory's research is directed to the study of the shoot apical meristems of flowering plants – the collection of stem cells at the tip of each branch that is the source for the cells that make stems, leaves, and flowers. The Meyerowitz laboratory detailed how flower formation is controlled, resulting in the ABC Model of flower development; discovered the first plant hormone receptor; and identified the genes that control cell numbers in the plant growing tip, providing a fundamental framework to help build the field of plant development.

Among his honours are the Genetics Society of America Medal (1996); the International Prize for Biology awarded by the Japanese Society for the Promotion of Science (1997); the Lounsbery Award of the US National Academy of Sciences (1999); the R.G. Harrison Prize of the International Society of Developmental Biologists (2005); the Balzan Prize (2006);

the Dawson Prize in Genetics from the University of Dublin (2013); and the Gruber Genetics Prize (2018). Professor Meyerowitz is past president of the Genetics Society of America, the International Society for Plant Molecular Biology, and the Society for Developmental Biology. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society. He is a foreign member of the Royal Society, a foreign associate of the Académie des Sciences of France, and an Associate Member of the European Molecular Biology Organization.

Plant Stem Cells: Live Imaging and Computational Models of the *Arabidopsis* Shoot Apical Meristem

It is a great honour to have given one of the Mendel Lectures. The 200th anniversary of Mendel's birth is a significant milestone in the history of science, as Mendel's work still serves as the basis for the greatest advances in modern biology in the 21st century.

Stephen C. West

*1952

Cancer Research UK, Clare Hall Laboratories, UK

April 10, 2008

Stephen Craig West is a British biochemist and molecular biologist specializing in research on DNA recombination and repair. He is known for pioneering studies on genome instability diseases including cancer.

West obtained his, BSc in 1974 and his PhD in 1977, both from Newcastle University. After finishing his PhD, he moved to the United States to work as a postdoc in the Department of Molecular Biophysics and Biochemistry at Yale University. In 1985, he moved back to the UK to set up a research group at the Imperial Cancer Research Fund's Clare Hall Laboratories at South Mimms. He is now a Senior Group Leader at the Francis Crick Institute in London.

West's research focuses on mechanisms of genetic recombination and DNA strand break repair. In particular, he has defined relationships between defective DNA repair processes and human diseases such as inheritable breast cancer and neurological disorders. While at Yale, West purified and characterized RecA protein, and in doing so discovered many key aspects of how cells mediate DNA-DNA interactions and strand exchange. Parallel studies were carried out by the groups led by Charles Radding (also at Yale) and Robert Lehman (Stanford University). The work at these three laboratories provided the groundwork for our current understanding of the enzymatic mechanisms of recombination. After moving to the UK in 1985, West continued his work in bacterial systems. He identified RuvC as the first cellular enzyme that resolves recombination intermediates and characterized how this nuclease cuts Holliday junctions. West's laboratory then moved into eukaryotic systems, where he discovered eukaryotic Holliday junction resolvases including GEN1 and the SMX complex. West was the first to purify the human RAD51 protein (the eukaryotic ortholog of RecA), and to show that it promotes homologous pairing and strand exchange reactions similar to those mediated by RecA. In addition, he purified and then visualized the BRCA2 breast cancer tumour suppressor.

West is a member of the European Molecular Biology Organization and a Fellow of the Royal Society, and has been awarded numerous prizes, including the 2007 Louis-Jeantet Prize for Medicine.

Stephen Craig West was elected Foreign Associate of the National Academy of Sciences in 2016, and an International Honorary Member of the Academy of Arts and Sciences in 2021. He was awarded the Leeuwenhoek Medal (2002) and the GlaxoSmithKline Medal (2010) of the Royal Society, the Genetic Medal (2012) and the Lifetime Achievement in Cancer Research Prize by Cancer Research UK (2018).

DNA Strand-Break Repair and Relationship to Human Disease


To present a lecture at the home and workplace of Mendel is the dream of every geneticist.

