EXCELLENCE IN SCIENCE

THE ROYAL SOCIETY

SATELLITE MEETING ON

Human evolution – plagues, pathogens and selection

Wednesday 8 – Thursday 9 June 2011

The Kavli Royal Society International Centre, Chicheley Hall, Buckinghamshire

Organised by Professor Danny Altmann, Dr Francois Balloux and Dr Rosemary Boyton

- **Programme schedule**
- **Programme and abstracts**
- **Speaker biographies**
- **Notes**
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Day 1 – Wednesday 8 June 2011

08.30 Registration & coffee

09.00 Welcome by Professor Sir Peter Knight, FRS, Principal, The Kavli Royal Society Centre
Welcome by Professor Danny Altmann, Organiser

Session 1 – Where anthropogenetics and history meet

Chair – Professor Peter Parham FRS, Stanford University, USA

09.10 Death comes to town: disease resistance, urbanisation and recent selection in human populations
Dr Ian Barnes, Royal Holloway, University of London, UK

09.40 Discussion

09.55 Hunting the molecular past
Professor Eske Willerslev, University of Copenhagen, Denmark

10.25 Discussion

10.40 Coffee

11.10 African population history inferred from genomic data
Dr Brenna Henn, Stanford University, USA

11.40 Discussion

11.55 Archaeogenetics and the settlement of the Remote Pacific
Professor Martin Richards, University of Leeds, UK

12.25 Discussion

12.40 Lunch

Session 2 – Human migration, genes and language
Chair – Professor Danny Altmann, Imperial College London, UK

13.40 Insights into human genome variation from the 1000 Genomes Project
Dr Chris Tyler-Smith, The Wellcome Trust Sanger Institute, UK

14.10 Discussion

14.25 Language evolution in time and space
Dr Quentin Atkinson, The University of Auckland, New Zealand

14.55 Discussion

15.10 Tea

15.40 Reconstruction of ancient migrations using multiple lines of evidence
Dr Stephen Oppenheimer, University of Oxford, UK

16.10 Discussion

16.25 Reconstructing the mode and tempo of the out-of-Africa migration of anatomically modern humans
Dr Andrea Manica, University of Cambridge, UK

16.55 Discussion

17.10 General discussion

17.40 End of day 1

18.30 Pre-dinner drinks

18.45 Dinner

Day 2 – Thursday 9 June 2011

Session 3 – Evolutionary pressure and the immune system
Chair – Dr Danny Douek, Vaccine Research Center, National Institutes of Health, USA

09.00 Evolution of the HLA-C 3'UTR and its effect on HIV control
Dr Mary Carrington, SAIC-Frederick Inc and Ragon Institute of MGH, MIT and Harvard, USA

09.30 Discussion

09.45 Population-specific evolution of Natural Killer cell diversity
Dr Paul Norman, Stanford University, USA

10.15 Discussion

10.30 Coffee

11.00 Origin of Amerindians and their genetic relatedness with Asian and Pacific islanders
Dr Antonio Arnaiz-Villena, Universidad Complutense, Spain

11.30 Discussion

11.45 Recognition of the Mtb-infected Cell: a fine line between innate and adaptive immunity
Dr David Lewinsohn, Oregon Health & Science University, USA

12.15 Discussion

12.30 Lunch

Session 4 – Plagues, epidemics and history
Chair – Sir Mark Walport FRS, The Wellcome Trust, UK

13.30 Are occasional human pathogens useful to their host?
Professor Robin Weiss, University College London, UK

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14.15 Should we blame agriculture on all our ills?
Dr Francois Balloux, Imperial College London, UK

14.45 Discussion

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15.30 The role of epistatic interactions between genetic disorders of haemoglobin in determining their global distribution
Professor Sunetra Gupta, University of Oxford, UK

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16.15 Overview and future directions

17.30 Close

18.30 Dinner (for those resident at Kavli on the night of 9 June)

Human evolution – plagues, pathogens and selection

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Session 1 – Where anthropogenetics and history meet

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09.10 Death comes to town: disease resistance, urbanisation and recent selection in human populations

