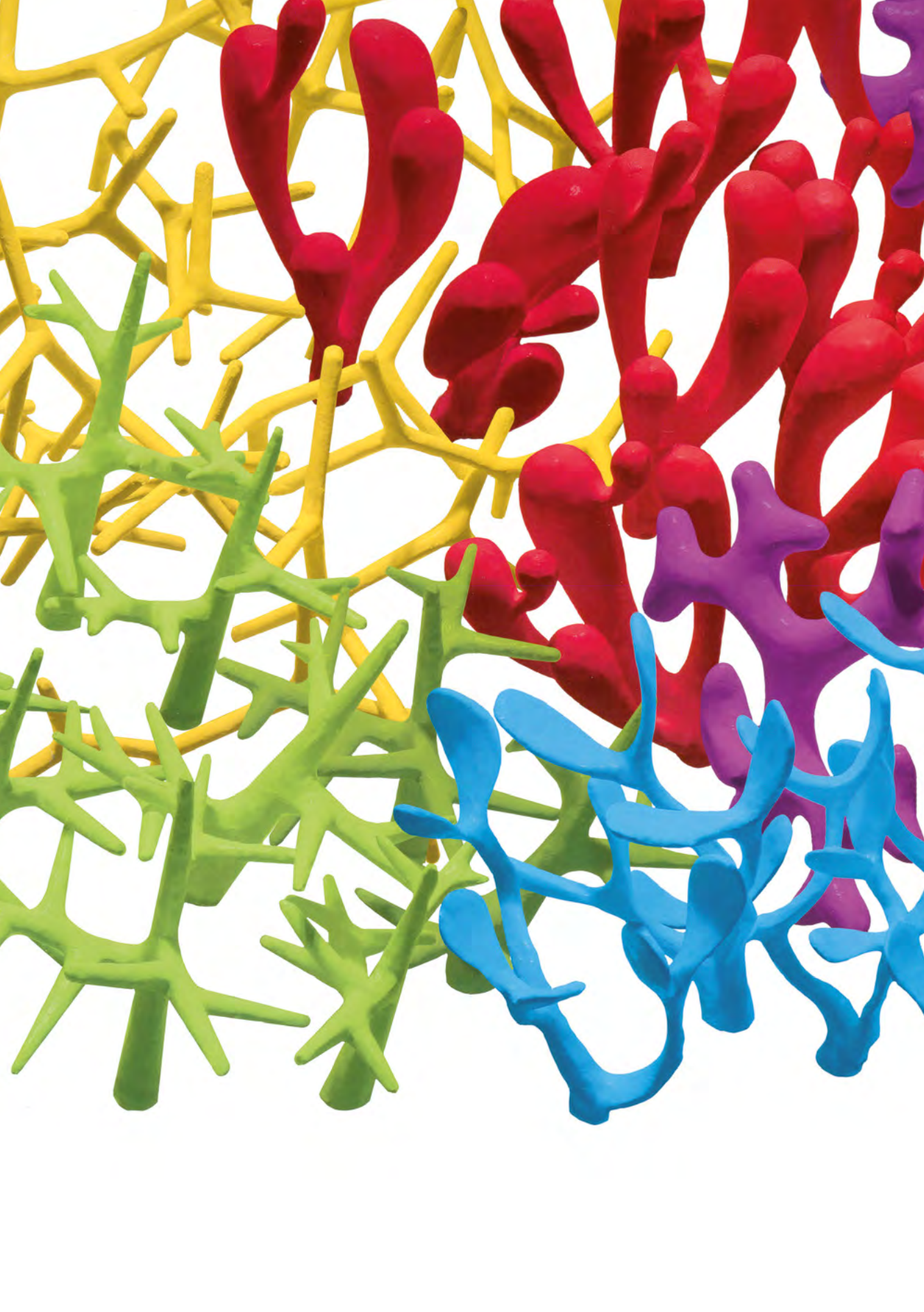
