
10th anniversary


2012

Gary Ruvkun

*1952

Harvard University, Massachusetts General Hospital, Department of Genetics, USA

October 8, 2012

Ruvkun attended the University of California at Berkeley, where he studied physics and biology, and graduated in 1973 with a degree in biophysics. In 1976 he enrolled in a PhD programme in biophysics at Harvard University. His PhD thesis, which explored bacterial nitrogen fixation genes, unlocked many of the genetic regulations of this process and showed that these genes have been conserved over 3 billion years of microbial evolution. After receiving his PhD in 1982, Ruvkun did postdoctoral research with Walter Gilbert at Harvard and Robert Horvitz at MIT, where he explored the genetic pathways controlling the developmental timing of *C. elegans*. Ruvkun became a professor at Harvard in 1985.

In collaboration with Victor Ambros at Harvard, Ruvkun established that the gene *lin-4* inhibits the activity of the gene *lin-14*. In 1991, Ruvkun showed that activating mutations of *lin-14* that escape repression by *lin-4* are RNA regulatory elements in the *lin-14* messenger RNA that follows the protein coding region. Ambros and his team discovered that *lin-4* encodes a tiny RNA of 22 nucleotides. Ambros and Ruvkun discovered that the 22-nt *lin-4* RNA is complementary to sections in the *lin-14* mRNA, and that activating mutations in *lin-14* delete these complementary regions. This complementarity to the *lin-4* miRNA was imperfect – the duplexes contained multiple bulges and loops both in the *lin-4* RNA strand and in the *lin-14* mRNA strand, like the secondary structures of the well-studied ribosomal RNAs. Ambros and Ruvkun's back-to-back studies in *Cell* (1993) announced the discovery of the first microRNA and of its mechanism of regulating target mRNA translation by imperfect base pairing.

The universality of miRNAs emerged in 2000 when Ruvkun's laboratory discovered the second miRNA, *let-7*, which was conserved in over 500 million years of animal phylogeny – including in humans. The *let-7* miRNA also repressed the activity of its target gene through its 3' UTR with imperfect complementary sequences in the target mRNA. The Ruvkun lab is now using genetic strategies to systematically discover the components of the microRNA pathways in *C. elegans*. These discoveries triggered an explosion of tiny RNA exploration across the tree of life, and led to the identification of the biochemical machinery by which tiny RNAs of different classes are generated and regulate their target genes in many genetic pathways. This work has revealed that miRNAs are key players in embryogenesis and totipotent cell decisions, as well as diseases ranging from coronary disease to cancer.

Ruvkun also has made key discoveries in aging research. His lab discovered the molecular mechanisms of the first two aging genes discovered by Tom Johnson at the University of Colorado and Cynthia Kenyon at the University of California at San Francisco, which enabled the study of aging to become molecular. He discovered essentially every element of an insulin-signalling pathway that is the most potent regulator of lifespan in *C. elegans*. Many of the genes identified by Ruvkun's comprehensive insulin-signalling genetics have been shown to mediate metabolic control and lifespan in humans as well.

Gary Ruvkun has received many awards (most of them with Ambros): the Rosenstiel Award in 2005, the Albert Lasker Award for Basic Medical Research in 2008, the Gairdner International Prize in 2008, the Warren Triennial Prize in 2008, the Massry Prize in 2008, and the Dan David Prize in 2011 (with Cynthia Kenyon for his discoveries in aging), the Paul Janssen Award in 2012, the Wolf Prize for Medicine in 2014, the Gruber Prize in 2014, the Breakthrough Prize in Life Sciences in 2014, and the March of Dimes Prize in Developmental Biology in 2016. He became a member of the National Academy of Sciences in 2008, the American Academy of Arts and Sciences in 2009, and the American Philosophical Society in 2019. Since 1997 and in collaboration with Chris Carr, Mike Finney and Maria Zuber, Ruvkun has been developing with NASA support a DNA sequencer to send to Mars or other planets to search for life on those planets that uses DNA, RNA, and ribosomes, like life on Earth. This is to test the hypothesis that life has spread between planets and perhaps across the galaxy.