Dr Ian Barnes, Royal Holloway, University of London, UK

The occurrence of infectious disease in the past can be inferred from historical records, artistic representation, and skeletal remains. However the timing of the emergence of key diseases - such as tuberculosis - and the extent to which these diseases have impacted human populations, remains unclear. While molecular genetics may be able to contribute to this area, there are still significant problems in utilising molecular clock techniques, identifying spatial structure in disease populations, and in the recovery of pathogen DNA from archaeological materials. In this talk I will discuss some recent work we have conducted to explore the extent to which the transition to urban living has resulted in an increase in disease-based mortality. If this is the case, we might expect to see evidence of increased disease resistance in longer-term urban populations, as a result of natural selection. Our results support this proposal, demonstrating a highly significant correlation between duration of urban settlement and a well-studied disease resistance allele. Further work is needed to establish the role of relatively recent changes in human ecology in determining health and the genetic structure of populations.

09.40 Discussion

09.55 Hunting the molecular past

Professor Eske Willerslev, University of Copenhagen, Denmark

In the past two decades, ancient DNA research has progressed from the retrieval of small fragments of mitochondrial DNA from a few relatively young specimens, to large-scale studies of ice age populations and whole genome sequencing of an ancient human. Recent methodological advances include DNA preserved in ancient hair shafts, coprolites, sediments and ice. Coupling

these with second generation sequencing technologies ancient DNA has positioned itself as a powerful tool in archaeology, paleontology, ecology and population genetics. Recent breakthroughs include evidence for human occupation in southwestern North America as early as 14,000 years ago (pre-Clovis), a previously unrecognized human migration from the Siberia to the New World around 5,500 years ago, the survival of mammoth and horse in central Alaska to at least 10,500 years ago – long after human arrival, and population dynamics underlying extinction of the ice age megafauna.

10.25 Discussion

10.40 Coffee

11.10 African population history inferred from genomic data
Dr Brenna Henn, Stanford University, USA

Africa is inferred to be the continent of origin for all modern human populations, but the details of human prehistory and evolution in Africa remain largely obscure due to the complex histories of hundreds of distinct populations. Dr Henn will present new genomic data for several African hunter-gatherer populations and seven North African populations. He describes patterns of geographic structure across the entire continent. We find that African hunter-gatherer populations today remain highly differentiated, encompassing major components of variation that are not found in other African populations. The observed patterns are consistent with an origin of modern humans in southern Africa rather than eastern Africa as is generally assumed. Additionally, we estimate demographic parameters such as the timing and magnitude of bottlenecks, and the time of divergence of North African populations. Genetic variation in African hunter-gatherer populations has been significantly affected by interaction with farmers and herders over the past 5,000 years, through both severe population bottlenecks and sex-biased migration. However, African hunter-gatherer populations continue to maintain the highest levels of genetic diversity in the world.

11.40 Discussion

11.55 Archaeogenetics and the settlement of the Remote Pacific
Professor Martin Richards, University of Leeds, UK

The Polynesians are usually thought, primarily on grounds of historical linguistics, to have originated in a dispersal of Austronesian speaking rice farming communities from Taiwan about 4000 years (4 ka) ago, but evidence from archaeogenetics is challenging this consensus. Y-chromosome evidence suggests a largely Near Oceanic ancestry for Polynesians, but until recently the mitochondrial DNA (mtDNA) has been assumed to support the "out of Taiwan" dispersal, suggesting overall a "slow-boat" model in which paternal lineages were picked up *en route* in Near Oceania. By analysing complete mtDNA genomes, we show that although ultimately arising in Island Southeast Asia, Polynesian maternal lineages gained a foothold in Near Oceania at least 3 ka earlier than dispersal from Taiwan 4–3 ka would predict. At the same time, we also find evidence for small-scale two-

way Holocene maternal gene flow between Island Southeast Asia and Near Oceania, likely reflecting movements along a "voyaging corridor" between them, as previously proposed on archaeological grounds. The associated mid-Holocene arrival in the Bismarck Archipelago of small numbers of Southeast Asian mtDNAs may reflect an élite cultural stimulus from the west, perhaps then providing the impetus for the expansion into Polynesia.

12.25 Discussion

12.40 Lunch

Session 2 – Human migration, genes and language
Chair – Professor Danny Altmann, Imperial College London, UK

13.40 Insights into human genome variation from the 1000 Genomes Project
Dr Chris Tyler-Smith, The Wellcome Trust Sanger Institute, UK

The 1000 Genomes Project is using next-generation sequencing technologies to sequence 2,500 individuals genomewide. We are learning a lot from the project about how to use these technologies, and, although not its main aim, it is also providing powerful insights into human evolution.

