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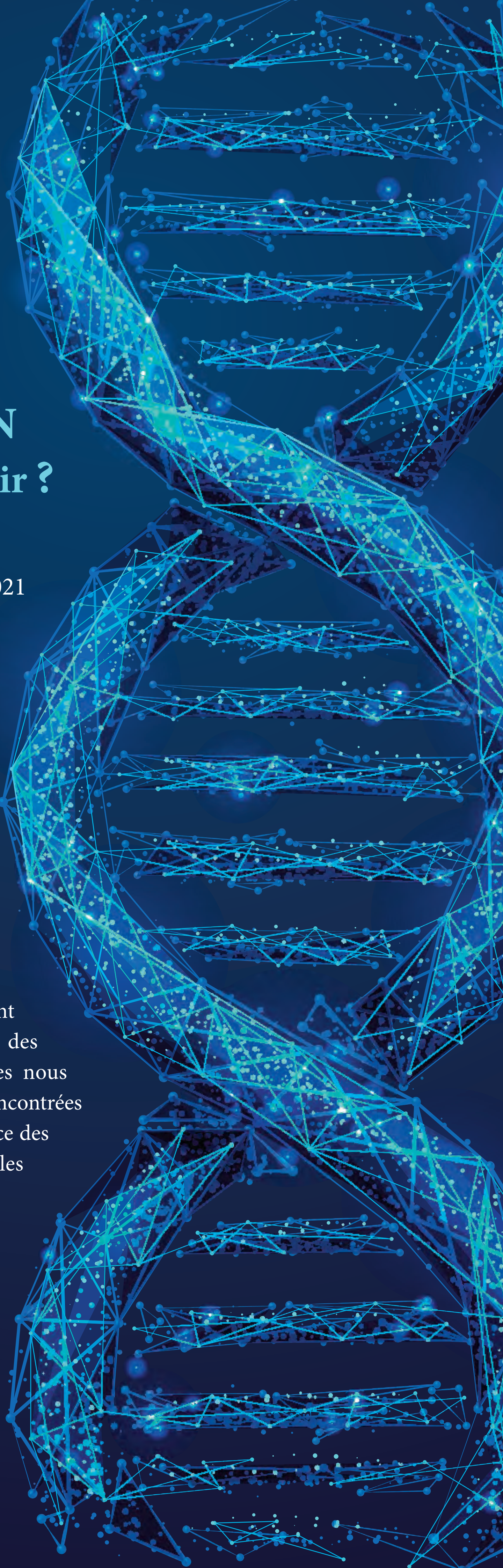
GRANDE CONFÉRENCE DE L'ACADÉMIE DES SCIENCES



50 000 ans d'épopée humaine dans notre ADN

Quelles conséquences pour l'avenir ?

Mardi 2 et mercredi 3 février 2021
Auditorium André et Liliane Bettencourt
3 rue Mazarine, 75006 Paris

Les découvertes remarquables de la paléo-anthropologie, basées sur l'étude des restes humains et de leurs environnements, ont ouvert le livre fascinant de nos origines, illustré de fragments de la vie et de l'histoire de nos ancêtres. Au cours des dernières années, les progrès spectaculaires de la génomique nous ont permis d'accéder au plus intime des individus qui nous ont précédés en différentes régions du monde en des temps reculés. Par analyse de leurs génomes et comparaison avec ceux des hommes modernes, l'épopée de l'espèce humaine au cours des quelques 50 derniers millénaires se reconstruit maintenant graduellement sous nos yeux en nous montrant la diversité des populations qui ont existé au cours du temps. Leurs gènes nous montrent leurs migrations, leurs adaptations aux conditions rencontrées (nourriture, agents pathogènes, domestications) et l'importance des métissages entre les populations. Les structures familiales ancestrales peuvent même être reconstituées.

En illustrant les plus récentes découvertes faites à partir d'ADN ancien, le colloque cherchera à faire apparaître comment l'histoire a laissé ses traces dans les gènes des hommes modernes, comment l'espèce humaine a façonné son environnement immédiat et quelles sont les conséquences pour notre futur.

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The organizers

Bernard Dujon

Professor, *Sorbonne Université, Institut Pasteur,* member of *Académie des sciences*

Bernard Dujon is member of *Académie des sciences*, professor at *Sorbonne Université* and *Institut Pasteur*. His scientific work has focused on genomes and molecular mechanisms of their evolution and dynamics. He discovered, from yeast mitochondria, the first intronic endonuclease, paving the way for site-specific editing of genomes.
He is also member of the *Academia Europaea* and EMBO.

Philippe Janvier

Research director, CNRS, *Muséum national d'Histoire naturelle, Sorbonne Université,* member of *Académie des sciences*

Philippe Janvier is a palaeontologist, research director at CNRS, member of *Académie des sciences*. He worked at the *Muséum National d'Histoire naturelle* on the first fossil vertebrates, dating from 535 to 360 million years ago, which he discovered and described in Paleozoic terrains in various regions. His book *Early vertebrates* synthesizes the evolutionary history of vertebrates and the major adaptations that have marked the first steps in the history of this zoological group.

Jean Weissenbach

Research director, *Génoscope,* member of *Académie des sciences*

Jean Weissenbach has directed the *Genoscope - Centre national de séquençage* within the CEA Genomics Institute (1997-2015). He played a pioneering role in the exploration and analysis of genomes, in particular the human genome. His current research focuses on the genomics and biochemical capabilities of the microorganisms in the environment. He is particularly interested in exploration of the biocatalytic biodiversity of living systems. Jean Weissenbach is a member of *Académie des sciences*, gold medal of the CNRS and has received prizes and distinctions in France and abroad.

Pascale Cossart

Professor, *Institut Pasteur, Secrétaire perpétuel* of *Académie des sciences*

Professor at *Institut Pasteur,* her research focuses on the study of molecular and cellular mechanisms implicated in bacterial infections, using the bacterium *Listeria monocytogenes* as a model. Pascale Cossart was a pioneer in a discipline that she named "Cellular Microbiology". She highlighted numerous strategies used by bacteria during infection. Her work has led to new concepts in infection biology, cellular biology, epigenetics and fundamental microbiology, and has been recognized by several international prizes. Pascale Cossart is a member of the *deutsche Akademie der Wissenschaften Leopoldina*, the National Academy of Sciences, the National Academy of Medicine and the Royal Society.