Richard M. Durbin

*1960

Department of Genetics, University of Cambridge, UK

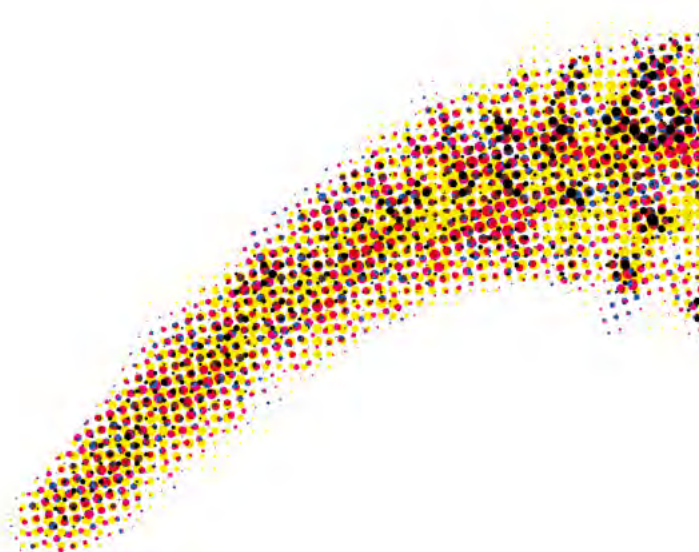
April 17, 2008

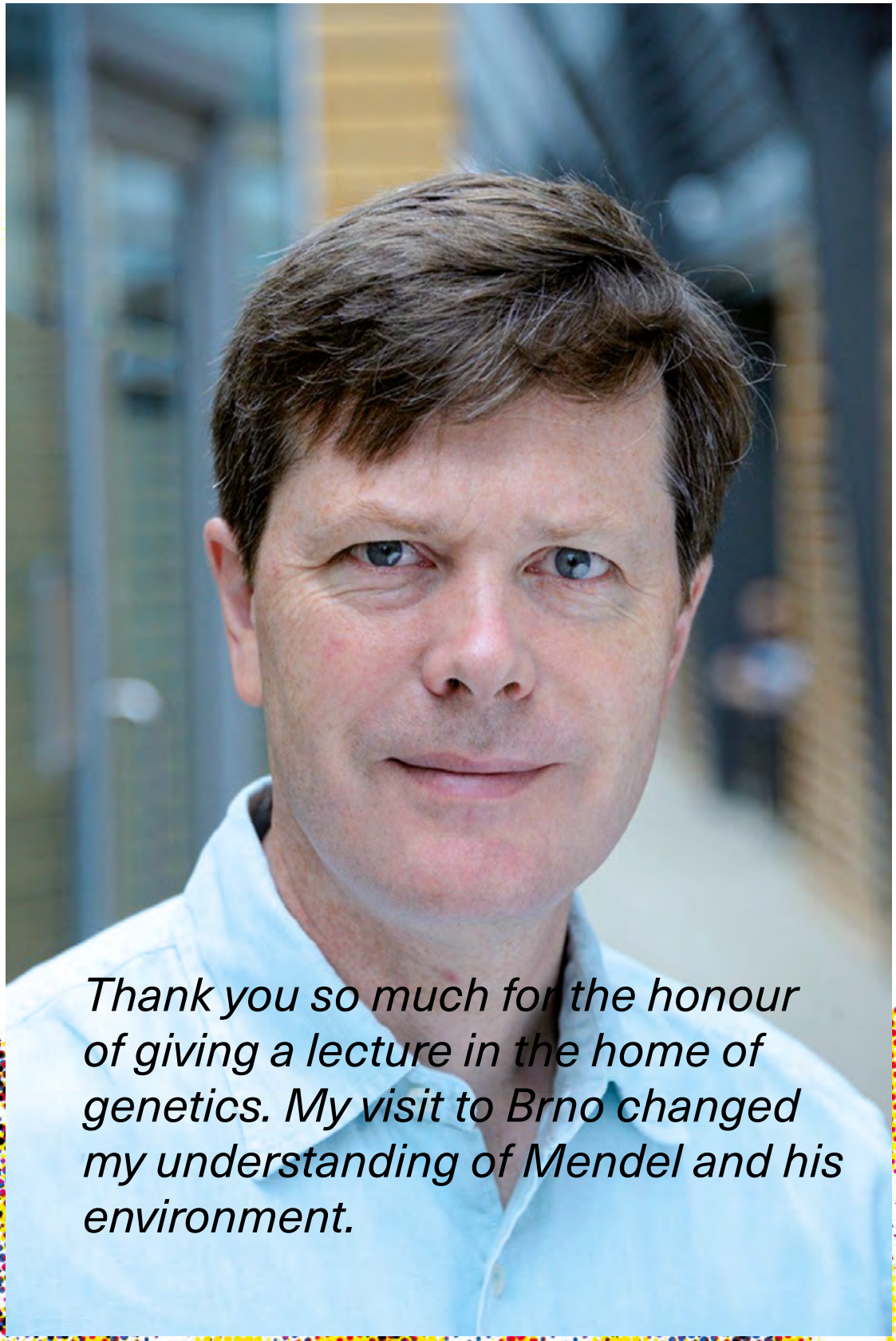
Richard Michael Durbin is a British computational biologist. He graduated from the University of Cambridge in 1982. Then he continued at Cambridge, studying for his PhD the development and organization of the nervous system of *Caenorhabditis elegans* while working at the Laboratory of Molecular Biology (LMB). In 1988 he moved to Stanford University, USA, for his postdoc, then returned to the UK in 1992 to the Wellcome Sanger Institute in Cambridge, where he worked for 25 years on genome sequencing and related areas before moving in 2017 to be Al Kindi Professor in the Department of Genetics, University of Cambridge.