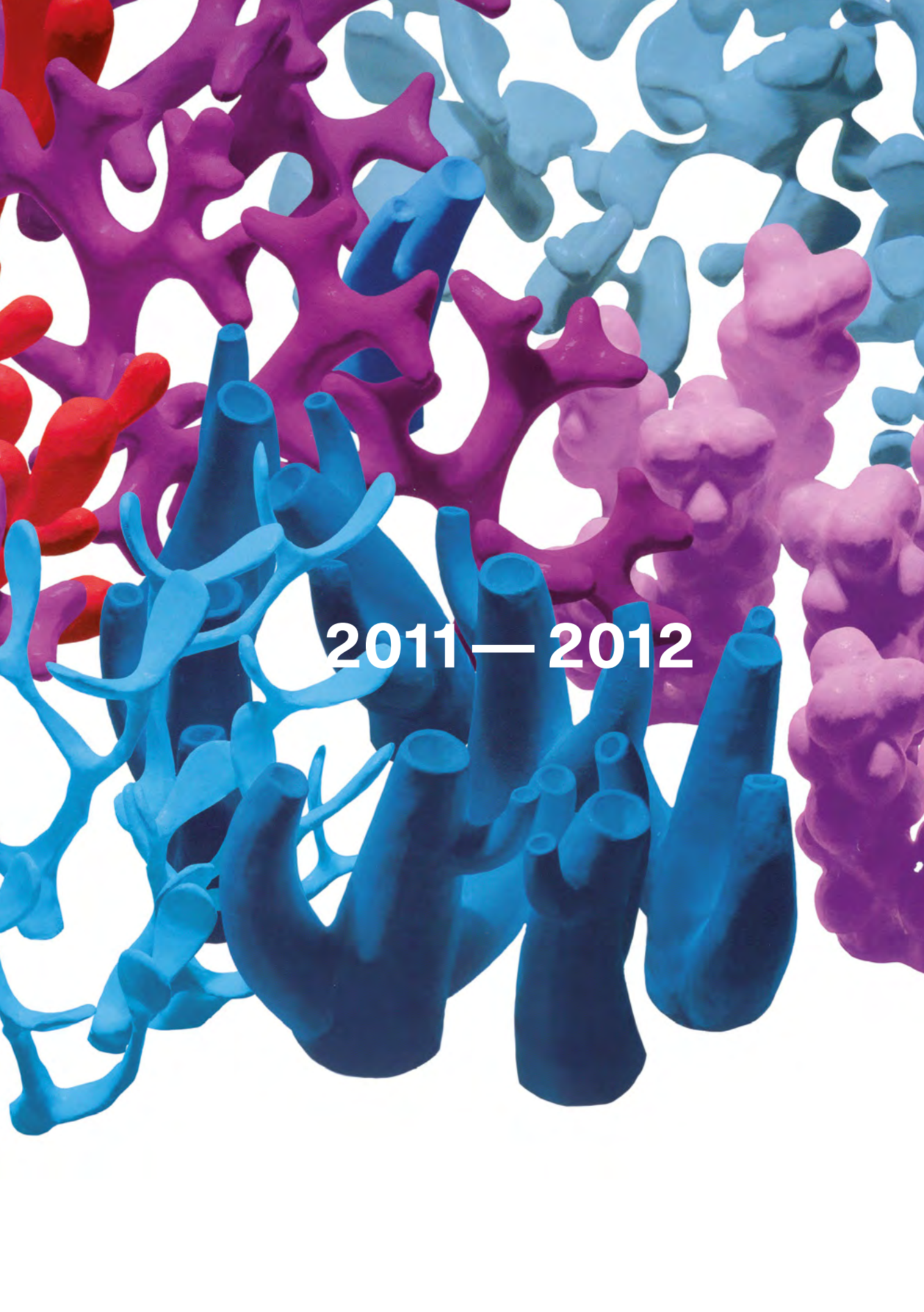
Mendel Lectures
2011—2012




