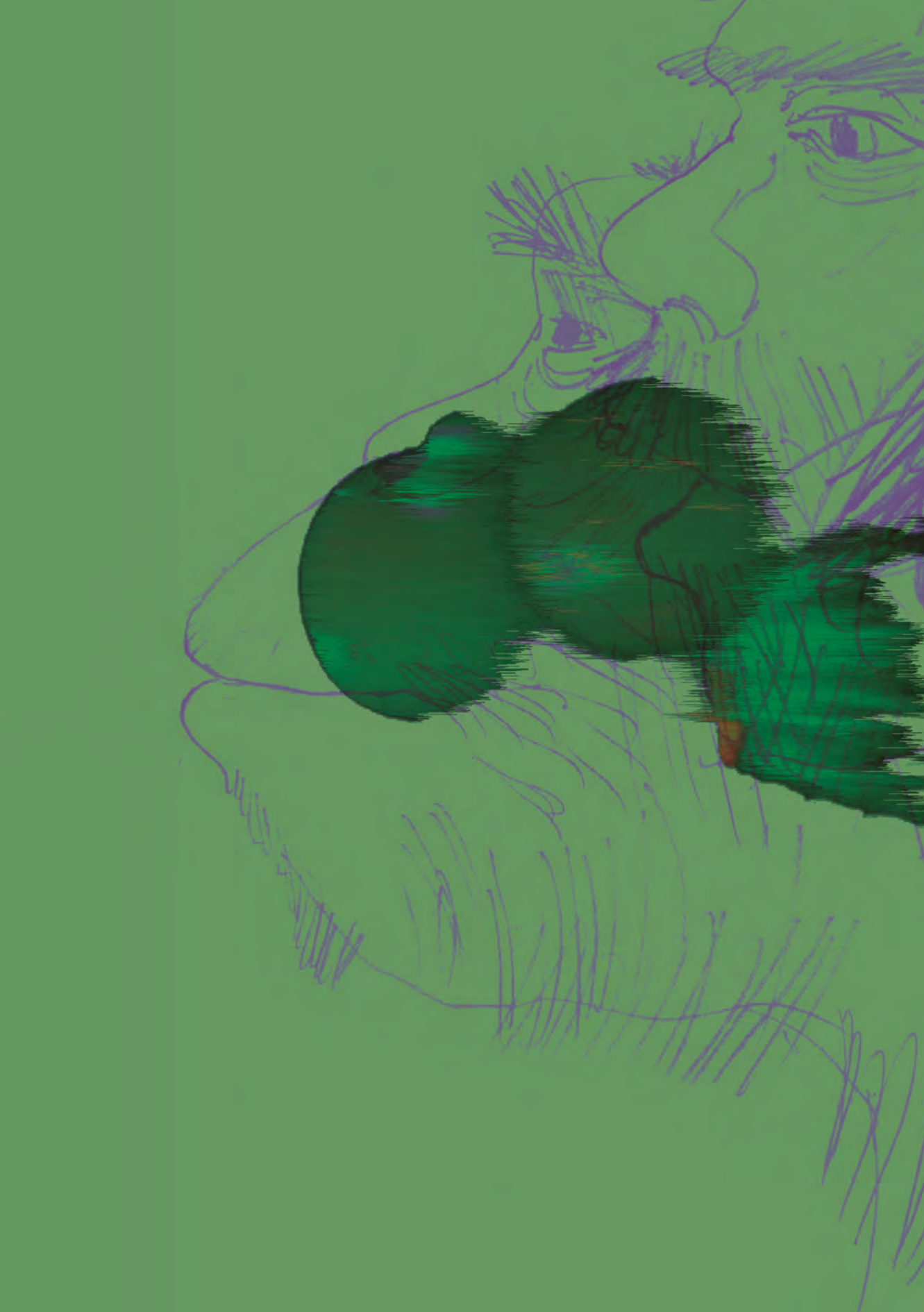