Program

Tuesday, February 2, 2021

Opening

https://youtu.be/jiTanXw2YNo

Chairperson : Pascale Cossart

02.30 pm **Welcome address**
Pascale Cossart, Professor, *Institut Pasteur, Secrétaire perpétuel* of *Académie des sciences*

02.40 pm **Opening**
Bernard Dujon, Professor, *Sorbonne Université, Institut Pasteur,* member of *Académie des sciences*
Philippe Janvier, Research director, CNRS, *Muséum national d'Histoire naturelle, Sorbonne Université,* member of *Académie des sciences*
Jean Weissenbach, Research director, *Génoscope*, member of *Académie des sciences*

03.10 pm **Three snapshots: the human settlement of the Earth 50.000, 25.000 and 5.000 years ago**
Yves Coppens, Professor, *Collège de France*, member of *Académie des sciences*

03.30 pm Discussion

Session I

Human populations, migrations, admixtures and peopling of continents from ancient and modern human DNA

https://youtu.be/jiTanXw2YNo

Chairperson : Bernard Dujon

03:40 pm **Deep human divergences and genomes**
Mattias Jakobsson, Professor, Department of Organismal Biology, Human Evolution, *Uppsala Universitet*

04:00 pm Discussion

04:10 pm ***Homo sapiens* meets Neandertal in Europe: where do we stand?**
Jean-Jacques Hublin, Director, Department of Human Evolution, Max Planck Institute for evolutionary Anthropology

04:30 pm Discussion

04:40 pm **Tracing the joint history of humans and dogs in ancient DNA**
Pontus Skoglund, Group leader, Ancient Genomics laboratory, Francis Crick Institute

05:00 pm Discussion

Wednesday, February 3, 2021

Session II

Molecular traces of ancient adaptations and selections in ancient and modern human DNA

https://youtu.be/wo42wYW17mw

Chairperson : Jean Weissenbach

10.00 am	**The demographic and adaptative history of *Homo sapiens:* a focus on Africa and the Pacific** **Lluis QUINTANA-MURCI,** Professor, *Collège de France* and *Institut Pasteur*, member of *Académie des sciences*
10.20 am	Discussion
10.30 am	**The genetic history of the plague: what we learn from ancient pandemics** **Johannes KRAUSE,** Director, Department of Archaeogenetics, Max Planck Institute for the Science of Human History
10.50 am	Discussion
11.00 am	**50.000 years of human history in our DNA: is our species still evolving?** **Pascale GERBAULT,** Researcher, Anthropology Unit, University of Geneva
11.20 am	Discussion
11.30 am	**How culture impacts genetic diversity** **Evelyne HEYER,** Professor, *Muséum national d'histoire naturelle*
11.50 am	Discussion
12.00 pm	End of session II - Break

Session III

Genetic and cultural co-evolution of humans and domesticated organisms

https://youtu.be/PfG-TFmcDFs

Chairperson : Philippe Janvier

02.00 pm	**A horse perspective on 50,000 years of human history** **Ludovic ORLANDO,** Research director, Laboratory of Molecular Anthropology and Image Synthesis, CNRS and *Université Paul Sabatier*
02.20 pm	Discussion
02.30 pm	**The tribulations of the cultivated apple tree in Eurasia: a complex history of domestication and towards the conservation of its wild apple relatives** **Amandine CORNILLE,** Researcher, *Génétique quantitative et évolution - Le Moulon*, INRAE - *Université Paris-Sud* - CNRS - *AgroParisTech*
02.50 pm	Discussion

03.00 pm **The impact of migration: prehistoric interactions in southern Africa and their linguistic and genetic consequences**
Brigitte PAKENDORF, Research director, *Dynamique du Langage* research lab, CNRS and *Université de Lyon*

03.20 pm Discussion

03.30 pm Break

Final Session

Human genetics

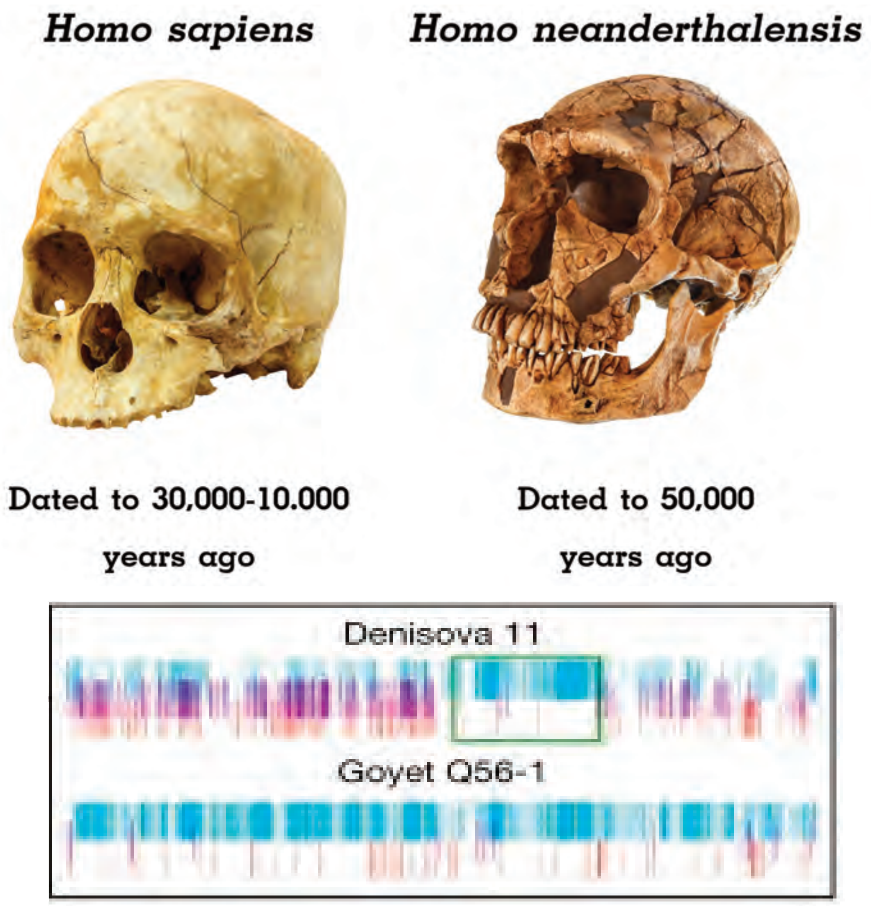
https://youtu.be/PfG-TFmcDFs

Chairperson : Jean Weissenbach

03.50 pm **From one human genome to 1+million genomes: how recent and very ancient genome evolution help us to understand human diseases and find novel therapeutic targets**
Jean-Louis MANDEL, Professor, *Université de Strasbourg*, member of *Académie des sciences*