The donors come from 27 populations from five continental regions: sub-Saharan Africa, Europe, South Asia, East Asia and the Americas. The primary aim of the project is to discover genetic variants of many kinds (SNPs, indels, structural variants) for subsequent medical genetics projects. The populations were consequently chosen for their relevance to medical rather than anthropological or evolutionary genetics: they include urban, admixed and expatriate samples. When the project was launched in 2008, the potential of the then-new sequencing technologies to produce reliable data on this scale was unclear, and so it began with a pilot phase, completed in 2010. The pilot showed that the variants the project set out to discover could be discovered very effectively by combining information from low-coverage sequencing of multiple individuals, and the project has subsequently gone on to sequence over 1,000 individuals using this strategy, with all information made freely available.

Genomewide sequencing has provided a nearly unbiased view of the distribution of genetic variation along the genome and within different populations. It shows expected features such as the highest diversity within Africa, but also less expected ones such as how the effect of negative selection has decreased diversity at distances of up to 100 kb from genes, implying that few regions of our genome entirely escape the influence of natural selection. Probably as a consequence of this ubiquitous negative selection, functional variants are both rarer and more geographically restricted than nearly-neutral ones. There is a surprising amount of variation in the number of functional genes in the genomes of different healthy individuals, with about 140 loss-of-function variants and 30 genes homozygously inactivated per individual. The project has also provided a comprehensive catalogue of genes showing a signature of positive selection, and while the selective force is completely unknown for most of these, this catalogue is an excellent starting point for further investigations. Overall, the project is providing information on human genetic variation on a scale that was inconceivable just a few years ago.

14.10 Discussion

14.25 Language evolution in time and space
Dr Quentin Atkinson, The University of Auckland, New Zealand

Recent work in computational historical linguistics has successfully applied phylogenetic methods from biology to linguistic data to test hypotheses about language family relationships, chronology, and the tempo and mode of language evolution. However, relatively little attention has focussed on explicitly modelling large-scale spatial processes of language change. Here Dr Atkinson reports results from collaborative research that uses tools from population genetics and phylogeography to analyze spatial information derived from comparative linguistic data. This work identifies clear spatial signal in the data that can be used to shed light on the origins of the world's major language families.

14.55 Discussion

15.10 Tea

15.40 Reconstruction of ancient migrations using multiple lines of evidence
Dr Stephen Oppenheimer, University of Oxford, UK

Speculation on origins of different human groups goes back to Herodotus, the first historian, and has relied on morphological, pigmentary, cultural and linguistic generalisations - and, over the last century, on comparisons of relative allele frequency at multiple loci. Geographically highly specific globin gene mutations, that protect against malaria, were used in the 1980's to trace migrations out of Africa and in the Pacific. Use of the distribution of geographically specific mutations was also extended, to the study of non-recombining uniparental loci, using genetic phylogeography with large, detailed, geographically-specific gene trees. Genetics has demonstrably replaced linguistics and archaeology as the most direct window on physical migration, but requires testable models, derived from archaeological, cultural, linguistic, morphological and Palaeo-climatic contexts. Language trees are the oldest, most tempting proxy, but being mainly culturally determined and liable to rapid switching, they suggest more people movement than the uniparental genetic record supports. Genetically-based models themselves offer predictions, which can be tested using genetic evidence, but also using context provided by the other disciplines. Examples are given of multidisciplinary synthesis including out-of-Africa and back, skin colour distribution, Pacific migrations and archaic human admixture.

16.10 Discussion

16.25 Reconstructing the mode and tempo of the out-of-Africa migration of anatomically modern humans
Dr Andrea Manica, University of Cambridge, UK

Current geographic patterns of genetic diversity have been influenced profoundly by ancient demographic events. Simple models reconstructing the expansion of anatomically modern humans out of Africa 50-70K years ago have been shown to do a remarkable job at explaining the major global trends in genetic diversity of modern populations. However, a close investigation of several descriptors of diversity reveals clear departures from the simple models.