2011— 2012

John Diffley

*1958

Chromosome Replication Laboratory – Clare Hall Laboratories, Cancer Research UK London Research Institute

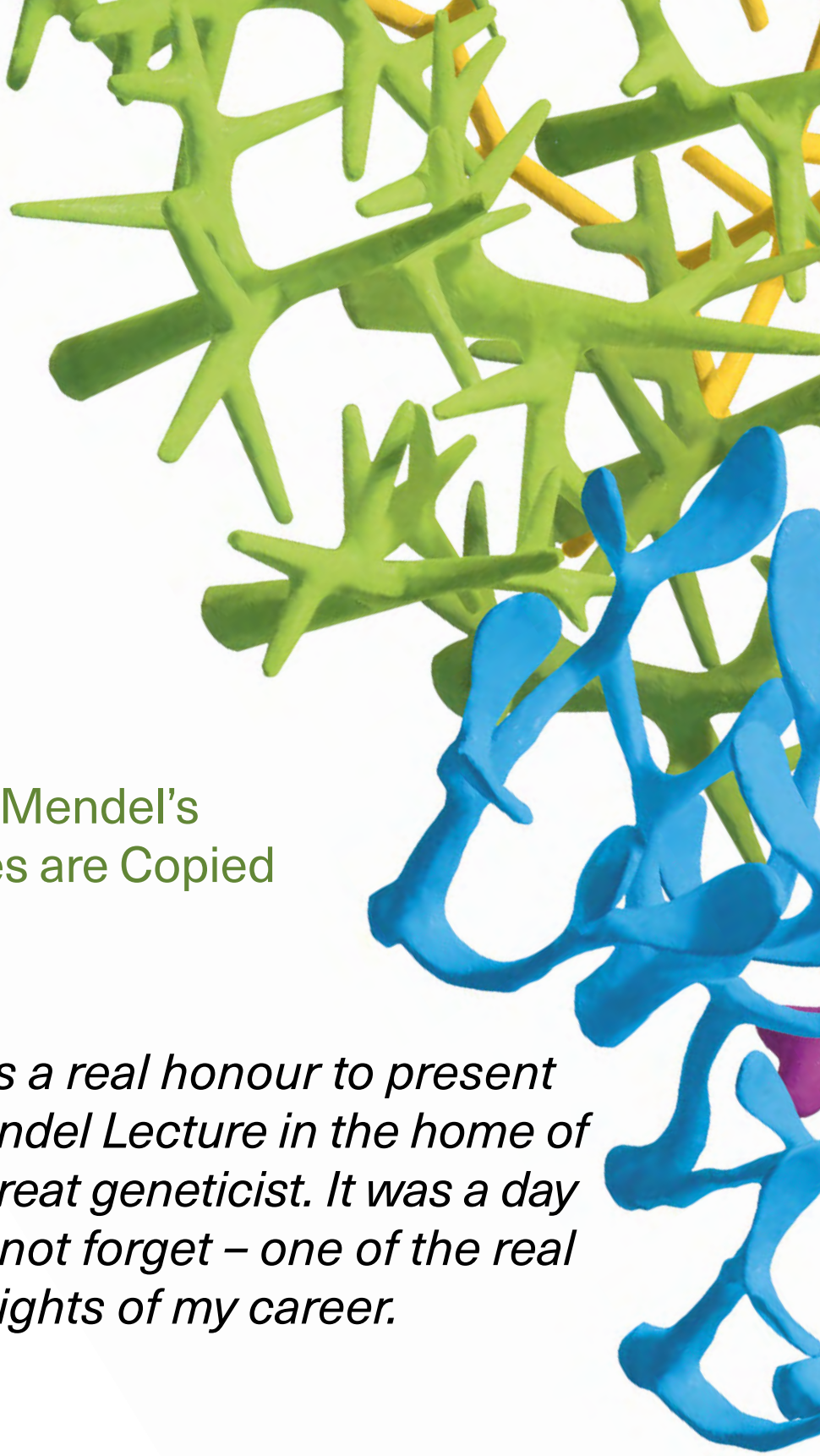
October 6, 2011

John Diffley is a molecular biologist who specializes in studying eukaryotic DNA replication.

He obtained his PhD from New York University, USA, in 1985 and was a post-doctoral fellow at Cold Spring Harbor Laboratory, USA, until 1990. After that he established a lab at the Imperial Cancer Research Fund, UK (which in 2002 was renamed Cancer Research UK). Since 2006 he has been the director of Clare Hall Laboratories and the deputy director of the Cancer Research UK London Research Institute. Since 2015 he has been Associate Research Director at the Francis Crick Institute.

Diffley's work studies the molecular machinery that copies DNA and ensures that each daughter cell receives a complete set of genetic instructions, and how the process is affected when DNA is damaged. Diffley discovered and characterized how DNA replication origins are regulated to ensure once per cell cycle replication. His group recently described the reconstitution of the initiation of eukaryotic DNA replication with purified proteins. They also showed how chromatinized templates are replicated, how nucleosomes displaced during replication are re-deposited on nascent DNA, and how chromatin influences DNA replication origin choice and lagging strand synthesis. He has also shown that DNA damage checkpoints regulate DNA replication on damaged DNA by inhibiting origin firing and that loss of this checkpoint or misregulation of normal cell cycle control can cause genome instability by interfering with normal DNA replication, with important implications in cancer biology.

Diffley was elected as a member of the European Molecular Biology Organization (EMBO) in 1998, awarded the Paul Marks Prize for Cancer Research in 2003, elected a Fellow of the Royal Society in 2005, and elected a Fellow of the American Association for the Advancement of Science (AAAS) in 2007. He was awarded the 2016 Louis-Jeantet Prize for Medicine for his contributions to understanding "how DNA replication, a process essential to life, initiates", and the 2016 Canada Gairdner International Award for his "pioneering research on the eukaryotic DNA replication cycles including initiation, regulation and responses to DNA damage".



How Mendel's Genes are Copied

It was a real honour to present a Mendel Lecture in the home of the great geneticist. It was a day I will not forget – one of the real highlights of my career.