Richard Durbin played a significant role in a series of large scale genome sequencing projects, contributing to the assembly and gene sequence analysis for the initial Human Genome Project, co-leading the 1000 Genomes Project to characterize genetic variation in 2504 humans from around the world, and co-founding the Earth Biogenome Project, which aims to assemble high quality reference genome sequences for all eukaryotic species. Alongside involvement in large projects he has developed numerous methods for computational sequence analysis. These include gene finding (e.g. GeneWise) and Hidden Markov model methods for sequence alignment and matching (e.g. HMMER) and for finding demographic history (PSMC). Using these methods, Durbin worked with colleagues to build a series of important genomic data resources, including the protein family database Pfam, the genome database Ensembl, and the gene family database TreeFam. Recently he started a research programme in evolutionary genomics, applying whole genome sequencing to study speciation and adaptation in the dramatic cichlid fish radiation of the East African great lakes.

Richard M. Durbin was a joint winner of the Mullard Award of the Royal Society in 1994, won the Lord Lloyd of Kilgerran Award of the Foundation for Science and Technology in 2004, and was elected a Fellow of the Royal Society (FRS) in 2004 and a member of the European Molecular Biology Organization (EMBO) in 2009. The Royal Society awarded its Gabor Medal to Durbin in 2017 for his contributions to computational biology.

Sequencing Hundreds of Human Genomes





Thank you so much for the honour of giving a lecture in the home of genetics. My visit to Brno changed my understanding of Mendel and his environment.

Sir Paul Nurse

*1949

Rockefeller University, New York, USA

May 5, 2008

Sir Paul Nurse is an English geneticist and cell biologist. He was awarded the 2001 Nobel Prize in Physiology or Medicine along with Leland Hartwell and Tim Hunt for their discoveries of protein molecules that control the division of cells in the cell cycle.

He received his BSc degree in biology in 1970 from the University of Birmingham and his PhD degree in 1973 from the University of East Anglia. Nurse continued his postdoctoral research at the laboratory of Murdoch Mitchison at the University of Edinburgh for the next six years (1973–1979). He also spent several months at both the University of Bern and the University of Copenhagen to gain experience in genetic analysis of the fission yeast (*Schizosaccharomyces pombe*).

Beginning in 1976, Paul Nurse identified the gene cdc2 in fission yeast. This gene is the key regulator of the progression of the cell cycle from G1 phase to S phase and the transition from G2 phase to mitosis. In 1987 Nurse also identified the corresponding human homologue of this gene, CDK1, which codes for a cyclin dependent kinase. He showed that CDK1 is responsible for reversible chemical modification (phosphorylation), discovering the key component of the molecular mechanism that drives cells through the cell cycle.

After a period at the University of Sussex, in 1984 he joined the Imperial Cancer Research Fund (Cancer Research UK). He left in 1988 to chair the Department of Microbiology at the University of Oxford. He then returned to the ICRF as Director of Research in 1993, and in 1996 was named Director General of the ICRF, and CEO of Cancer Research UK in 2002. In 2003, he became President of Rockefeller University in New York City where he continued to work on the cell cycle of fission yeast.

Paul Nurse has received numerous awards and honours. He was elected an EMBO Member in 1987 and a Fellow of the Royal Society (FRS) in 1989, and the Founder Member of the Academy of Medical Sciences in 1998. He has received the Royal Society's Royal and Copley Medals and is a foreign associate of the US National Academy of Sciences. He received the Gairdner Award in 1992, the Albert Lasker Award for Basic Medical Research in 1998, was knighted in 1999, awarded the French Legion d'Honneur in 2002, and the Order of the Rising Sun, Japan, in 2018.

In 2010, he was elected President of the Royal Society for a five-year term and became the first Director and Chief Executive of the UK Centre for Medical Research and Innovation, now the Francis Crick Institute.


Mendel was a great scientist whose research paved the way to the concept of the gene and led to the foundation of genetics. It was an honour to give a lecture in Brno where his work was carried out which celebrated his achievements.