We have developed a geographically and demographic explicit model that incorporates climate and vegetation reconstructions for the last 100K years. This model shows that climate was an important factor in determining the timing and tempo of human expansions, and provides a powerful null model for the investigation of selection through time and space.

16.55 Discussion

17.10 General discussion

17.40 End of day 1

18.30 Pre-dinner drinks

18.45 Dinner

Day 2 – Thursday 9 June 2011

Session 3 – Evolutionary pressure and the immune system
Chair – Dr Danny Douek, Vaccine Research Center, National Institutes of Health, USA

09.00 Evolution of the HLA-C 3'UTR and its effect on HIV control
Dr Mary Carrington, SAIC-Frederick Inc and Ragon Institute of MGH, MIT and Harvard, USA

Differential expression of HLA-C allotypes is mediated by the binding of miR-148a to the 3'untranslated region of some, but not all HLA-C alleles. The binding results in lower levels of HLA-C expression, which associates with higher levels of HIV-1 viral load among infected individuals. The alternative set of HLA-C alleles has several substitutions in the miR-148a binding site that prevent binding and HLA-C downregulation; these high expression alleles associate with control of HIV-1 viral load. Our analyses show that the common ancestor of all extant HLA-C alleles was suppressed by miR-148a. Substitutions that prevent miR-148a binding arose by a sequence exchange event between an HLA-C allele and an HLA-B allele of a B*07-like lineage. The event occurred 3-5MYA, resulting in an HLA-C variant that escaped from miR-148a downregulation. Selection appears to have played a role in the successful spread of the HLA-C escape alleles, giving rise to seven of the fourteen extant HLA-C lineages. Notably, critical peptide and KIR binding residues of the escape variants have selectively converged to resemble the sequence of their inhibited counterparts such that the inhibited and escape groupings differ primarily by their levels of expression.

09.30 Discussion

09.45 Population-specific evolution of Natural Killer cell diversity
Dr Paul Norman, Stanford University, USA

Human population survival requires both disease resistance and reproductive success, but the immune functions that enable response to diverse pathogens and ensure successful pregnancy are not always mutually beneficial. Natural Killer cells mediate these distinct activities through Killer-cell Immunoglobulin-like Receptors (KIR) that interact with Human Leukocyte Antigen (HLA) Class I molecules on tissue cells. Strong inhibitory interactions favour infection control and weak activating interactions favour reproduction. Segregating independently, three *HLA Class I*, and 5-14 *KIR* are among the most polymorphic human genes. Study of human populations and comparison with primate species show that KIR are evolving rapidly, with natural selection highly focused towards modifying KIR/HLA interactions. Distinct HLA alleles have increased in frequency in isolated human populations, likely in response to specific pathogen threat. In turn, unique KIR mutations have evolved that affect HLA binding strength or alter its specificity, and thus promote or diminish the infection-response. Through cycles of relative importance between disease and reproduction, a balance of distinct KIR and HLA interactions has been maintained in all human populations.

10.15 Discussion

10.30 Coffee

11.00 Origin of Amerindians and their genetic relatedness with Asian and Pacific islanders
Dr Antonio Arnaiz-Villena, Universidad Complutense, Spain

The classical three-waves theory of American peopling through Beringia (Amerindians, Athabascans, Eskimos) was based on a mixed anthropological and linguistic methodology. The use of mtDNA, Y chromosome and other DNA markers offers different results according to the different markers and methodologies chosen by different authors. At present, the peopling of Americas remains uncertain, regarding time of population, number of peopling waves and place of peopling entrance among other related issues. We have gathered our own and most available autosomal HLA data already obtained about First Native American populations, which raise some doubts about the classical three waves of American peopling hypothesis. Our conclusions by using both population frequency and genealogy markers study conclusions are: North West Canadian Athabaskans have had gene flow with Asians, Amerindians and Pacific Islanders; Amerindians entrance to America may have been different to that of Athabaskans and Eskimos and Amerindians may have been in their lands long before Athabaskans and Eskimos; Amerindians show very few "particular alleles", almost all are shared with other Amerindians, Athabaskans and Pacific Islanders, including East Australians and Siberians; our results do not support the three waves model of American peopling, but another model where the people entrance is not only Beringia, but also Pacific Coast. Reverse migration (America to Asia) is not discarded and different movements of people in either direction in different times are supported by the Athabaskan(North West Canada) population admixture with Asian-Pacific population and with Amerindians; HLA haplotype variability is more common than allele variability in Amerindians.