Timothy John Mitchison

*1958

Department of Systems Biology, Harvard Medical School, Boston, USA

October 13, 2011

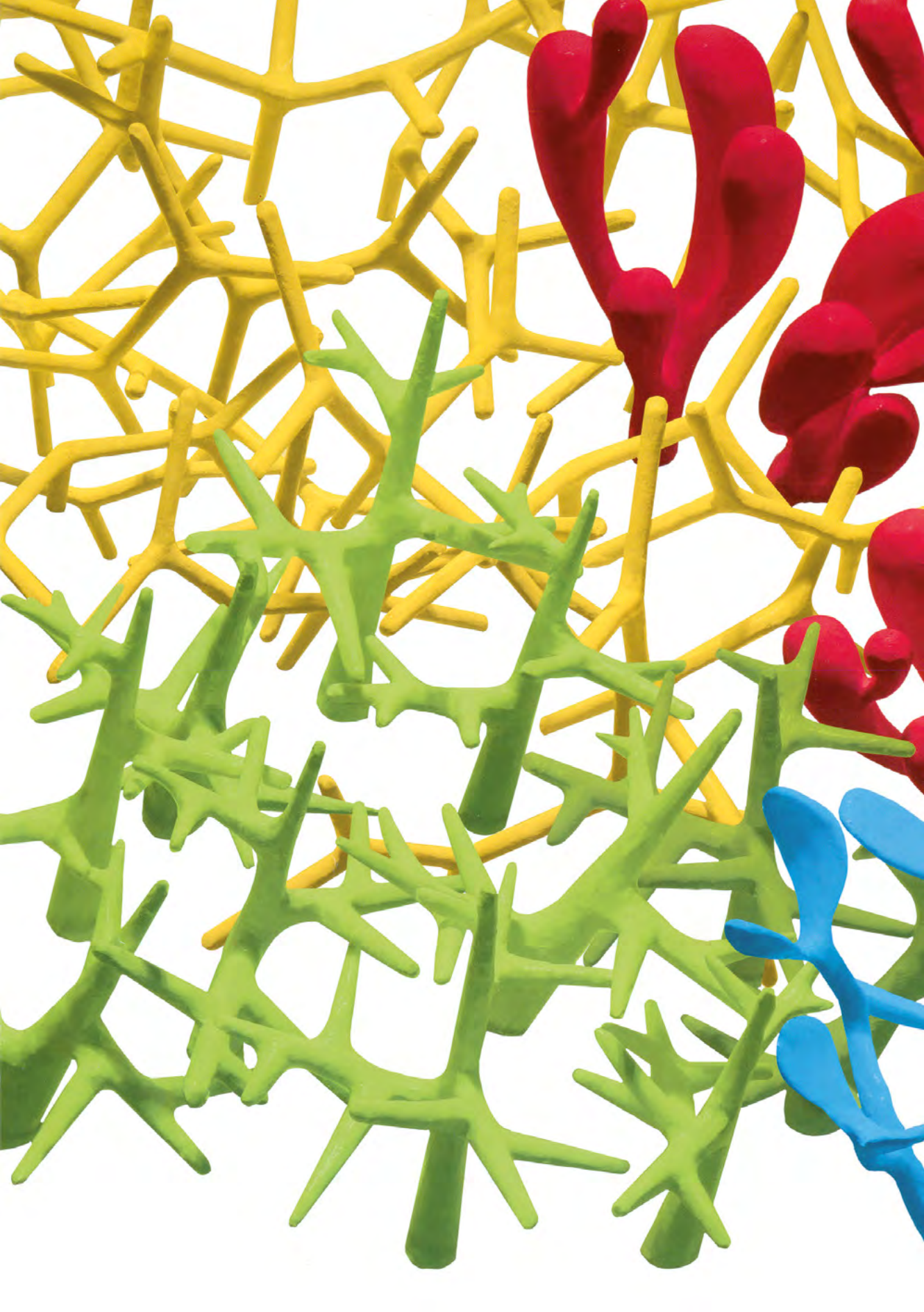
Timothy John "Tim" Mitchison is a British cell biologist and systems biologist interested in the structure, dynamics, and function of the cytoskeleton.

After completing his undergraduate degree at Merton College, Oxford, he moved to the University of California, San Francisco in the United States in 1979, to work on his PhD. He returned to the UK for postdoctoral research at the National Institute for Medical Research (NIMR) in London. In the late 1980s he returned to San Francisco to become an assistant professor at UCSF. In the late 1990s he become co-director of the Institute for Chemistry and Cell Biology at Harvard Medical School. In 2004 he was a founding faculty member of the new Department of Systems Biology at HMS, where he continues to work on cell division mechanisms and the pharmacology of anti-cancer drugs.

Mitchison was elected Fellow of the Royal Society in 1997 and was president of the American Society for Cell Biology. He delivered the Keith R. Porter Lecture in 2013 and was elected a member of the National Academy of Sciences of the United States in 2014.

Mitchison's lab uses imaging-based assays in living cells and *in vitro* extracts, in conjunction with molecular biology and biochemical fractionation approaches, as well as theory and modelling to study the function of the cytoskeleton. Together with Marc Kirschner, he discovered dynamic instability in microtubules and is studying the cell division mechanism. The lab is increasingly interested in cancer chemotherapy directed at the mitotic spindle to understand how current chemotherapy works, and how it can be improved. Current foci include understanding monopolar cytokinesis, and the mechanism by which actin filaments turn over rapidly in the cytoplasm.

How Does a Large Cell Find its Center?