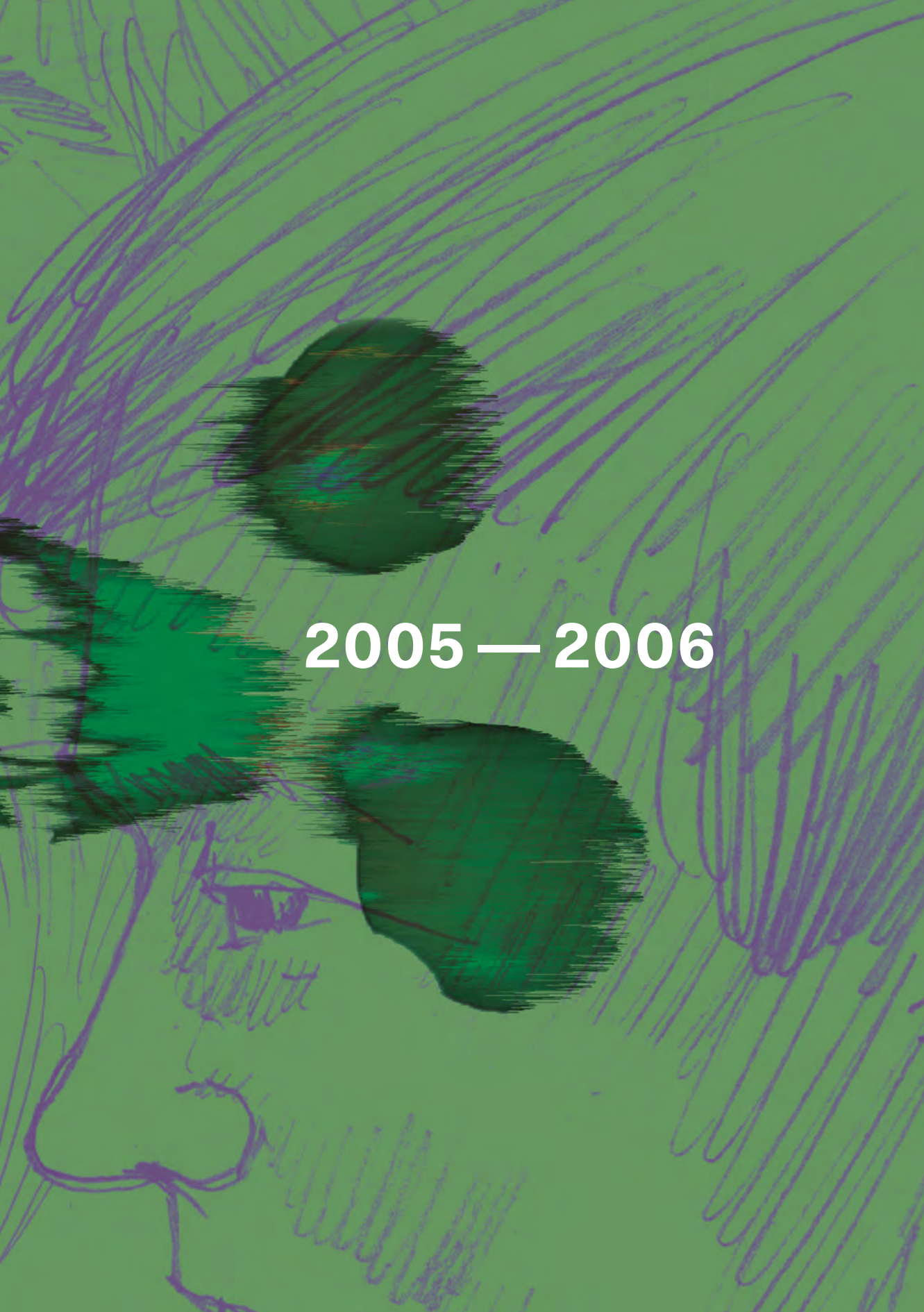
Mendel Lectures
2005—2006