11.30 Discussion

11.45 Recognition of the Mtb-infected Cell: a fine line between innate and adaptive immunity
Dr David Lewinsohn, Oregon Health & Science University, USA

Mycobacterium tuberculosis (Mtb), which causes tuberculosis (TB), remains a leading cause of infectious disease mortality worldwide. Control of Mtb is critically dependent on the ability of immune cells to detect those cells infected with Mtb and in this regard CD8+ T cells are uniquely able to detect intracellular infection.

In humans, CD8+ T cell recognition of intracellular infection requires the interaction of a specific receptor on the T cell (the T cell receptor; TCR) with ligand presented in the context of the major human histocompatibility system (HLA). Diversity in both TCR and HLA allow for broad recognition of peptide ligands. These classical, or HLA-Ia restricted responses allow for the successful development of memory following antigenic exposure. In contrast, non-classical, or HLA-Ib restricted responses often reflect limited diversity of both TCR and HLA molecules, and hence are often associated with recognition of unique features of the intracellular pathogen. While HLA-Ia restricted CD8+ T cells predominate in those with active TB infection, both TB-exposed and unexposed humans contain high frequencies of Mtb-reactive non-classically restricted CD8+ T cells. Interestingly, these Mtb-reactive cells expressed the Vα7.2 T- TCR and were restricted by the HLA-Ib molecule MR1. These properties are all characteristics of mucosal associated invariant T cells (MAIT), an "innate" T-cell population of previously unknown function. These MAIT cells also detect cells infected with other bacteria. Direct ex vivo analysis demonstrates that Mtb-reactive MAIT cells are decreased in peripheral blood mononuclear cells

(PBMCs) from individuals with active tuberculosis, are enriched in human lung, and respond to Mtb-infected MR1-expressing lung epithelial cells.

Here we report that human MAIT cells from the thymus are naive cells yet have innate effector capacity in response to Mtb-infected cells. In addition, MAIT cells in the thymus and periphery express the transcription factor PLZF, a marker associated with innate effector function. However, MAIT cells phenotypically differentiate from the thymus to the peripheral blood suggesting MAIT cells mature after thymic egress. These findings, then, suggest that innately derived T cells have the capacity to undergo further maturation, presumably the result of environmental exposures.

12.15 Discussion

12.30 Lunch

Session 4 – Plagues, epidemics and history
Chair – Sir Mark Walport FRS, The Wellcome Trust, UK

13.30 Are occasional human pathogens useful to their host?
Professor Robin Weiss, University College London, UK

Human pathogens may be regarded as having two main origins: 'family heirlooms' which co-evolved with their host, and 'new acquisitions' which have recently originated from zoonotic infections and which adapted to human-to-human transmission. The former tend to be endemic infections and the latter epidemic. I shall argue that some heirloom viruses may be of selective value to humans in two ways. First, the virus may protect the host against a more virulent infection, analagous to the selection for genetic haemoglobinopathies because heterozygotes are protected against malaria. Second, viruses which cause mild symptoms or seldom cause disease in the human host may have been lethal to competing hominid species, analogous to the virulence of New World myxomatosis virus when introduced into Old World rabbits.

14.00 Discussion

14.15 Should we blame agriculture on all our ills?
Dr Francois Balloux, Imperial College London, UK

The advent of agriculture is often blamed for all sorts of afflictions affecting humans and essentially all major human pathogens have been hypothesised to have started infecting our ancestors as a consequence of the Neolithic revolution. The tremendous progress in sequencing technology over the last years has allowed revisiting the age of such host-pathogen associations for a variety of human pathogens. While many of these dates remain questionable and may need being revisited in the future, it is fair to say that the vast majority of studies exculpate agriculture as the source of all ailments. Estimates for bacteria and parasites tend to point to more ancient associations, whereas dates for viruses tend to point to far more recent associations. I will highlight a few particularly interesting examples from the most recent literature, and finish the talk by a critical assessment of the limitation of the current estimates.