Jürgen Knoblich

*1963

Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Austria

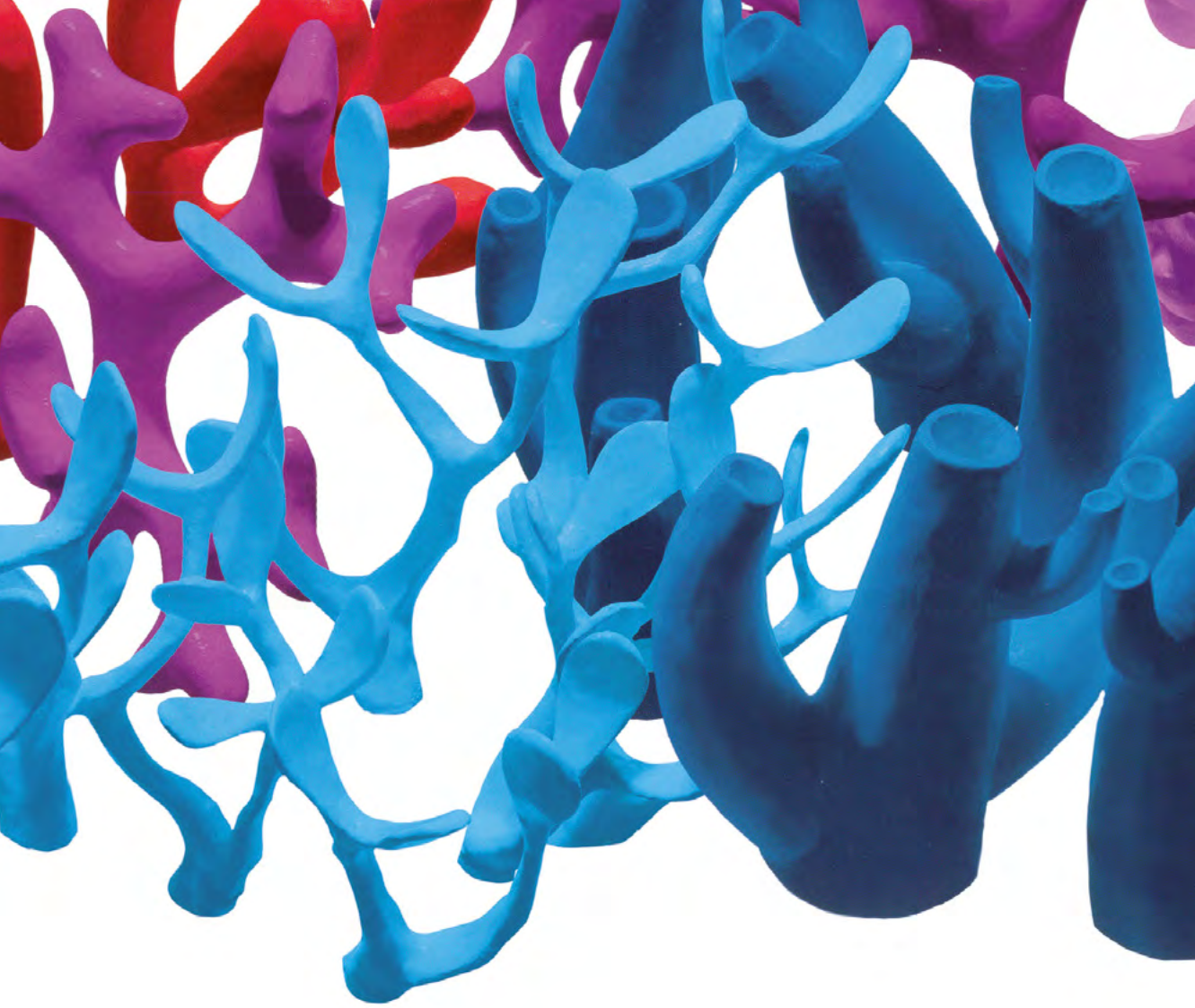
November 10, 2011

Jürgen Knoblich started his scientific career as a graduate student at the Max Planck Institute in Tübingen where he worked on cell cycle control in *Drosophila*. In 1994 he became a postdoctoral fellow at the University of California, San Francisco, where he discovered his interest in asymmetric cell division, a topic that has remained the main focus of his research ever since. In 1997, Jürgen Knoblich returned to Europe to become a group leader at the Institute of Molecular Pathology (IMP) in Vienna, Austria. In 2004, he moved to the newly founded Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA). He became a senior scientist and was appointed deputy director of the institute in 2005 and director in 2018.