04.10 pm Discussion

04.20 pm **Round table with speakers, organizers and invited students**



Slon et al., Nature 2018

Programme

Mardi 2 février 2021

Ouverture

https://youtu.be/jiTanXw2YNo

Présidente de séance : Pascale Cossart

14:30 **Accueil**

Pascale Cossart, Professeur, Institut Pasteur, Secrétaire perpétuel de l'Académie des sciences

14:40 **Ouverture**

Bernard Dujon, Professeur, Sorbonne Université, Institut Pasteur, membre de l'Académie des sciences

Philippe Janvier, Directeur de recherche, CNRS, Muséum national d'Histoire naturelle, Sorbonne Université, membre de l'Académie de sciences

Jean Weissenbach, Directeur de recherche, Génoscope, membre de l'Académie de sciences

15:10 **Trois images instantanées : le peuplement humain de la Terre il y a 50.000, 25.000 et 5.000 ans**

Yves Coppens, Professeur, Collège de France, membre de l'Académie des sciences

15:30 Discussion

Session I

Populations humaines, migrations, mélanges et peuplement des continents à partir de l'ADN humain ancien et moderne

https://youtu.be/jiTanXw2YNo

Président de séance : Bernard Dujon

15:40 **Divergences humaines profondes et génomes**

Mattias Jakobsson, Professeur, *Department of Organismal Biology, Human Evolution, Uppsala Universitet*

16:00 Discussion

16:10 ***Homo sapiens* rencontre Néandertal en Europe : où en sommes nous ?**

Jean-Jacques Hublin, Directeur, *Department of Human Evolution, Max Planck Institute for evolutionary Anthropology*

16:30 Discussion

16:40 **Retracer l'histoire commune des hommes et des chiens à partir de l'ADN ancien**

Pontus Skoglund, Chef d'équipe, *Ancient Genomics laboratory, Francis Crick Institute*

17:00 Discussion

Mercredi 3 février 2021

Session II

Traces moléculaires d'anciennes adaptions et sélections dans l'ADN humain ancien et moderne

https://youtu.be/wo42wYW17mw

Président de séance : Jean Weissenbach

10:00	**L'histoire démographique et adaptative d'*Homo sapiens* : un regard sur l'Afrique et le Pacifique** **Lluis Quintana-Murci,** Professeur, Collège de France et Institut Pasteur, membre de l'Académie des sciences
10:20	Discussion
10:30	**L'histoire génétique de la peste : ce que nous apprennent les anciennes pandémies** **Johannes Krause,** Directeur, *Department of Archaeogenetics, Max Planck Institute for the Science of Human History*
10:50	Discussion
11:00	**50.000 ans d'histoire humaine dans notre ADN : notre espèce évolue-t-elle encore?** **Pascale Gerbault,** chercheur, unité d'Anthropologie, Université de Genève
11:20	Discussion
11:30	**Comment la culture impacte-t-elle la diversité génétique** **Evelyne Heyer,** Professeur, Museum national d'histoire naturelle
11:50	Discussion
12:00	Fin de la session II - Pause

Session III

Co-évolution génétique et culturelle des hommes et des organismes domestiqués

https://youtu.be/PfG-TFmcDFs

Président de séance : Philippe Janvier

14:00	**50.000 ans d'histoire humaine du point de vue du cheval** **Ludovic Orlando,** Directeur de recherche, Laboratoire d'anthropologie moléculaire et imagerie de synthèse, CNRS et Université Paul Sabatier
14:20	Discussion

14:30 **Les tribulations du pommier cultivé en Eurasie : une histoire complexe de domestication et vers la conservation de ses parents sauvages**

Amandine Cornille, Chercheur, Génétique quantitative et évolution - Le Moulon, INRAE - Université Paris-Sud - CNRS - AgroParisTech

14:50 Discussion

15:00 **L'impact de la migration : les interactions préhistoriques en Afrique australe et leur conséquences linguistiques et génétiques**

Brigitte Pakendorf, Directeur de recherche, Laboratoire Dynamique du Langage, CNRS et Université de Lyon

15:20 Discussion

15:30 Pause

Session finale

Génétique humaine

https://youtu.be/PfG-TFmcDFs

Président de séance : Jean Weissenbach

15:50 **D'un seul génome humain à "*1+million genomes*" : comment l'évolution des génomes récents et très anciens nous aide à comprendre les maladies humaines et à trouver de nouvelles cibles thérapeutiques**

Jean-Louis Mandel, Professeur, Université de Strasbourg, membre de l'Académie des sciences

16:10 Discussion

16:20 **Table ronde avec les intervenants, les organisateurs et des étudiants invités**

Biographies and abstracts

Yves COPPENS

Professor, *Collège de France*, member of *Académie des sciences*

Né en 1934, entré dans la vie professionnelle en 1956 (CNRS), Yves Coppens a été titulaire de la Chaire d'Anthropologie (biologique) du Muséum national d'Histoire naturelle, puis de celle de Paléoanthropologie et Préhistoire du Collège de France.
Paléontologue et Préhistorien, après de nombreuses fouilles archéologiques en Bretagne, Yves Coppens a monté et conduit, à partir de 1960, d'importantes expéditions, seul ou en collaboration, en Afrique d'abord (Tchad, vallée de l'Omo et désert de l'Afar en Ethiopie, Tunisie, Mauritanie) et en Asie (Chine, Mongolie, Sibérie russe) ; il en a rapporté des tonnes de fossiles, dont des centaines de restes d'Hominidés, parmi lesquels 6 espèces nouvelles qu'il a signées ou co-signées. Il en a tiré, évidemment, un certain nombre d'idées originales dont la plus importante est incontestablement la découverte de la raison pour laquelle est apparu le genre humain, une simple nécessité d'adaptation à un changement climatique (1975).