14.45 Discussion

15.00 Tea

15.30 The role of epistatic interactions between genetic disorders of haemoglobin in determining their global distribution
Professor Sunetra Gupta, University of Oxford, UK

It is widely recognised that human genetic disorders of haemoglobin have risen in frequency due to the protection they offer against death from malaria. We propose that the complex geographical distribution of globin mutants can be explained by their specific intracellular interactions. We have shown that cancellation of malaria protection among individuals inheriting both α-thalassaemia and sickle cell trait can explain why α-thalassaemia fails to reach fixation in sub-Saharan Africa. By combining into this model the observation individuals co-inheriting α- and β-thalassaemia sustain a reduction in blood disorder severity, we can also explain why the highly protective sickle mutant is uncommon in Mediterranean populations which instead harbour a diverse range of thalassaemic haemoglobin disorders. I will discuss some of the implications of this theoretical framework for other regions such as South-East Asia, and also what it can tell us about the mechanisms of malaria protection.

16.00 Discussion

16.15 Overview and future directions

17.00 Close

18.30 Dinner (for those resident at Kavli on the night of 9 June)

Biographies

Professor Danny Altmann, Imperial College London, UK (Organiser/Chair)
Danny Altmann is Professor of Immunology in the Department of Medicine, Imperial College London and, as of 2011, Head of Pathogens, Immunity and Population Health at the Wellcome Trust. He is also Editor in Chief of Immunology. As Head of the Human Disease Immunogenetics Group, his major research interest has been in the immunogenetics of autoimmune diseases and bacterial infections. This has in recent years included a major emphasis on T cell immunity to serious bacterial infections. Prior to joining Imperial College he was a senior scientist in the Medical Research Council Clinical Sciences Centre.

Dr Antonio Arnaiz-Villena, Universidad Complutense, Spain (Speaker)
Antonio Arnaiz Villena is presently Head of Immunology and Microbiology I Department at University Complutense and Hospital 12 de Octubre in Madrid, Spain. He was born and studied Biology and Medicine in Madrid. He accomplished post-doctoral research during 9 years in the UK at the Middlesex Hospital Medical School (Professor Roitt) and at the London Hospital Medical College (Professor Festenstein). He came back to Spain and set up Immunology and Genetics laboratories in the Spanish National Health Service in Madrid (Hospital Ramon y Cajal, The Madrid Regional Blood Center and Hospital 12 de Octubre). He was also appointed in Madrid Full Professor of Immunology by an International Board, including Pablo Rubinstein and Antonio Coutinho. He has established Immunology teaching at Biochemistry, Medicine, Biology, Pharmacology, Veterinary Faculties at University Complutense, Madrid. He has served 5 years as elected President of the Spanish Society for Immunology and 14 years in the Government Spanish Board for Specialists. He has published 341 papers in international magazines, published 8 books and directed 48 PhD Doctoral Theses in Immunology,Human and Bird Population Genetics and Linguistics.

Dr Quentin Atkinson, The University of Auckland, New Zealand (Speaker)
Dr Atkinson has recently taken up a post as Senior Lecturer in the Department of Psychology at the University of Auckland. Prior to this, he spent 3 years at the University of Oxford as a Research Fellow in the Institute of Cognitive and Evolutionary Anthropology. His research interests cover a range of areas related to genetic and cultural evolution in modern humans. This includes work on the evolution of language, religion, large-scale cooperation, and the human expansion from Africa.

Dr François Balloux, Imperial College London, UK (Organiser/Speaker)
François Balloux is a Reader in the Department of Infectious Disease Epidemiology at Imperial College. He was trained as a population geneticist and obtained his PhD in 2000 from the University of Lausanne (Switzerland). After a postdoc at the University of Edinburgh, he was offered a faculty position in the Department of Genetics in Cambridge in 2002. There, he led a group working on human evolutionary genetics for five years but became increasingly interested in the evolution of human pathogens and the interplay with their host. In 2007, he joined the Department of Infectious Disease Epidemiology at Imperial College and the newly founded MRC Outbreaks Centre.