An Animal Surveillance Pathway for Microbial Inhibition of Conserved Cellular Components and Induction of Defence Responses

Josef Jiřičný

*1951
Institute of Molecular Cancer Research, University of Zurich, Switzerland

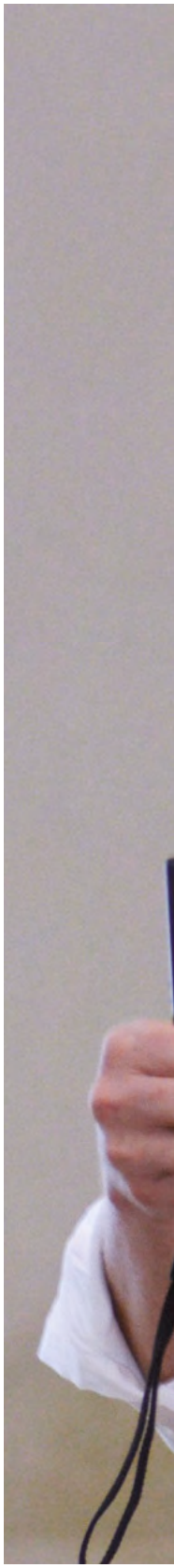
October 8, 2012

Josef Jiřičný was born in Prague in 1951. Following the occupation of Czechoslovakia in 1968, he emigrated to England. He studied chemistry at the University of Aston in Birmingham and then at the University of London, where he obtained his PhD in 1977. After three years of postdoctoral research at King's College London, he moved to the Imperial Cancer Research Fund laboratories in London, where he began to explore repair mechanisms of damaged or carcinogen-modified DNA. In 1983 he transferred his research to the Friedrich Miescher Institute in Basel, where he became a senior group leader in 1989. One year later he accepted the position of senior director of biochemistry at the newly-founded Istituto di Richerche di Biologia Molecolare (IRBM) near Rome, where he continued to study DNA repair mechanisms, as well as coordinating research programmes aimed at the discovery of novel antiviral substances. In 1996 he moved to Zurich as director of the Institute of Molecular Cancer Research of the medical faculty of the University of Zurich (UZH). In 2003 he was elected joint UZH/ETH professor and joined the Department of Biology at the ETH in Zurich.

Jiřičný's group has been primarily interested in studying the biochemistry and biology of the postreplicative mismatch repair (MMR) system in human cells. They identified and characterized several key components of this system. They have also been studying the link between MMR and colon cancer, as mutations in MMR genes are associated with one of the most common inherited cancer predisposition syndromes, hereditary non-polyposis colon cancer (HNPCC). Having discovered that MMR-associated proteins participate in other pathways of DNA metabolism as well, Jiřičný's lab shifted its focus to the characterization of these processes, particularly the repair of interstrand cross-links such as those induced by the cancer chemotherapeutic cisplatin.

Josef Jiřičný has been a member of EMBO since 1996 and of Academia Europaea since 2000. In 2003 he was awarded the Gregor Mendel Medal of the Czech Academy of Sciences for his contribution to the elucidation of the genetics of inherited cancer. In the same year, he was nominated the Bonizzi-Theler Professor of functional genomics and received the Swiss Bridge Award. In May 2006, he received the San Salvatore Prize for cancer research and the International Award of the Slovak Academy of Sciences. In 2010 he was awarded the Ernst-Theophile Jucker Prize for Cancer Research.

FAN 1, a Novel Enzyme Involved in the Processing of Cisplatin Adducts in DNA



I feel highly honoured to be among the speakers who have had the great privilege to participate in the Mendel Lecture series during the past two decades.