Knoblich's research focuses on brain development and cell division. Initially, he characterized a complete mechanism for the asymmetric stem cell division in *Drosophila* neural stem cells. His group was also the first to carry out a genome-wide *in vivo* RNAi screen demonstrating the ability to simultaneously analyze gene functions across the whole genome in a tissue's specific manner. Recent findings suggest that tumours can be based on stem cells that keep their unique stem cell characteristics and thus divide uncontrollably, without ever differentiating into specific somatic cell types. In 2013, Knoblich's lab developed an *in vitro* culture system called Cerebral Organoids that recapitulates the development of a human brain at a remarkable level of detail. Their models made possible the investigation of the migration of neurons and neuronal activities. By fusing two separate organoids, it became possible to study interactions between distinct brain areas. They have also successfully modelled patient-specific disease phenotypes and used them to describe disease mechanisms.

Jürgen Knoblich holds the professorship in Synthetic Biology at the Medical University of Vienna. He received the EMBO young investigator award in 2001, the ELSO early career award in 2003, the Wittgenstein Prize in 2009, the 2012 Erwin Schrödinger-Preis, and the 2015 Sir Hans Krebs Medal of the Federation of European Biochemical Societies (FEBS). He is also a member of the Academia Europaea and of the Pontifical Academy of Sciences.

Proliferation Control and Tumorigenesis in Stem Cell Lineages of the Nervous System: Lessons from *Drosophila* and Mouse Genetics



Gregor Mendel, a great mind, far ahead of his time would be delighted to see, that still, after 200 years, the world's leading scientists assemble every year to hold a lecture in his name. I am very honoured to be part of this scientific legacy.

Angelika Amon

*1967

Massachusetts Institute of Technology (MIT), Cambridge, USA

March 8, 2012

Angelika Amon was an Austrian-American molecular and cell biologist focusing on cell growth, division and chromosome imbalance.

She received her BS from the University of Vienna and continued her doctoral work there at the Research Institute of Molecular Pathology, receiving her PhD in 1993. She completed a two-year postdoctoral fellowship at the Whitehead Institute in Cambridge, Massachusetts, and was subsequently named a Whitehead Fellow for three years. She joined the MIT Center for Cancer Research and MIT's Department of Biology in 1999 and was promoted to full professor in 2007.

In the earliest stages of her career, Amon made profound contributions to deciphering the regulatory networks governing cell division and proliferation in various model organisms and shedding light on how chromosome segregation is regulated. More recently she studied the consequences of chromosome mis-segregation on cell and organismal physiology, and how these repercussions can lead to human disease. She found that aneuploidy can interfere with a cell's normal DNA repair mechanism, allowing genetic mutations to quickly accumulate in tumour cells. Amon's work also led to understanding how aneuploidy results in some of the health problems associated specifically with Down syndrome.

Her pathbreaking research was recognized by several awards and honours, including the 1998 Presidential Early Career Award for Scientists and Engineers, the 2003 National Science Foundation Alan T. Waterman Award, the 2007 Paul Marks Prize for Cancer Research, the 2008 National Academy of Sciences (NAS) Award in Molecular Biology, the 2013 Ernst Jung Prize for Medicine, the 2019 Breakthrough Prize in Life Sciences, the Vilcek Prize in Biomedical Science, and the 2020 Human Frontier Science Program Nakasone Award. She was also named to the Carnegie Corporation of New York's annual list of Great Immigrants, Great Americans and was elected a member of the National Academy of Sciences and the American Academy of Arts and Sciences.

Angelika Amon, professor of biology and a member of the Koch Institute for Integrative Cancer Research, died on 29 October 2020 at age 53, following a two-and-a-half-year battle with ovarian cancer.

Causes and Consequences of Aneuploidy


ΑΠΟ

Anthony A. Hyman

*1962

Cell Biology/Microtubules and Cell Division, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

March 22, 2012

Anthony Hyman studied zoology at University College in London, was awarded a PhD in 1987 at King's College (Cambridge) and completed his postdoctoral studies at the University of California in San Francisco. He subsequently became a group leader at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. In 1999 he become one of the four founding directors of the Max Planck Institute of Molecular Cell Biology and Genetics (MPI–CBG) in Dresden, where he was managing director from 2010–2013.

Located at the interface between cell biology and developmental biology, his research has focused primarily on the organization of cellular biochemistry. Hyman is known for his studies on the role of so-called microtubules in cell division. Functioning as dynamic "molecular machines", these cytoskeletal components organize the distribution of a cell's components to its daughter cells. Hyman has developed a range of innovative physical and genomic methods for studying the microtubular cytoskeleton, including laser microsurgery techniques. Using video microscopy and high-throughput processes, he has successfully identified hundreds of genes which cause cell division defects.

More recently he has been studying the mechanisms by which cells compartmentalize their biochemistry by phase separation. Aberrant phase transitions within liquid-like compartments may underlie amyotropic lateral sclerosis and other neurodegenerative and age-related diseases. His current work focuses on the physical-chemical basis by which intrinsically disordered proteins phase separate. Using this knowledge, he is studying the roles of phase separation in physiology and disease.