Dr Ian Barnes, Royal Holloway, University of London, UK (Speaker)
Ian Barnes is Reader in Molecular Palaeobiology at Royal Holloway, University of London. Since completing his DPhil at the University of York, he has worked at the University of Oxford, and University College London (as a Wellcome Trust Fellow). In 2005 he was awarded a NERC Fellowship, moving to Royal Holloway. He has worked in the field of ancient DNA since 1994, conducting studies on plant, fungi, bacterial, avian and mammal DNA, with a focus on the study of ecological and evolutionary change through time. Dr Barnes has a first degree in archaeological science, and continues to work at the interface of archaeology, palaeontology and molecular biology. He has been particularly involved in exploring the potential for the recovery of bacterial pathogens in archaeological material, and more recently the use of host disease resistance as a proxy for long-term population exposure to pathogens.

Dr Rosemary Boyton, Imperial College London, UK (Organiser)
Dr Rosemary Boyton heads the Lung Immunology Group, Department of Medicine that is focused on the molecular immunology of lung disease. Research interests include innate and adaptive immune mechanisms in the regulation of infectious and allergic lung inflammation. She is a Consultant Physician in Respiratory Medicine at Royal Brompton Hospital with a specialist interest in Respiratory Infection.

Dr Mary Carrington, SAIC-Frederick Inc and Ragon Institute of MGH, MIT and Harvard, USA (Speaker)
Dr Carrington obtained her PhD in Immunobiology at Iowa State University in 1982. She performed her postdoctoral studies in the departments of Immunology and Microbiology at Duke University and the University of North Carolina, respectively. Subsequently she joined the Immunology Department at Duke University as a faculty member from 1985-1989. Dr Carrington began her career at the NCI-Frederick in 1989 as a Principal Scientist in the HLA Immunogenetics Laboratory and later became Head of the laboratory. Her laboratory has been involved in characterizing the influence of host genetics on cancer, autoimmunity and, in particular, infectious disease pathogenesis. She is a member of the International Council on Immunogenetics and Histocompatibility, the steering committee of the Ragon Institute of MGH, MIT and Harvard, the CCR/DCEG Human Genomics & Genetics Leadership group, the Center of Excellence in Integrative Cancer Biology and Genomics steering committee, the Center of Excellence in HIV/AIDS, and the Global HIV Vaccine Enterprise. Dr Carrington became Director of the Basic Sciences Program in 2002. As Director, she is responsible for the guidance and oversight of a large and diverse group of scientists in investigator-initiated hypothesis-driven basic research.

Dr Danny Douek, Vaccine Research Center, National Institutes of Health, USA (Chair)
Dr Douek studied medicine at the Universities of Oxford and London. He then practiced internal medicine, before pursuing a PhD in Immunology at the University of London. Dr Douek was appointed to the NIH Vaccine Research Center in November 2000. His laboratory, the Human Immunology Section, studies the processes that determine the course of human diseases in which the immune system, particularly its T cell arm, plays a central role in their pathogenesis and outcome. He aims to use the knowledge gained to initiate clinical studies of new therapeutic and vaccine approaches. Dr Douek is a widely published author in the field of human immunology and currently the main focus of his lab is both the pathogenesis and immune control of HIV infection. In 2007 Dr Douek was given the World AIDS day Award.

Professor Sunetra Gupta, University of Oxford, UK (Speaker)
Sunetra Gupta is Professor of Theoretical Epidemiology in the Department of Zoology at the University of Oxford. She graduated in 1987 from Princeton University with a degree in Biology, and received her PhD from Imperial College, London in 1992. Her research focuses on the dynamics of parasite population diversity and the evolution of host genetic diversity in infectious disease systems.

Dr Brenna Henn, Stanford University, USA (Speaker)
Brenna Henn began her PhD by studying the deep population structure and complex migration patterns of African hunter-gatherer groups. She continues to have an abiding interest in diverse, indigenous populations from around the world who harbor genetic (and linguistic and phenotypic) variation that is often absent in regularly studied populations. Motivated by her prior PhD (2009) training in anthropology and evolutionary genetics at Stanford University, she aims to approach questions of genetic and phenotypic diversity from an interdisciplinary standpoint. After a 'personal genomics' interlude at 23andMe, Inc, she began a postdoctoral position in Dr Carlos Bustamante's lab at the Stanford University School of Medicine. She currently leads projects to infer African demographic history from genomic data and model selection in hunter-gatherer populations.