2005 — 2006

Steven McKnight

*1949

University of Texas, Southwestern Medical Center, Dallas, USA

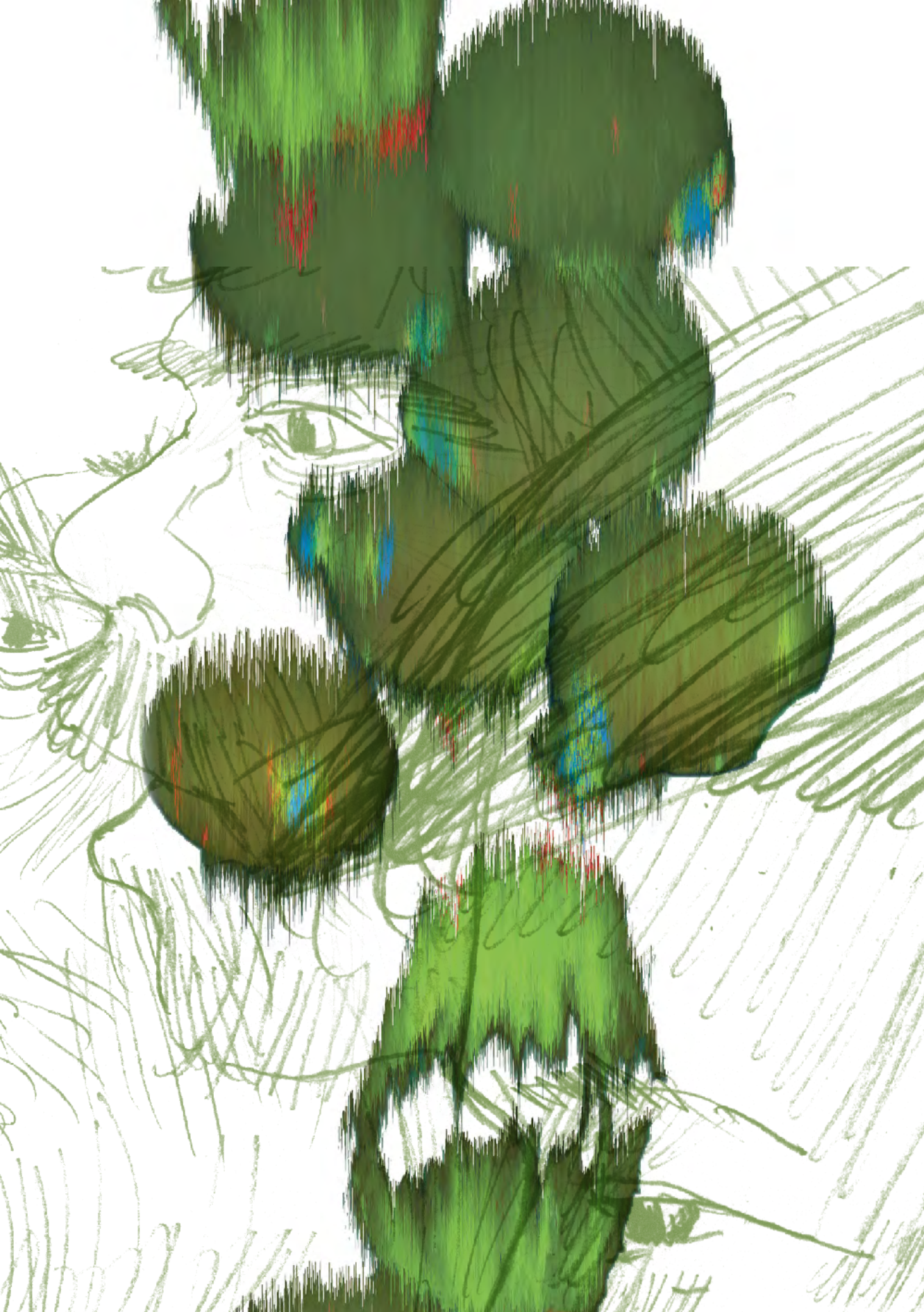
October 3, 2005

Steve McKnight received his bachelor's degree in biology from the University of Texas in 1974 and his PhD degree in biology from the University of Virginia in 1977. He conducted postdoctoral research at the Carnegie Institution of Washington under the mentorship of Donald Brown and was appointed as a staff member at that institution in 1983. He was appointed as a Howard Hughes Medical Institute investigator in 1988. His research focus at the Carnegie Institution was on gene regulation. He used molecular biological methods to define the regulatory DNA sequences constituting the promoter of the herpes simplex virus thymidine kinase gene, and then employed biochemical methods to purify gene-specific transcription factors, including members of the C/EBP and GABP families of transcription factors.

In 1991 Dr. McKnight left academia to co-found Tularik, a San Francisco-based biotechnology company devoted to the discovery of ethical drugs acting to treat disease via the regulation of gene expression. In 1995 Dr. McKnight moved from Tularik to UT Southwestern and in 1996 he was appointed chairman of the Department of Biochemistry. At UT Southwestern Dr. McKnight has directed an active research laboratory and has guided the Department of Biochemistry to substantial growth in the disciplines of chemistry, biochemistry and biophysics. Dr. McKnight is a member of the National Academy of Sciences, the Institute of Medicine and the American Academy of Arts and Sciences.

McKnight's awards and honours include: the Eli Lilly and Company-Elanco Research Award, the Award in Molecular Biology of the National Academy of Sciences, Member of the National Academy of Sciences, Member of the American Academy of Arts and Sciences, the National Institutes of Health Director's Pioneer Award, Fellow of the American Association for the Advancement of Science, and the Wiley Prize.

Schizophrenia, Stem Cells and Sprouty Signalling



Kim Ashley Nasmyth

*1952

Institute of Molecular Pathology (IMP), Vienna, Austria

November 10, 2005

Professor Kim Nasmyth is an English geneticist best known for his work on the segregation of chromosomes during cell division. He attended Eton College and then the University of York where he studied biology and graduated in 1974. For his PhD research, he joined the lab of Murdoch Mitchison at the University of Edinburgh and focused on cell cycle regulation in yeast – a topic that would remain at the centre of his scientific interest.