Three snapshots: the human settlement of the Earth 50.000, 25.000 and 5.000 years ago

N'étant pas généticien, je ne peux qu'apporter les images que ma discipline, la Paléoanthropologie, a construites au terme de 200 années de fouilles, de découvertes et de leur analyse et de 80 ans de datations ; ce sera « ma livraison » à la Science soeur, celle qui lit les molécules.

50.000 ans. L'Humanité a déjà 3 millions d'années, elle s'est déjà répandu sur l'ensemble de l'Ancien Monde ; l'*Homo sapiens*, notre espèce, né en Afrique, s'est déjà déployé sur son continent d'origine, sur l'Asie qu'il a rejointe par le Sinaï et où il a rencontré bien d'autres espèces humaines (dont des insulaires de petite taille) et sur l'Australie où il s'est rendu en radeau à partir de l'Asie. Mais il ne connait pas encore l'Europe, déjà peuplée, ni l'Amérique qui ne l'est pas.

25.000 ans. L'*Homo sapiens* est partout, ou presque, sur le globe, en partie hybridé avec les populations qu'il a rencontrées. Le peuplement de l'Amérique, du Nord où il est majoritairement arrivé, à la Patagonie, donne une bonne idée de l'étonnante vitesse de cette expansion, évidemment associée à une certaine croissance démographique.

5.000 ans. Il restait quelques îles à peupler, c'est ainsi le cas du Groenland, qui, de ce point de vue, est américain d'origine. Le dernier Interglaciaire a eu lieu, celui dans lequel nous nous trouvons toujours aujourd'hui, la « révolution » néolithique aussi, et, avec elle, la sédentarisation, l'invention de l'élevage et de l'agriculture, le début des OGM, de l'architecture monumentale et le premier baby-boom indiscutable. Le développement demeure alors durable, bien que l'anthropisation de la Terre ait sérieusement commencé.

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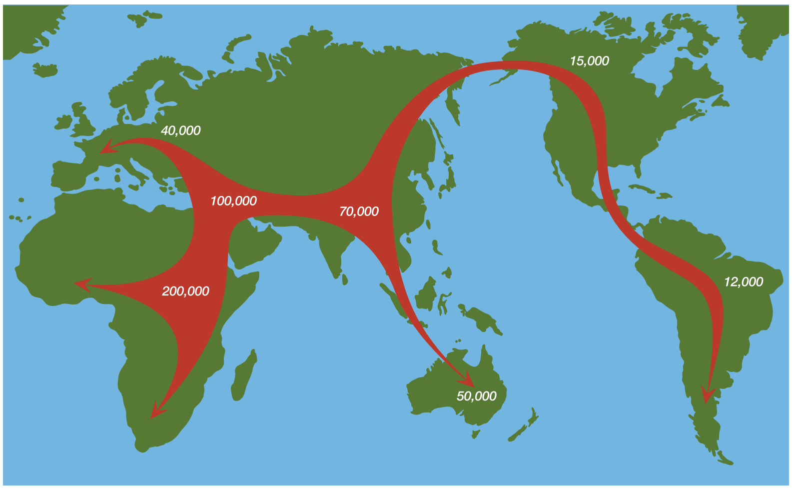
Jean-Jacques Hublin, Nikolay Sirakov, Vera Aldeias et al., « Initial Upper Palaeolithic Homo sapiens from Bacho Kiro Cave, Bulgaria », Nature, Mai 2020

Lorena Becerra-Valdivia et Thomas Higham, « The timing and effect of the earliest human arrivals in North America », Nature, Août 2020.

Anne Lehoërff, Le Néolithique, « Que sais-je », PUF, Paris, 2020.



Mattias JAKOBSSON

Professor, Department of Organismal Biology, Human Evolution, Uppsala Universitet

Dr. Mattias Jakobsson received his PhD in Genetics from Lund University, Sweden in 2005. After postdoctoral research at University of Michigan, USA, he joined Uppsala University as an assistant professor in 2008. Dr. Jakobsson was appointed full professor 2014, and chair of Human Evolution in 2018 at Uppsala University.

Dr. Jakobsson has a broad interest in population genetics and human evolution. His lab uses computational approaches for deciphering complex patterns of large-scale human genomic variation from both modern-day and ancient humans in order to understand human evolutionary history. The lab focus on interrogating long-standing questions in human evolution, including the colonization and migration in Stone Age Eurasia and the population history of sub-Saharan Africans, and Dr. Jakobsson team has recently published a series of papers that push the emergence of modern humans further back in time. Dr. Jakobsson is a Wallenberg Scholar, an ERC grantee, and have received the Tage Erlander prize and the Göran Gustafsson prize from the Royal Academy of Sweden.

Deep human divergence and genomes

Advances in the sequencing and the analysis of the genomes of both modern and ancient individuals have led to breakthroughs in understanding human evolutionary history. As an example, I will discuss recent discoveries about human history in Africa, leading to a fundamental revision of the age of our species. Sequencing of seven ancient individuals from KwaZulu-Natal, South Africa, of which three were dated to ~2000 years old, provided direct evidence for migration, admixture and adaptation in southern Africa that had important consequences for interpreting our human past. Using traditional and new population genomics analysis approaches, we estimate the deepest human population divergence time to between 350,000 and 260,000 years ago. This estimate increases the deepest divergence amongst modern humans, coinciding with anatomical developments of archaic humans into modern humans as represented in the local fossil record, and suggest that modern humans emerged around 300,000 years ago. As we uncover new pieces to the human evolution puzzle, a complex interplay between migration, admixture and adaptation often appear.