Jan Hoeijmakers

*1951

Department of Genetics, Erasmus MC, Rotterdam, Netherlands

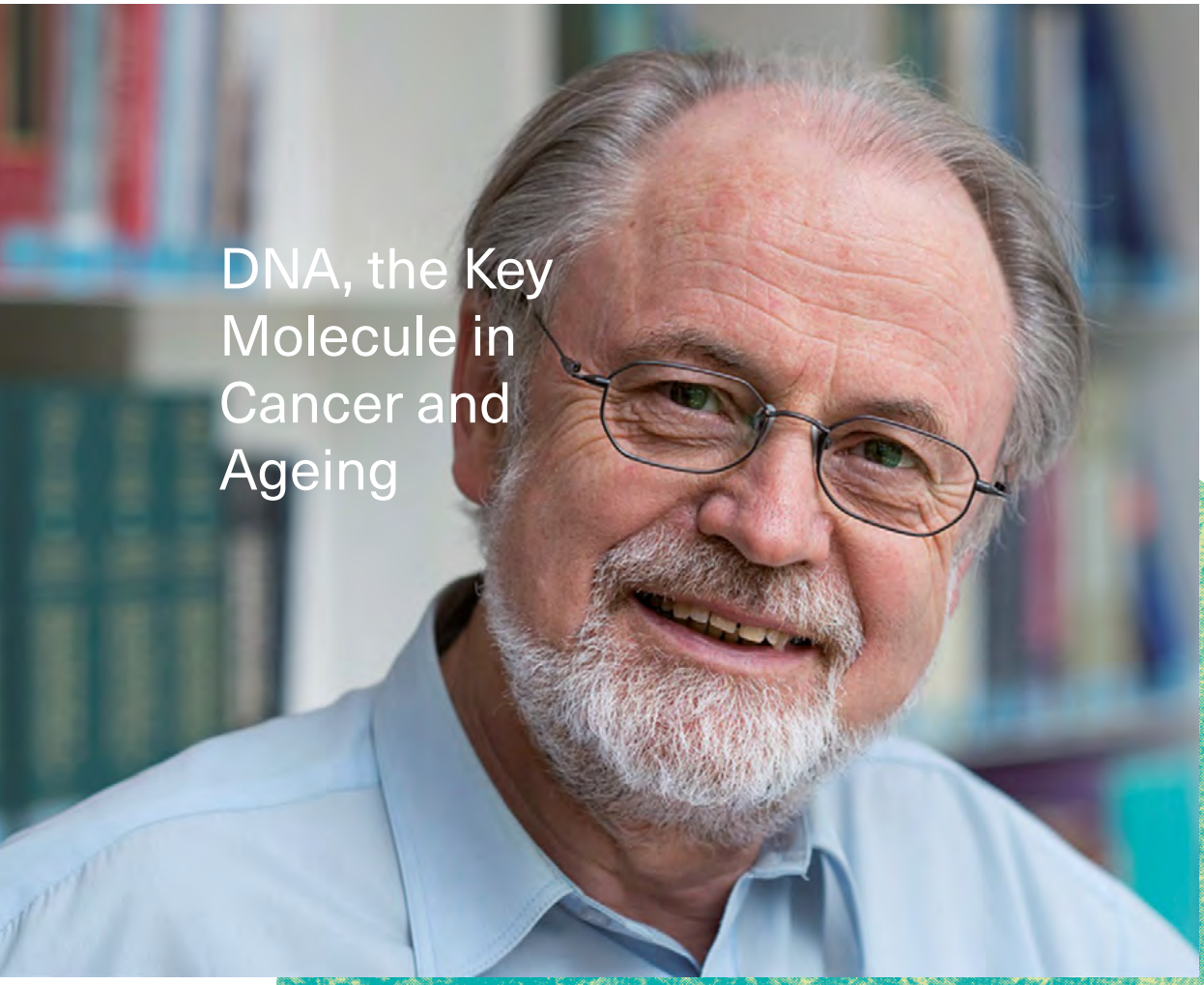
October 8, 2012

Jan Hoeijmakers graduated in 1975 in molecular biology from the Radboud University Nijmegen, Netherlands, and finished his PhD at the University of Amsterdam (under supervisor Piet Borst) in 1979. He was given a position in the Department of Cell Biology and Genetics of Erasmus University in Rotterdam where he became professor of Molecular Genetics in 1993 and head of the Department in 2001.

His PhD work provided insight into the curious fishnet-structure and function of the unusual mitochondrial DNA of trypanosomes, called kinetoplast DNA. In addition, by cloning four genes for surface antigens he discovered – at that time unexpected – DNA rearrangements enabling these parasites to constantly change their surface coat and thereby escape the host immune system, causing sleeping sickness. For this work he received the Harold-Quintus-Bosz Prize in 1983.