After a postdoctoral fellowship at the University of Washington in Seattle and at Cold Spring Harbor Laboratory in New York, Kim Nasmyth became a staff member at the MRC Laboratory of Molecular Biology in Cambridge. Here he studied yeast mating type genes and demonstrated that gene expression can be regulated through specific control elements distant from the start of transcription. He also identified cell-cycle specific transcription factors.

In 1987, Max Birnstiel recruited Kim Nasmyth to the newly founded Research Institute of Molecular Pathology in Vienna. Among the most important scientific achievements of his team was the discovery of the cohesin complex that holds sister chromatids together until they separate during anaphase. They also discovered separase, the protease that triggers loss of cohesion at the metaphase to anaphase transition. Cohesin and separase are essential for the correct distribution of the genetic material to daughter cells.

In 1997, Kim Nasmyth succeeded Max Birnstiel as director of the IMP and relocated to the University of Oxford in 2006 to take over the Whitley Chair of Biochemistry. He served as head of the Department of Biochemistry in Oxford for five years and was a Professorial Fellow in Biochemistry at Trinity College. Nasmyth continues to head a research group at the Department of Biochemistry in Oxford.

His work has been recognized by several awards, including the Louis Jeantet Prize (1997), the Austrian Wittgenstein Prize (1999), the Croonian Lecture of the Royal Society (2002), the Boveri Award (2003) for Molecular Cancer Genetics, the Gairdner Foundation Prize (2007), the Golden Medal of the Faculty of Natural Sciences of Charles University in Prague, the Breakthrough Prize (2018), and the Biochemistry Society Centenary Award (2021). He is a fellow of the Royal Society, a member of the Austrian Academy of Sciences, and a foreign honorary member of the American Academy of Arts and Sciences.

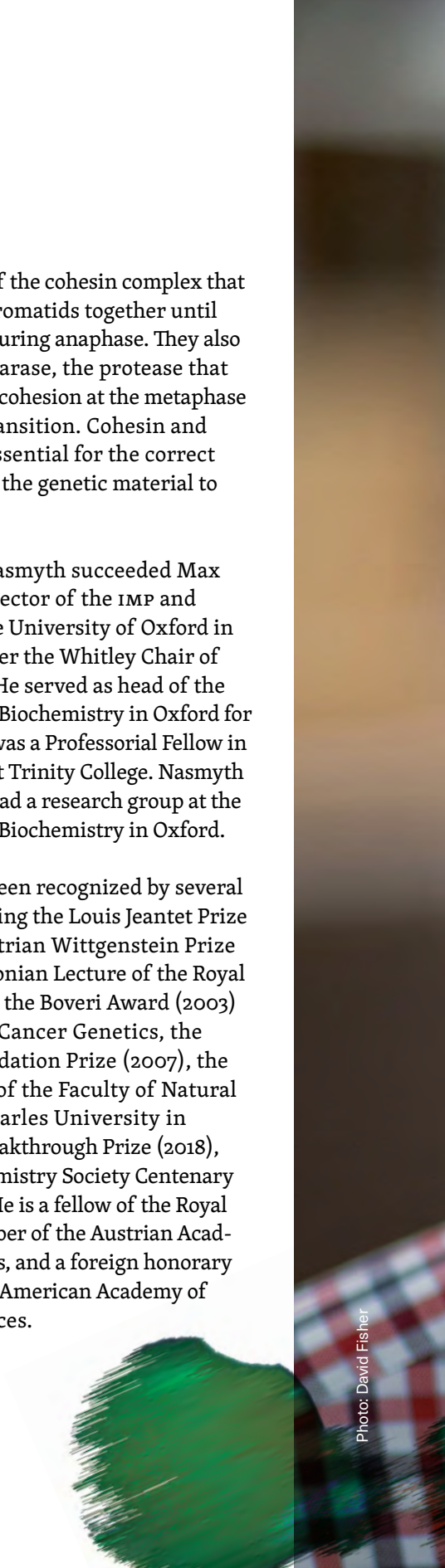


Photo: David Fisher

Molecules Behind Mendel's Laws of Heredity:

How Cohesin Holds Sister DNAs Together During Mitosis and Meiosis

Richard Henderson

*1945

MRC Laboratory of Molecular Biology, Cambridge, UK

March 30, 2006

Richard Henderson is a Scottish molecular biologist and biophysicist and pioneer in the field of electron microscopy of biological molecules.