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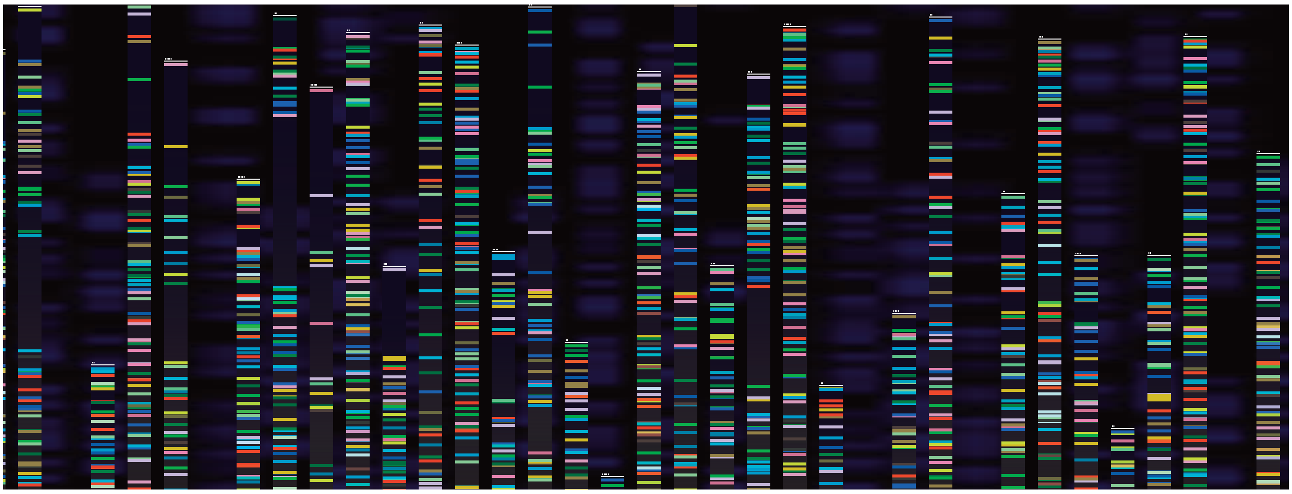
Carina M. Schlebusch, Helena Malmström, Torsten Günther,Per Sjödin, Alexandra Coutinho,Hanna Edlund, Arielle R. Munters, Mário Vicente, Maryna Steyn, Himla Soodyall, Marlize Lombard, Mattias Jakobsson, Southern African ancient genomes estimate modern human divergence to 350,000 to 260,000 years ago, Science 358, 652–655 (2017)



Jean-Jacques Hublin

Director, Department of Human Evolution, Max Planck Institute for evolutionary Anthropology

Professor Jean-Jacques Hublin is the Director of the Department of Human Evolution at the Max Planck Institute for Evolutionary Anthropology, Leipzig. He is an honorary Professor at the University of Leipzig and holds the International Chair in Paleoanthropology at the *Collège de France*, Paris. He is best known for pioneering the field of virtual paleoanthropology. The origins of Neandertals and *Homo sapiens*, and most notably, the interactions between the two groups have occupied a central place in his career. To address these issues, he led fieldworks in Europe and North Africa. He is the founder of the European Society for the Study of Human Evolution.

Homo sapiens meets Neandertal in Europe: where do we stand?

To date, the detailed process of replacement and partial absorption of local Neandertals by *Homo sapiens* populations of African origins remains largely unknown in most parts of Eurasia. Debates mostly center on the interpretation of diverse archeological assemblages of the transitional period and on the biological nature of their makers. A group of lithic industries rooting in south-east Asia and spreading from central Europe to Mongolia before 45,000 cal BP has been described as representing an "Initial Upper Paleolithic" and a possible marker of the first dispersal of *Homo sapiens* in the mid-latitudes of Eurasia. Recent excavations at the site of Bacho Kiro Cave (Bulgaria) have demonstrated the direct association of IUP assemblages dated between 46,000 and 44,000 cal BP with well identified *H. sapiens*. In contrast to later Upper Paleolithic European hominins, the available paleogenetic data suggests that the IUP early wave of peopling is unrelated to present-day European populations. Recent advances highlight the long chronological overlap of *Homo sapiens* and Neandertals at the scale of Europe during which biological and cultural interactions between the two groups took place and the complex nature of the replacement process.

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Hublin, J.-J. et al. 2020. Initial Upper Palaeolithic Homo sapiens from Bacho Kiro Cave, Bulgaria. Nature 58: 299-302.

Pontus Skoglund

Group leader, Ancient Genomics laboratory, Francis Crick Institute

Pontus Skoglund is the group leader of the Francis Crick Institute's Ancient Genomics laboratory. Originally from Sweden, he obtained his PhD in evolutionary genetics from Uppsala University in 2013, and thereafter did his postdoctoral research at Harvard Medical School. His past research has focused on developing new approaches to propel the field of ancient DNA into the genomic era, revealing population migrations as catalyzers for the transition from hunter-gatherer lifestyles to agriculture in Europe, Africa, and Southeast Asia. He has also studied gene flow between archaic- and modern humans, early human evolution in Africa, the peopling of the Americas, and the origin of domestic dogs. He is a Wellcome Trust Investigator, an ERC starting grantee and a Vallee Foundation Scholar.

Tracing the joint history of humans and dogs in ancient DNA

Dogs were the first domestic animal, but little is known about their population history and to what extent it was linked to humans. I will discuss recent evidence from ancient dog genomes of limited gene flow from wolves since domestication, but substantial dog-to-wolf gene flow. By 11,000 years ago, at least five 5 major ancestry lineages had already diversified, demonstrating a deep genetic history of dogs during the Paleolithic. Co-analysis with human genomes reveals aspects of dog population history that mirror humans, including Levant-related ancestry in Africa and early agricultural Europe. Other aspects differ, including the impacts of steppe pastoralist expansions in West- and East Eurasia, and a complete turnover of Neolithic European dog ancestry.

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Lluis QUINTANA-MURCI

Professor, *Collège de France* and *Institut Pasteur*, member of *Académie des sciences*

Dr Lluis Quintana-Murci was born in Palma de Mallorca, Spain. He earned his Ph.D. in Population Genetics at the University of Pavia, and his MSc in Biology at the University of Barcelona. He heads the Unit of Human Evolutionary Genetics (CNRS UMR2000) at I*nstitut Pasteur* since 2007, and has been Scientific Director of the Institut during 2016-2017. He is presently Professor at *Collège de France* (Chair of Human Genomics and Evolution) and *Institut Pasteur*. His team focuses on demographic and adaptive inference in humans, using population genetics approaches, with a strong focus on the history of African hunter-gatherers and farmers. He is also interested in how pathogens have exerted selective pressures on the human genome. In this context, his research focuses on the study of the genetic, epigenetic and environmental factors driving variation in immune responses, as this helps to lay the foundations of precision medicine related to infectious and immune-related disorders.