After completing his PhD, Hoeijmakers studied the molecular biology of DNA repair by cloning many human DNA repair genes, allowing elucidation of the molecular-genetic basis of multiple rare and very severe human repair syndromes, and understanding repair mechanisms *in vitro*, in live cells and intact mice by developing GFP-tagging and dynamic innovative photobleaching techniques. His team generated the largest collection of mouse models for DNA repair deficiencies, enabling insight into the biological and clinical importance of DNA damage for cancer and aging. He pioneered the link between DNA damage, repair and aging and succeeded in influencing aging in mice. Recently, his group also identified DNA damage-driven transcriptional stress as a major cause of systemic aging, explaining the basis of proteinopathies, and discovered a surprising effect of nutritional interventions, with implications for repair syndromes, dementias, chemotherapy and ischemia reperfusion injury in surgery and organ transplantation. This work has led to a complete reversal of nutritional guidelines for DNA repair syndrome patients suffering from dramatic premature aging.

Jan Hoeijmakers has been honoured with many prizes. In 1986 he received the De Snoo-van 't Hoogerhuijs Prize; in 1995 the Louis-Jeantet Prize together with Bootsma for cloning the first human DNA repair gene; and in 1998 the Spinoza Prize, the highest award in Dutch science. In 2000 he was awarded the Descartes Prize and the Van Gogh Prize, and in 2001 the Josephine Nefkens Prize for cancer research. In 2011 he and Bert Vogelstein received a prize from the Charles Rodolphe Brupbacher Foundation for their research into genome stability and its role in aging and cancer. In that year he also received the Queen Wilhelmina Research Prize from the Dutch Cancer Society. Hoeijmakers became Academy Professor at the Royal Netherlands Academy of Sciences in 2011. He was knighted in 2013 in the Order of the Dutch Lion, received the NVHG Galjaard Prize of the Netherlands Society of Human Genetics in 2016, the International Olav Thon Foundation personal Award in 2017, the "EMGS Award" in 2019, and jointly with other lab members the Ammodo Award in 2020.



DNA, the Key Molecule in Cancer and Ageing

The amazing discovery of the basic genetic principles by Mendel has provided the basis of genetics today and the enormous impact it has on our society, most importantly health and well-being of mankind. This major discovery deserves lasting commemoration by the Mendel Lectures.

Jiří Lukáš

*1961

Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Denmark

October 8, 2012

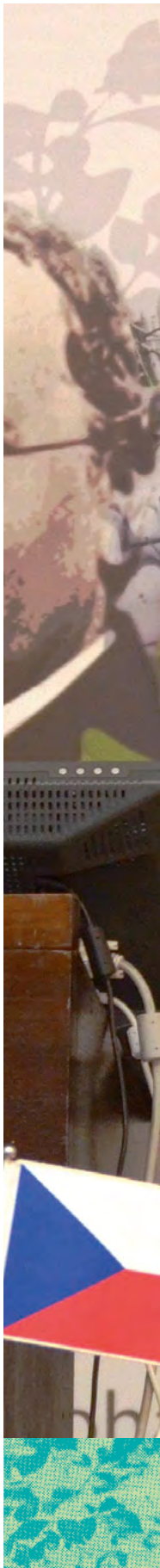
Jiří Lukáš was born in the Czech Republic and studied at the Veterinary University in Brno, Czech Republic and obtained a PhD in zoology from the Czech Academy of Science. He worked as a visiting scientist with Nobel laureate Paul Nurse at the Department of Biochemistry, Oxford, UK and as a postdoc with Giulio Draetta at EMBL, Heidelberg, Germany. In 1993 he became a senior scientist in the Danish Cancer Society, Copenhagen, Denmark, where he later served as Director of the Center for Genotoxic Stress Research. For much of his career he created a remarkable partnership with Jiří Bártek, placing replication stress among the hallmarks of cancer. In 2012, Jiří Lukáš moved to the University of Copenhagen where he was appointed Professor at the Faculty of Health and Medical Sciences and Executive Director of the Novo Nordisk Foundation Center for Protein Research.