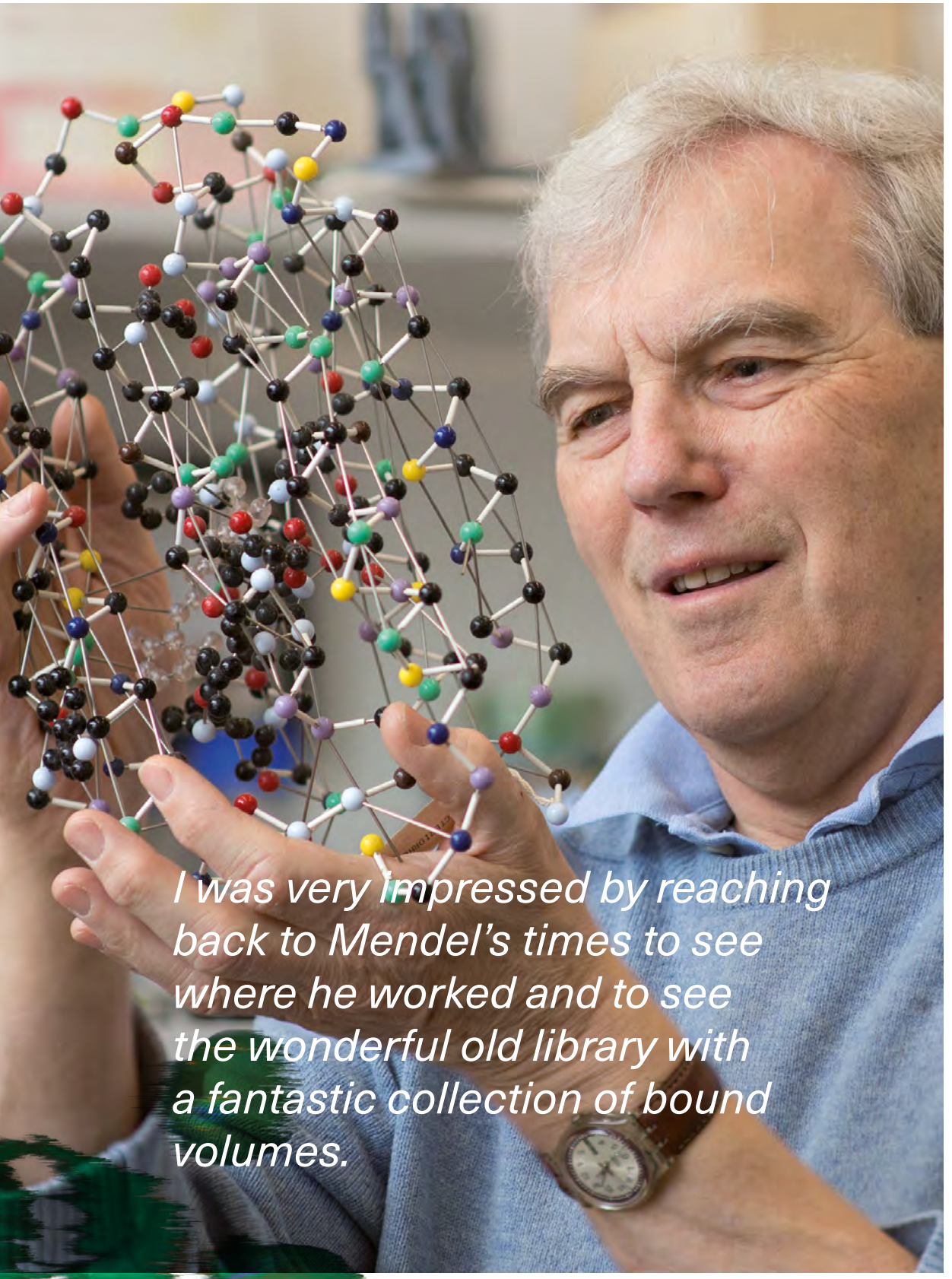
Henderson studied physics at the University of Edinburgh and received his doctorate at the University of Cambridge in 1969. His interest in membrane proteins led to his work on voltage-gated sodium channels as a postdoctoral researcher at Yale University. Returning to the MRC Laboratory of Molecular Biology in Cambridge in 1973, Henderson worked with Nigel Unwin to study the structure of the membrane protein bacteriorhodopsin by electron microscopy. In 1990 Henderson published an atomic model of bacteriorhodopsin by electron crystallography. This model was the second-ever atomic model of a membrane protein. Henderson has worked at the Medical Research Council Laboratory of Molecular Biology in Cambridge since 1973, and was its director between 1996 and 2006. The techniques Henderson developed for electron crystallography are still in use.

Together with Chris Tate, he developed conformational thermostabilization: a method that allows any protein to be made more stable while still holding a chosen conformation of interest. This method has been critical in crystallizing and determining the structures of several G protein-coupled receptors (GPCRs). Henderson and Tate founded the MRC start-up company Heptares Therapeutics (now Sosei-Heptares), which continues to develop new drugs targeting medically important GPCRs linked to a wide range of human diseases.