Widely regarded as one of the world's leading cell biologists, Professor Hyman was elected a member in 2000 of the European Molecular Biology Organization (EMBO) and was awarded its Gold Medal in 2003. He was elected a fellow of the Royal Society (FRS) in 2007. In 2011, Hyman was awarded the Gottfried Wilhelm Leibniz Prize, Germany's most prestigious research award, for his work on microtubules and cells. In 2020 he was awarded the Wiley Prize in Biomedical Sciences for his work on biomolecular condensates, and was also given the NOMIS Distinguished Scientist Award by the NOMIS Foundation. In the same year Hyman was elected as an international member of the US National Academy of Sciences. In 2021 he received the Nakasone Prize from the HFSP.

Cytoplasmic Organization through Phase Transitions

Roland Kanaar

*1961

Department of Molecular Genetics, Oncode Institute, Erasmus University Medical Center, Rotterdam, Netherlands

April 19, 2012

Roland Kanaar is a Dutch biochemist and molecular biologist.

Kanaar studied chemistry (BSc) and biochemistry (MSc) at Leiden University. He obtained his PhD degree in molecular biology in 1988 for research on the action of an enhancer in site-specific DNA recombination and the elucidation of how nucleoprotein complexes assembled at distant sites along a DNA chain communicate with each other to provide selectivity during recombination. His postdoctoral work at the University of California, Berkeley, aimed at understanding mechanisms of homologous recombination and how proteins and RNA interact to achieve accurate but flexible recognition of splice sites. He returned to the Netherlands in 1995 and started working in the Department of Genetics at Erasmus University in Rotterdam. In 2015 Kanaar became the Director of the Joint Erasmus MC/TU Delft, master's degree programme in nanobiology. In 2016, Kanaar was appointed Head of the Department of Molecular Genetics, and in 2020 Chair of the Theme of Biomedical Sciences at Erasmus University Medical Center.

His research focuses on the molecular mechanisms and physiological relevance of homologous DNA recombination and DNA break metabolism. Work in his team spans the experimental range from single-molecule biophysics to mouse genetics. His research has revealed that homologous recombination plays an important role in repairing radiation-induced DNA breaks in mammals, and his team's discovery of the pathway responsible for random integration of exogeneous DNA in the genome has had important implications for gene targeting efficiency in mammalian cells. His team is developing functional *ex vivo* tests on patient tumour material to guide precision therapy and design novel precision cancer treatments.

Professor Kanaar was elected a member of the European Molecular Biology Organization in 2002 and in 2013 to the Royal Netherlands Academy of Arts and Sciences (KNAW).

How DNA Recombination Maintains Genome Integrity

Óscar Fernández-Capetillo

*1974

Genomic Instability Group, Spanish National Cancer Research Centre (CNIO), Madrid, Spain and the Karolinska Institute, Stockholm, Sweden