Prof. Lukáš studies chromosomal dynamics in the mammalian cell cycle and after DNA damage. He has made revolutionary discoveries enhancing our knowledge of essential mechanisms required for genome maintenance, and has provided key evidence of how the failure of post-translational protein modifications contribute to the development of cancer. His laboratory is also renowned for pioneering advanced imaging techniques combined with genetic silencing and computation-based phenotypic readouts, which elucidate fundamental principles of protein function in their physiological environment and generate powerful resources of previously unknown genome caretakers including rate-limiting guardians of DNA repair as potentially druggable targets of cancer.

Prof. Lukáš has received numerous prestigious awards for his research including the Young Danish Cancer Researcher Prize (1995), the Alfred Benzons Foundation Prize (2002), the Novo Nordisk Foundation Prize (2003), the GJ Mendel Honorary Medal (2003), the Danish Cancer Society Senior Research Prize (2008), the Danish Society for Cancer Research Award (2010), the Leopold Griffuel Award (2014), and the Fernström Foundation Grand Nordic Prize (2016). Lukáš is an elected member of EMBO, Academia Europaea, the European Academy of Cancer Sciences, and the Royal Danish Academy of Sciences and Letters. He is also Honorary Member of the Learned Society of the Czech Republic.

Most recently, Prof. Lukáš received the Anders Jahre Medical Prize in 2020 for his many years of outstanding research and work on cell cycle regulation and genome integrity in cancer.

Spatial and Temporal Organization of Genome Maintenance




ANNIVERSARY MENDEL LECTURES

Günter Blobel

*1936

Howard Hughes Medical Institute & The Rockefeller University, New York, USA

October 9, 2012

Günter Blobel was born in 1936 in Waltersdorf, Germany (now part of Poland). In January 1945 he fled with his family from their native Silesia to Dresden to escape from the advancing Red Army. He received his MD from the University of Tübingen in 1960 and his PhD in 1967 from the University of Wisconsin, Madison, where he worked with Van R. Potter in the McArdle Laboratory for Cancer Research. He did postdoctoral work at Rockefeller University in the laboratory of George E. Palade, and remained at the university from that time. He was named the John D. Rockefeller, Jr. Professor in 1992, and became an Investigator at the Howard Hughes Medical Institute in 1986.

In a series of ground-breaking experiments conducted over the course of 30 years, Günter Blobel discovered how the cell's protein distribution system operates. It was for this work that he won the Nobel Prize in Physiology or Medicine in 1999. Blobel found that proteins carry built-in signals that act like postal codes to direct proteins to their proper locations within each cell. His studies also demonstrated that special receptors on the surfaces of membranes read those signals and allow the appropriate proteins either to pass through or to lodge within the membrane.

Günter Blobel received the King Faisal International Prize in 1996, the Albert Lasker Award for Basic Medical Research in 1993, the Louisa Gross Horwitz Prize in 1989, and the Gairdner Foundation International Award in 1982. He was a member of the National Academy of Sciences, the American Philosophical Society, the Pontifical Academy of Sciences, and received the German Order of Merit.

Blobel became well known for his direct and active support of the rebuilding of Dresden in Germany, becoming in 1994 the founder and president of the non-profit "Friends of Dresden, Inc.". He donated all of his Nobel award money for the rebuilding of the Frauenkirche (completed in 2005) and the building of a new synagogue.

Günter Blobel died on February 18, 2018, at the age of 81.

Molecular Design of Nature's Largest and Most Versatile Channel Anchored in the Center of the Nuclear Pore

Julius Lukeš

*1962
Institute of Parasitology, Biology Centre, CAS, České Budějovice, Czech Republic

October 9, 2012

Julius Lukeš studied at Charles University in Prague, Czech Republic, graduating in 1986. After completing a PhD in 1991 in parasitology in the Czech Republic, Lukeš went for several postdoc stays in the Netherlands and USA, and since 1999 has established his independent laboratory at the Institute of Parasitology, Czech Academy of Sciences, of which he became director in 2012.