For his seminal contributions to many aspects of electron microscopy of biomolecules, he was honoured with a number of awards and fellowships, including as a Fellow of the Royal Society, a Foreign Associate of the US National Academy of Sciences, the William Bate Hardy Prize in 1978, the Sir Hans Krebs Medal by the Federation of European Biochemical Societies in 1984, and the Louis-Jeantet Prize for Medicine in 1993.

In 2016 Henderson was awarded the Copley Medal of the Royal Society, and the Nobel Prize in Chemistry in 2017 together with Jacques Dubochet and Joachim Frank for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution. In 2018 he was appointed Member of the Order of the Companions of Honour (CH) in the Queen's Birthday Honours and in the same year he was awarded the Royal Medal of the Royal Society of Edinburgh.

High Resolution Electron Miscroscopy in Biological Structure Determination


I was very impressed by reaching back to Mendel's times to see where he worked and to see the wonderful old library with a fantastic collection of bound volumes.

Jiří Bártek

*1953

Institute of Tumour Biology, Danish Cancer Society, Copenhagen, Denmark

April 6, 2006

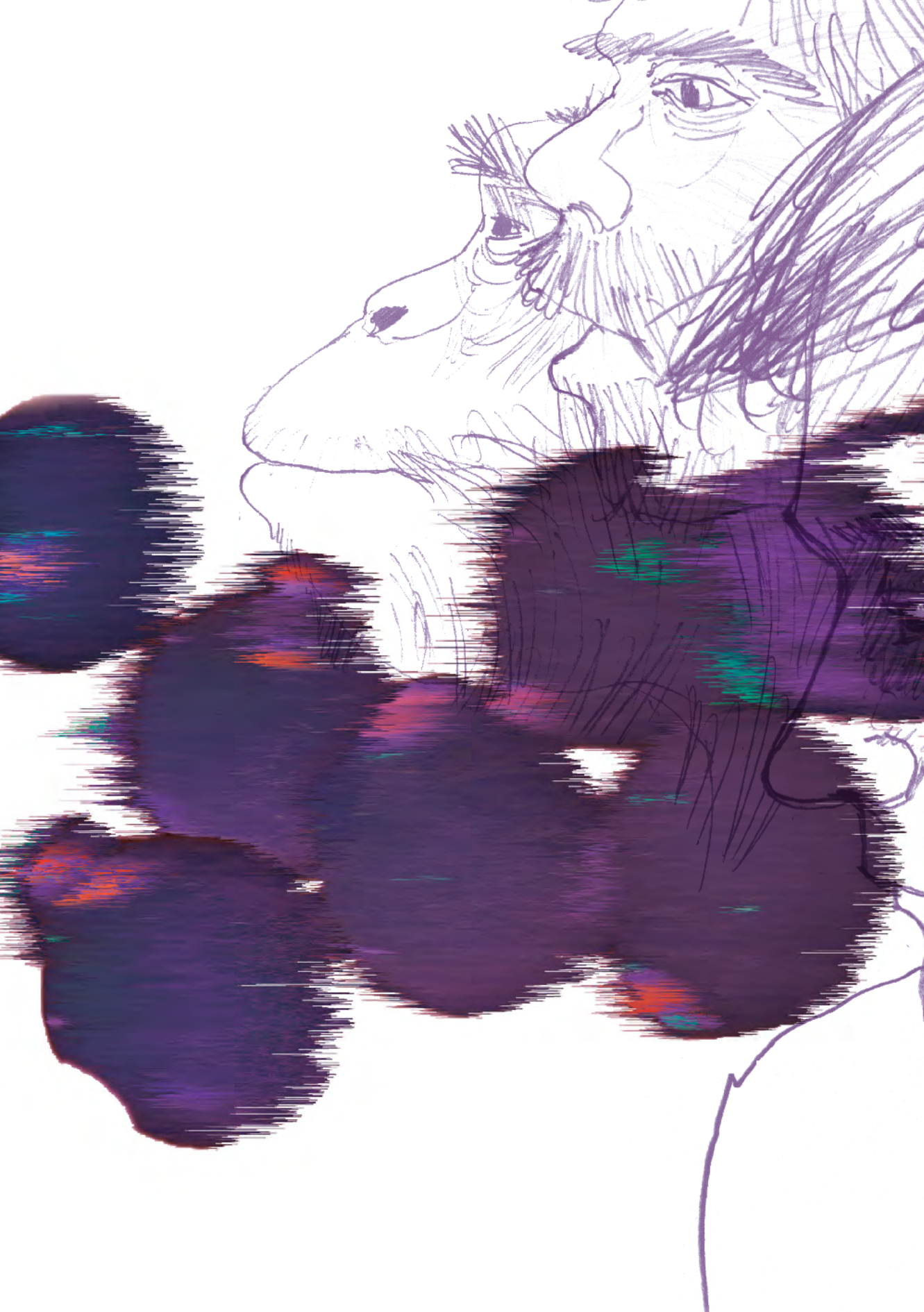
Jiří Bártek is Czech-born scientist, the head of the Genome Integrity Unit at the Danish Cancer Society Research Center in Copenhagen, Denmark. His work focuses on molecular mechanisms of cell cycle control and genome integrity maintenance, and aberrations of these pathways in human disease, particularly cancer.