Lluis Quintana-Murci was a laureate of the European Research Council (ERC) in 2012 and is a member of EMBO and the *Academia Europaea* since 2014.

The demographic and adaptative history of *Homo sapiens*: a focus on Africa and the Pacific

Population genomics approaches allow to elucidate migration routes, admixture between populations and events of genetic adaptation to challenging environments. I will review our most recent studies on the genomic history of human populations, with a focus on African rainforest hunter-gatherers and Pacific islanders. On the one hand, Central Africa hosts the world's largest group of hunter-gatherers, who live in close proximity with groups that have adopted agriculture over the past 5,000 years. Over the last years, we have provided evidence that admixture between hunter-gatherers and farmers have conferred an advantage to increased adaptation to their respective environments, involving functions related to growth and immunity against infectious agents. On the other hand, the Pacific region is of major importance for addressing questions regarding human dispersals, interactions with archaic hominins and natural selection processes. Our studies show marked differences in the proportion and nature of the Neandertal and Denisovan heritage among Pacific groups, suggesting that interbreeding with highly-structured populations of archaic hominins was a common phenomenon in the region.

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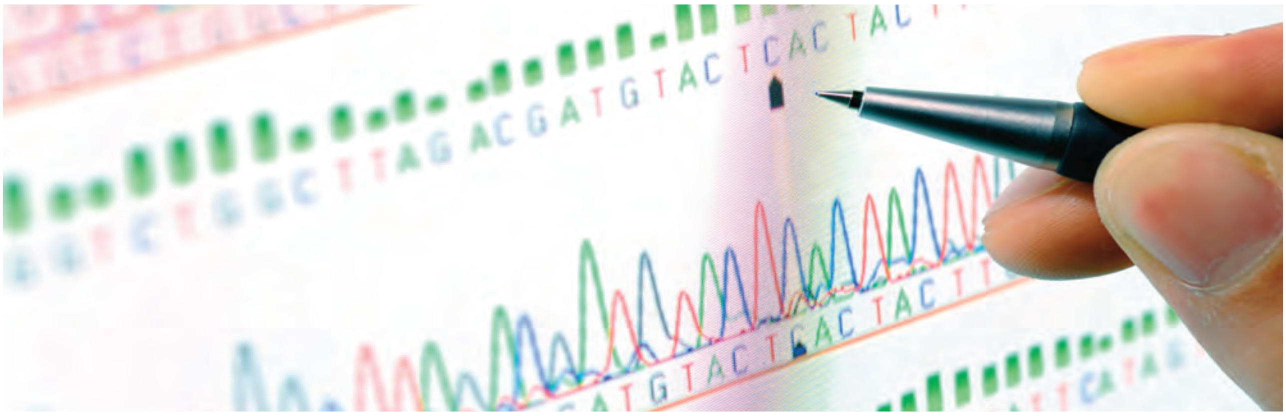

Johannes Krause

Director, Department of Archaeogenetics, Max Planck Institute for the Science of Human History

Prof. Dr. Johannes Krause obtained his Ph.D. in Genetics at Leipzig University. He is currently heading the department of Archaeogenetics of the Max Planck Institute for Evolutionary Anthropology. Prof. Dr. Krause focuses on the analysis of ancient DNA to investigate such topics as pathogens from historic and prehistoric epidemics, human genetic history and human evolution. He contributed substantially to deciphering the Neanderthal genome and the shared genetic heritage of Neanderthals and modern humans. In 2010, while working at the Max Planck Institute for Evolutionary Anthropology in Leipzig, he discovered the first genetic evidence of the Denisovans, an extinct hominin discovered in Siberia. His recent work includes revealing the genetic heritage of ancient Egyptians, reconstructing the first Pleistocene African genomes, uncovering the source of the epidemic plague bacteria that periodically caused historic and prehistoric epidemics in Europe, and clarifying the complex history of Europe's prehistoric mass migrations.

The genetic history of the Plague: what we learn from ancient pandemics

High throughput DNA sequencing has revolutionized the field of archaeogenetics in the past decade, providing a better understanding of human genetic history, past population dynamics and host pathogen interactions through time. Targeted DNA capture approaches have allowed reconstructing complete ancient bacterial genomes providing direct insights into the evolution and origin of some of the most infamous bacterial pathogens known to humans such as *Yersinia pestis*, *Mycobacterium tuberculosis* or *Mycobacterium leprae.* Here we discuss the potential of ancient pathogen genomics using Yersinia pestis as a model organism. Phylogenetic comparisons of modern and ancient *Y. pestis* strains spanning over 5000 years of human history from the Stone Age to modern times are discussed. They provide direct evidence for the timing and emergence of major virulence factors essential for the transmission of bacteria by fleas. We furthermore present the oldest reconstructed genomes of *Y. pestis* that are fully capable of causing the bubonic form of plague from the Eastern European Bronze Age. Suggesting that the emergence of this form of the disease happened more than 1000 years earlier than previously suggested. Temporal studies of pathogens might thus throw new light on the origin of human diseases and potentially allow predicting and preventing further transmissions and disseminations in the future.

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Pascale Gerbault

Researcher, Anthropology Unit, University of Geneva

Pascale Gerbault completed her PhD in evolutionary genetics at University College London in the UK. She recently joined the *Unité d'Anthropologie* at the *Université de Genève* in Switzerland to investigate human evolutionary history using the molecular and statistical analysis of the major histocompatibility complex, HLA.

Pascale Gerbault is an evolutionary biologist, experienced in analysing genetic data using simulation modeling approaches to infer evolutionary processes shaping patterns of genetic diversity. Fascinated by our species ability to adapt to various environments she seeks to understand how the diverse pathogenic environments we have encountered have shaped our evolution. Additional research interests include the pathogens causing syphilis and yaws in humans. Pascale Gerbault does collaborative research in Ghana that aims to investigate the evolution and spread of the pathogens that cause these infectious diseases

50.000 years of human history in our DNA : is our species still evolving?