His lab is generally interested in protists belonging to the eukaryotic supergroup *Excavata*. While his team was until relatively recently primarily focused on parasitic kinetoplastid flagellates, the lab also became interested in ecologically relevant euglenids and a group of marine protists called diplonemids that are extremely diverse and abundant in the oceans, yet markedly understudied. The aim is a holistic understanding of this enigmatic group of marine protists, from studying their morphology and life cycles, to mapping their diversity and abundance, to turning them into model organisms, which would allow dissecting mechanistic details underlying their biology. The inquiries into these three groups are unified by consideration of their evolution and the structure and function of their single reticulated mitochondrion.

Lukeš has also retained interest in field research, each year collecting protists to culture and analyze, for example, from the *Tara* Polar Circle expedition and from Papua New Guinea, Ecuador, Madagascar, Ghana, Vietnam, Cuba, the Philippines, China etc.

Julius Lukeš has been recognized by the scientific community by a number of honours. In 2002, he received the Otto Wichterle Prize from the Czech Academy of Sciences, in 2004 he became a Member of the Learned Society of the Czech Republic, and in 2009 he became a Laureate *Praemium Academiae*.

Between 2012 and 2017 he was a Senior Fellow of the Canadian Institute for Advanced Research. He has been a Fellow of the American Academy for Microbiology since 2014, a Fellow of the European Academy of Microbiology since 2015, and a Fellow of the American Association for the Advancement of Science since 2018.

RNA Editing in Trypanosomatid Protists


ARIZONA
DESERT

Jiří Friml

*1973

VIB Ghent, Belgium

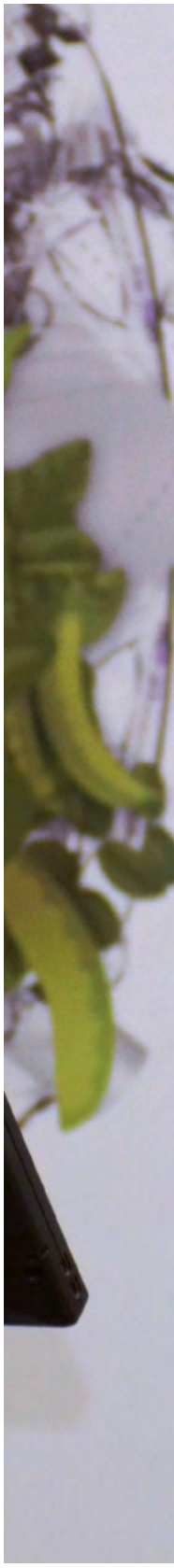
October 9, 2012

Jiří Friml was born in the Czech Republic and studied biochemistry at Masaryk University in Brno, Czech Republic. Immediately after receiving his master's degree in 1997 he obtained a fellowship at the Max Planck Institute in Cologne, Germany. He finished with a PhD degree in biology at the University of Cologne in 2000. In 2001 he moved to the Centre for Plant Molecular Biology at the University of Tübingen. There he headed a research group before gaining a further doctorate in biochemistry at Masaryk University. From 2007 to 2012 he was a professor of plant systems biology at the University of Ghent, Belgium, where he led a research group.

The research of Jiří Friml has always focused on the cellular and molecular mechanisms behind adaptive development in plants. He proposed a general model that explains how plants capture multiple internal and external signals and translate them into the extraordinary plasticity and adaptability that characterizes their development. At the centre of Friml's research work is the growth hormone auxin. Its distribution regulates what is up and what is down in a plant, how much it grows in a particular direction and where individual organs are located. These findings are seen as a milestone in gaining a greater understanding of numerous physiological processes in plants. They are also of pre-eminent importance to agronomic and medical research.

For his work, Jiří Friml has been recognized with many prestigious awards including the EMBO Young Investigator Award (2004), the Heinz Maier-Leibnitz Prize (2005), and the prestigious European Science Prize awarded by the Körber Foundation (2010). In 2015 he was selected for the list of the World's Most Influential Scientific Minds.

How Cells Make a Plant: Role for Directional Auxin Transport




It is a great honour to follow in the footsteps of Gregor Johann Mendel with my molecular genetic research. It is great to see that Mendel's tradition in Brno is revived and continued.