Bártek and colleagues discovered several cell cycle checkpoints ensuring that our cells sense and respond to various stressors that damage DNA and studied differences in these processes between normal and cancer cells. He also pioneered the thesis that cancer cells may depend on some mechanisms that represent as cancer vulnerabilities in innovative cancer treatment. His group identified several such vulnerabilities and suggested how these could be used to sensitize cancer. He and his colleagues also helped to understand mechanisms of cancer cell resistance to standard-of-care treatments and found ways to overcome it, together with identification of biomarkers to guide cancer therapy.

Bártek studied medicine at Palacký University in Olomouc, Czech Republic, and obtained his PhD in 1983 at the Institute of Molecular Genetics of the Czech Academy of Science in Prague. Before moving to his current position in Copenhagen in 1992, he worked as a postdoctoral fellow at the Imperial Cancer Research Fund in London and the German Cancer Research Center in Heidelberg, and as a group leader at the Cancer Research Institute in Brno and as head of a department at the Institute of Haematology in Prague. His work has been acknowledged by a number of prestigious awards in Denmark, Sweden, Israel and the Czech Republic, including the 1998 Prize of the Danish Association for Cancer Research, the 2003 Novo Nordisk Prize, and the G. J. Mendel Honorary Medal for Merit in the Biological Sciences. He was elected as a member of EMBO in 2000.

Bártek is a founding member of the European Academy of Cancer Sciences (2009) and was elected to the Danish Royal Academy of Sciences and Arts in 2012. In 2013 he was awarded the Silver Medal of Merits from the Senate of the Czech Republic.

DNA Damage Response: Molecular Mechanisms and Relevance for Cancer



Václav Pačes

*1942

Institute of Molecular Genetics, Czech Academy of Sciences, Prague, Czech Republic

April 13, 2006

Václav Pačes is Czech biochemist and a well-known figure in the popularization of science in the Czech Republic.

Pačes studied biochemistry at the Faculty of Science at Charles University in Prague, Czech Republic. After obtaining a master's degree in 1965 he joined the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences, where he obtained his PhD in 1968. He then spent a year as a postdoctoral fellow at the University of Chicago and another year at McMaster University in Hamilton, Canada. Since 1976 he has worked at the Institute of Molecular Genetics in the field of genomics, where he was asked to establish a methodology for DNA sequencing. A complete sequence of bacteriophage PZA was finished in 1986, which made his group one of the very first to read the complete DNA information of any organism. Professor Pačes followed on his studies of DNA with a focus on its regulatory role and evolutionary importance. He spent another year (1990–91) as a visiting professor at Yale University in New Haven, USA, and later became one of the first Czech members of EMBO.

From 1999 to 2005 he served as the Director of the Institute of Molecular Genetics in Prague and is a founding member of the Czech Learned Society.

Pačes served as chair of the Czech Academy of Sciences, and from 2010 until 2012 as chair of the Czech Learned Society.

In Brno you have the only Mecca of science in the Czech Republic – the place where modern life science originated. And that is why, but not the only reason why, we all appreciate being invited to the lecture here.

On the Origin of Life on Earth

Sir Adrian Bird

*1947

Buchanan Professor of Genetics, Wellcome Trust Centre for Cell Biology, University of Edinburgh, UK