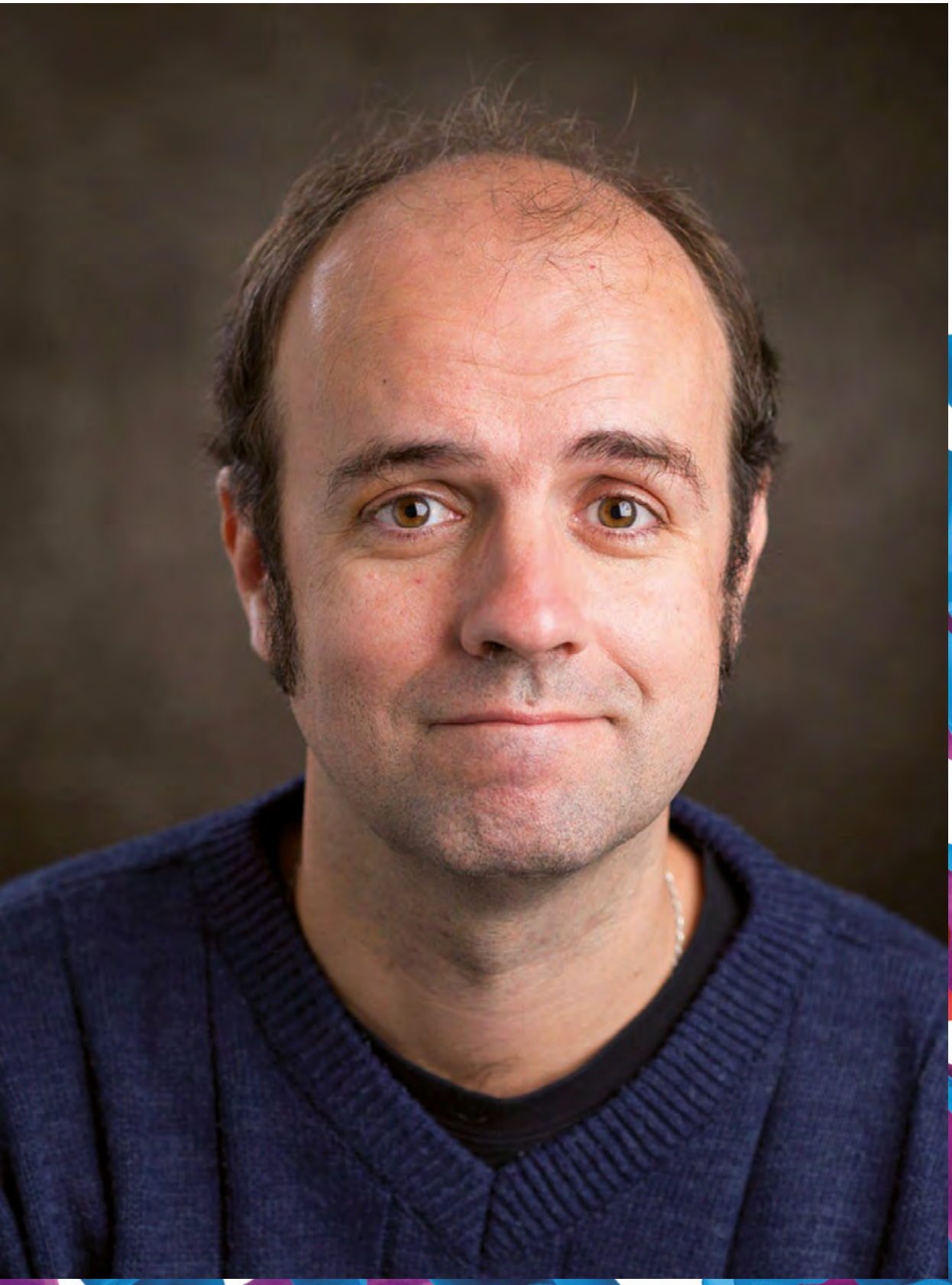
May 16, 2012

Óscar Fernández-Capetillo is a Spanish biochemist. He obtained his PhD in 2001 from the Universidad del País Vasco working on the role of E2F transcription factors on the immune system. He then joined the laboratory of A. Nussenzweig at the National Cancer Institute, USA, where he started to work on the cellular response to DNA damage, focusing particularly on the role of the histone variant H2AX and other chromatin-related aspects. After that he joined the CNIO to lead the Genomic Instability Group with a particular focus on developing cellular and animal tools to investigate the role of the ATR/Chk1 signalling cascade in protection against cancer and ageing. He is currently the Deputy Director at CNIO as well as Director of its Molecular Oncology Program. Since 2015 he has also been a professor of "Cancer Therapy" at the Karolinska Institute in Stockholm, Sweden.

The laboratory at CNIO combines mouse models, molecular and cellular biology, and genetic screens, while the laboratory at Karolinska has specialized in cell-based phenotypic chemical screens. While the initial focus of Fernandez-Capetillo was on ATR signalling, today his interests are spread across many independent topics which include mechanisms of DNA replication and repair, ageing, neurodegeneration, and academic drug development.

His work has been recognized through several national and international awards and honours including the Swiss Bridge Award (2005), selection as an EMBO Young Investigator (2008) and Member (2016), the Eppendorf Award for Young Investigators (2009), the International Early Career Scientist, from the Howard Hughes Medical Institute of the USA (2011), and being named by CELL in their "40-under-40" list of the 40 most influential scientists under 40 years of age (2014).

Exploring the Role of Replicative Stress in Cancer and Ageing



Doug Koshland

*1953
Department of Molecular and Cell Biology, University of California, Berkeley, USA

May 24, 2012

Douglas E. Koshland earned his BA degree in chemistry from Haverford College and his PhD degree in microbiology at the Massachusetts Institute of Technology, where he studied the secretion of beta-lactamase in *Salmonella typhimurium*. His postdoctoral work at the University of Washington, Seattle, studied yeast chromosome segregation, and at the University of California, San Francisco, focused on vertebrate kinetochore function. Douglas Koshland was a staff scientist and then senior staff scientist at the Carnegie Institution for Science's Department of Embryology from 1987 to 2010. During that time, he was also an adjunct professor in the Department of Biology at the Johns Hopkins University, and a Howard Hughes Medical Institute Investigator from 1997 to 2012. In 2010, Koshland was named Professor of Molecular and Cell Biology at the University of California, Berkeley. Recently he was appointed Richard and Rhoda Goldman Distinguished Chair in the Biological Sciences at the University of California, Berkeley.

Dr. Koshland's laboratory uses genetic, cell biological and biochemical approaches in budding yeast to understand cell division, higher-order chromosome structure, genome integrity and evolution, and stress biology. He was the first to identify cohesins, made a major contribution to the understanding of cohesins and condensins, and employed minichromosomes to illuminate universal chromosome transitions and the specific protein involved.

Doug Koshland was inducted into the National Academy of Science in 2010, and was also elected to the American Academy of Arts and Sciences.

Preventing Chromosomes from Going Rogue