It could be presumed that human genetic adaptations occurred between 65,000 and 55,000 years ago, when our species started to inhabit environments as diverse as the tropical Oceania and the polar Greenland. Advances in molecular genomics technologies and in the analyses of genome-wide data have shed new light on our understanding of human evolutionary biology[1]. These advances have enabled the comparison of genomes of humans living thousands of years ago to those living today, thereby providing snapshots of our evolutionary history and elucidating many aspects of human evolutionary biology[2]. These include (i) the interbreeding between our species and our close relatives, such as Neanderthals, and how it has affected our adaptation, (ii) bringing more details into the complex migrations of our species and its dispersal worldwide, and (iii) a finer characterisation of genetic adaptations of our species to various environments (e.g.[3]), whether they are due to climatic conditions, pathogens or cultural innovations. This talk focusses on (iii), and discusses specific examples of human genetic adaptations that have occurred recently in our evolutionary history.

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Evelyne Heyer

Professor, *Muséum national d'histoire naturelle*

E Heyer is Professor in Genetical Anthropology at *Muséum National d'Histoire Naturelle* in Paris where she develops researches in Human evolutionary Genetics. Her laboratory is located at the *Musée de l'Homme* where she is the head of the research unit UMR7206 Eco-Anthropology. Her research topics are on Human evolutionary Genetics that she develops along three axes: tracing back population history, evaluating adaptation and natural selection, gene-culture co-evolution. She does field works in Central Africa and Central Asia and has published more than 100 papers, her works on the impact of culture on genetic evolution in humans are widely known and she is regularly invited on this subject in international meetings.

On top of her research work, she is strongly involved in dissemination of knowledge: she became involved in the renovation project of the *Musée de l'Homme* and she is the scientific general commissioner for the renovated *Musée de l'Homme* that opened in October 2015. She was in charge of the first temporary exhibition at the *Musée de l'Homme :* "Us and them – from prejudices to racism" in 2017.

How culture impacts genetic diversity

A specificity of our species is the fact that we transmit several cultural traits. Since some of these transmitted traits impact our survival, reproduction and migration, cultural transmission can influence the biological evolution of our species. One way to assess the importance of cultural variation on our evolution is to measure the impact of these cultural traits on genetic diversity. This lecture will specifically assess the importance of various cultural factors in shaping patterns of genetic variation in human populations, in particular focusing on sex-specific migration, social organization, inbreeding, and cultural transmission of reproductive success. I will present results of our field studies in Central Asia, Central Africa and South East-Asia where we collected ethnological and genetic data. These studies clearly show how different cultural processes have impacted human genetic diversity supporting the hypothesis of co-evolution between genes and cultures.

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L'Odyssée des genes, Flammarion (2020)

Ludovic ORLANDO

Research director, Laboratory of Molecular Anthropology and Image Synthesis, CNRS and *Université Paul Sabatier*

Ludovic Orlando was born in 1977, the year when the first DNA sequencing technology was developed. He graduated his PhD in 2003, twenty years after the first ancient DNA molecule was ever sequenced. He was appointed as a permanent Associate Professor at *Ecole Normale Supérieure de Lyon* where he lectured and performed research on ancient DNA until 2010. He then joined the Centre for GeoGenetics at the University of Copenhagen, Denmark to become Professor of Molecular Archaeology and form his own research group. Now back to France, his home country, he built the Centre for Anthropobiology and Genomics of Toulouse at *Université Paul Sabatier.* Amongst his early career achievements feature the sequencing of the oldest genome, the characterization of the first ancient epigenome, and the reconstruction of the domestication history of the species that most impacted human evolution: the horse.

A horse perspective on 50,000 years of human history

The horse is one of the most frequently represented species in the cave art record of Western Europe, where it was central to the subsistence economy of Pleistocene hunter-gatherer societies. Its domestication by the mid-Holocene represents one turning point in human history. It truly globalized the world for the first time as not only people but their genes, their culture and their diseases could then spread across the Old World at an unprecedented pace. Charriots launched at full speed against the enemy lines or charging cavalries also provided warfare revolutionary tactics, often decisive to the fate of some of the most famous battles in history. The horse was in fact paramount to the world economy up until the early 20th century when societies became increasingly mechanized. The global needs for horse meat, speed and power thus deeply impacted human history. They did not changed the horse anyless. In this talk, I will unfold 50,000 years of history in the human-horse relationship and will show how humans have reshaped the horse genome through space and time. Reciprocally, I will illustrate how horse speed transformed patterns of human mobility from the Bronze Age onwards.

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Amandine CORNILLE

Researcher, *Génétique quantitative et évolution - Le Moulon*, INRAE - *Université Paris-Sud* - CNRS - *AgroParisTech*

Amandine Cornille is CNRS researcher and a group leader of a young ATIP / AVENIR CNRS-Inserm team created in January 2019 at the Génétique Quantitative et Evolution - Le Moulon (France, Université Paris Saclay, INRAE, CNRS, AgroParisTech) working on plant and insect evolutionary genomics, in particular on the ecological genomics of apple-aphid interaction. Amandine Cornille has recently been awarded of the CNRS Paoletti prize 2020.

The tribulations of the cultivated apple tree in Eurasia: a complex history of domestication and towards the conservation of its wild apple relatives

What is the origin and the genetic make-up of the apple varieties you eat nowadays? Despite its economic, cultural and historical importance, the evolutionary histories of the cultivated apple and of its wild relatives still remained unresolved 10 years ago. The use of genetic markers on multiple wild and cultivated populations across Eurasia has since made great strides toward answering this question. Genetic markers revealed a complex apple domestication history in Eurasia that has been shaped by human history and practices. Domesticated in Central Asia more than 4000 years ago, several wild apple species then contributed to the genetic make-up of the cultivated apple genome during its journey along the Silk Roads towards Europe. These wild apples are currently threatened, and active conservation programs are settled to preserve them, especially in Europe.

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Brigitte Pakendorf
Research director, *Dynamique du Langage* research lab,
CNRS and *Université de Lyon*

Brigitte Pakendorf is a senior scientist ("*directrice de recherche*") at the CNRS. A linguist and molecular anthropologist, she led a multidisciplinary Max Planck Research Group at the MPI for Evolutionary Anthropology in Leipzig, Germany, before joining Dynamique du Langage in Lyon. Her research, which is based on data collected during numerous field trips to Siberia and southern Africa, focuses on the interdisciplinary investigation of population history, on the documentation and description of Northern Tungusic languages, and on language contact in Siberia. She was awarded a silver medal of the CNRS in 2016 and is a member of the *Academia Europaea*.