May 18, 2006

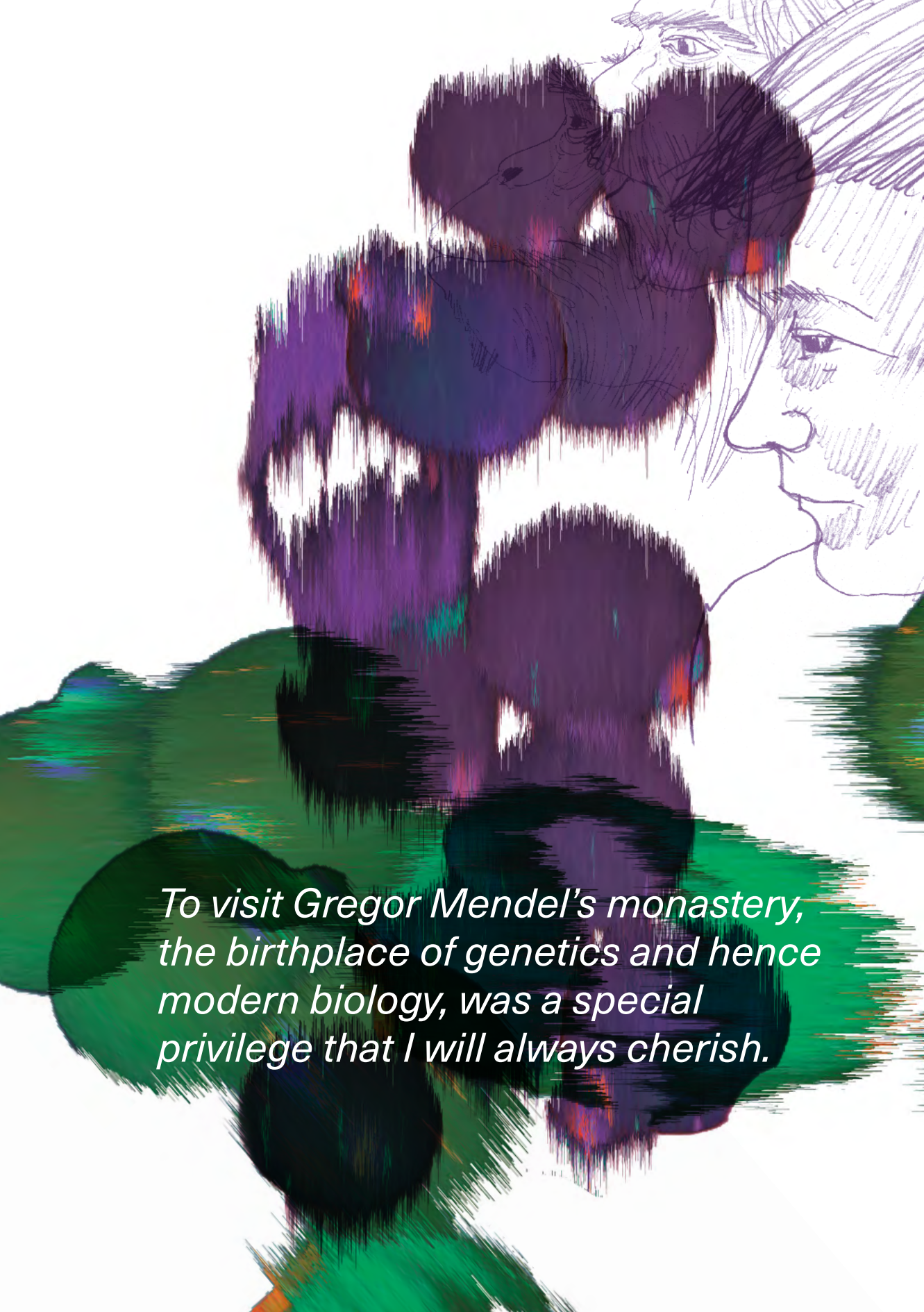
Professor Adrian P. Bird is a British geneticist and the world's leading expert in understanding the molecular mechanism underlying Rett Syndrome.

Adrian Bird graduated in biochemistry from the University of Sussex and obtained his PhD at Edinburgh University in 1970. Following postdoctoral experience at Yale University and the University of Zurich, he joined the Medical Research Council's Mammalian Genome Unit in Edinburgh. In 1987 he moved to the Institute for Molecular Pathology in Vienna. After returning to Edinburgh

in 1990 he became Buchanan Professor of Genetics and played a prominent role in setting up the Wellcome Trust Centre for Cell Biology, where he was Director from 1999–2010. Professor Bird was a Governor of the Wellcome Trust, one of the world's largest medical research charities, from 2001–2011. He has received numerous awards and honours, including the Louis-Jeantet Prize for Medicine, the Gairdner Prize, the Shaw Prize and the 2020 Brain Prize. He is a Fellow of the Royal Societies of London and Edinburgh and of the Academy of Medical Sciences.

Professor Bird's research focuses on the basic biology of DNA methylation and other epigenetic processes. He identified CpG islands as gene markers in the vertebrate genome and discovered proteins that read the DNA methylation signal to influence chromatin structure. Mutations in one of these proteins, MeCP2, cause the severe neurological disorder Rett Syndrome, which he showed to be reversible and therefore potentially curable. Professor Bird's recent work indicates that DNA base composition can be read as a signal to influence cell fate.

Proteins that Read the DNA Methylation Signal


To visit Gregor Mendel's monastery, the birthplace of genetics and hence modern biology, was a special privilege that I will always cherish.