The impact of migration: prehistoric interactions in southern Africa and their linguistic and genetic consequences

Although the so-called "Khoisan" foragers in southern Africa are often thought to have been isolated for millennia, there is evidence for two waves of migration into the region in the past 2000 years: one that brought pastoralists from East Africa and a later one that brought farmers speaking Bantu languages. As can be shown with studies of both ancient and modern DNA, the impact of these migrations on both the autochthonous and the immigrant peoples was diverse, leading to genetic replacement, admixture, and language change. Some Khoisan-related groups were completely replaced and can be detected only through traces of admixture in Bantu-speaking groups. Other Khoisan communities interacted with the immigrants to various degrees in a sex-biased fashion: Khoisan women married into Bantu groups and Bantu men fathered children with Khoisan women. There were linguistic effects as well: one of the three Khoisan language families may have been brought to southern Africa by the East African pastoralists. Furthermore, some of the Bantu groups adopted 'click' consonants from Khoisan languages, while others must have shifted to a Khoisan language and partly foraging life-style in the past.

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Jean-Louis Mandel

Professor, *Collège de France,* member of *Académie des sciences*

Jean-Louis Mandel is a professor at *Collège de France*. His research concerns the identification of genes and their mutations responsible for monogenic neurological diseases, development of diagnostic tests and analysis of pathophysiological mechanisms, using in particular animal or cellular models. He has in particular carried out numerous studies on diseases caused by unstable expansion of trinucleotide repetition.

Repeat expansions

Sequencing of « THE » (almost complete) human genome was published in 2003, an achievement of considerable cost. At the time, one would not have dreamed that whole genome sequence (WGS) would be obtained by 2018 for 100 000 british individuals with cancer or rare diseases. A 1 million genome project is discussed at the European level. This has a large impact for human diseases. I will give a historical perspective on some large scale projects and databases, regretting that France has been largely absent from them.

The HAPMAP project was key to the explosion of GWAS studies for the common multifactorial diseases, that cover all of medicine. Curiously, the X chromosome is absent from almost all such studies. For monogenic diseases, the explosion started with the technology of exome sequencing, and now cheap WGS, but interpretation of such data for diagnosis requires large databases of control individuals from diverse populations and of genomes throughout the tree of life. Extensive databases including phenotype information are still needed, despite useful initiatives. Difficult to sequence non coding regions have been recently a treasure trove for identification of novel disease mechanisms. Identification of novel drug targets also benefits from large databases of genomic sequences linked to electronic health records.

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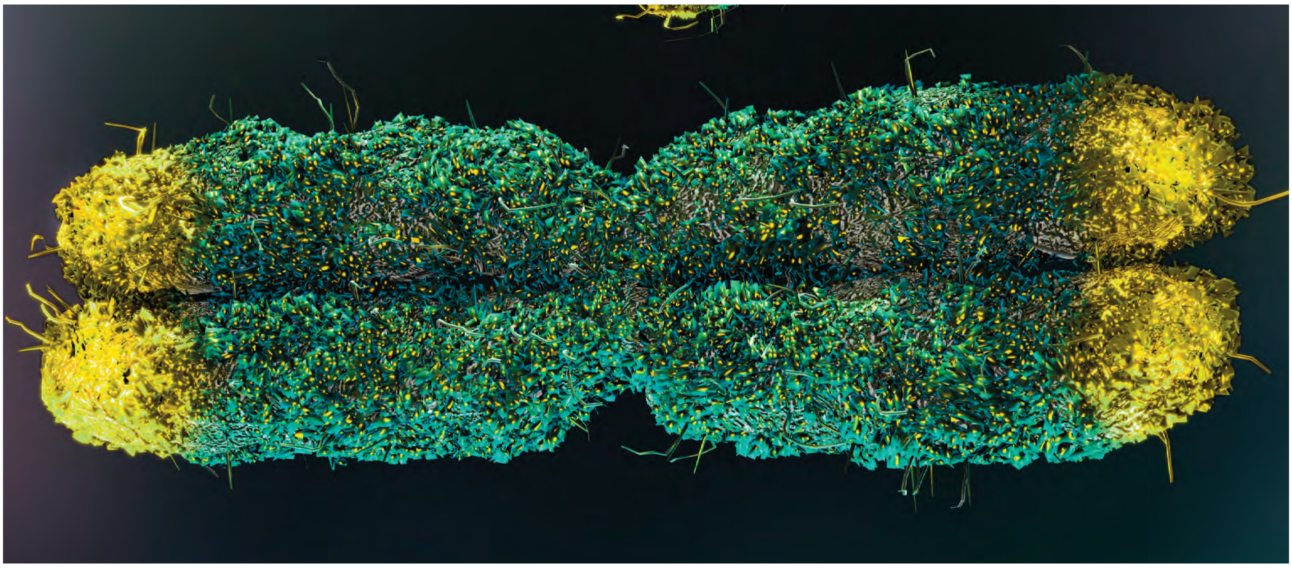

INSTITUT DE FRANCE
Académie des sciences

50 000 years of human history in our DNA: what consequences for the future?

The remarkable discoveries of paleo-anthropology, based on the study of human remains and their environments, have opened the fascinating book of our origins, illustrated with fragments of the life and history of our ancestors. In recent years, spectacular advances in genomics have given us access to the most intimate knowledge of the individuals who preceded us in different parts of the world in remote times. By analyzing their genomes and comparing them with those of modern humans, the epic journey of the human species over the last 50 millennia is now gradually being reconstructed before our eyes, showing us the diversity of populations that have existed over time. Their genes show us their migrations, their adaptations to the conditions encountered (food, pathogens, domestication) and the importance of admixtures between populations. Ancestral family structures can even be reconstructed. By illustrating the most recent discoveries made from ancient DNA, the colloquium will seek to show how history has left its traces in the genes of modern humans, how the human species has shaped its immediate environment and what are the consequences for our future.

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