Dr David Lewinsohn, Oregon Health & Science University, USA (Speaker)
David M Lewinsohn is Professor of Medicine and Adjunct Professor of Molecular Microbiology & Immunology at Oregon Health and Sciences University, and the Portland VA Medical Center. Dr Lewinsohn received his undergraduate degree from Haverford College, his MD and PhD from Stanford University School of Medicine, internal medicine training at the University of California, San Francisco, and fellowship training in Pulmonary and Critical Care Medicine at the University of Washington.
Dr Lewinsohn's research interest is in Tuberculosis Immunology. He is particularly interested in the mechanisms by which the human immune system can recognize those cells harboring Mtb. Dr Lewinsohn's research program has focused on the role of both classically and non-classically restricted CD8+ T cells such as those restricted by HLA-E and more recently MR1. More recently, the laboratory has begun to explore the ability of lung epithelial cells to become infected with Mtb, and the mechanisms by which recognition of these cells may lead to the control of intracellular infection. Dr Lewinsohn's research has been supported by the ALA, the NIH, and the VA. His is also the recipient of an NIH Bioterrorism contract to comprehensively define human CD8 antigens and epitopes in Mycobacterium tuberculosis.

Dr Andrea Manica, University of Cambridge, UK (Speaker)
Andrea Manica is a Senior Lecturer in Zoology at the University of Cambridge. His group uses spatial models to look a variety of ecological and evolutionary questions. His work in population genetics has mostly focussed on reconstructing the out-of-Africa migration by anatomically modern humans that led to their spread across the globe.

Dr Paul Norman, Stanford University, USA (Speaker)
Paul Norman's long-term research goal is to understand how genetic factors lead to individual differences in immune responses, with application towards improving human health. His initial training was in the clinical transplantation laboratory of Guy's Hospital London where he studied the genetics of HLA, arguably the most highly variable molecules in humans. Whilst at Guy's he also investigated genes that govern individual variation in the number of circulating immune cells, in collaboration with the Human Genetics Department at the University of Utah. During his PhD at King's College London and subsequent research career at Stanford University in the laboratory of Professor Peter Parham he has continued to explore the genetics of immune cell receptors. He has been specializing on the 'KIR' natural killer cell

receptors, their impact on immune function through interaction with HLA and, importantly, their extraordinary genetic diversity. KIR genes vary in number between individuals and populations and are also highly polymorphic. By studying how natural selection has defined HLA and KIR variants and their distribution in modern human populations we have begun to understand how they interact with each other and ultimately modulate immune function.

Dr Stephen Oppenheimer, University of Oxford, UK (Speaker)
Dr Oppenheime qualified in medicine Oxford 1971.1972-97: he spent a total of 17 years, located in the tropics as a paediatrician, with intervening time spent in English universities (London, Oxford, and Liverpool) as bases for overseas secondment. He has published extensively, focussing on the interactions between iron, nutrition, genetics (particularly α+-thalassaemia) and infections esp malaria. He was Professor of Paediatrics in Malaysia then HK from 1987-94.

1997-present: he returned to Oxford for children's education. He published first book 'Eden in the East: the drowned continent of Southeast Asia' in 1998, a multidisciplinary reconstruction of prehistoric migrations in Southeast Asia and the Pacific using climatology, oceanography, archaeology, genetics, linguistics and cultural anthropology. This was followed by two similar, more genetically focussed books "Out of Eden: the Peopling of the World" 2003 and "The Origins of the British: a genetic detective story", 2006.

He has continued collaborative research with numerous peer-reviewed publications supporting the original reconstructions in his three books. He is adviser and talking head in a number of related TV documentaries.

Professor Peter Parham FRS, Stanford University, USA (Chair)
Growing up in London, Peter Parham studied Natural Sciences at Cambridge University and then went as a Kennedy Scholar to Harvard University, where he obtained a PhD for structural studies on HLA class I performed in Jack Strominger's laboratory. As a Junior Fellow of the Harvard Society of Fellows Parham spent a year in Walter Bodmer's group at Oxford University, where with Frances Brodsky he developed monoclonal antibodies against HLA class I and II. Peter Parham joined the faculty at Stanford University in 1980, where he is now Professor of Structural Biology and Microbiology & Immunology. Parham's research concentrates on the genetics and evolution of MHC class I polymorphisms and their functional interactions with rapidly evolving and comparably polymorphic lymphocyte receptors.

Professor Martin Richards, University of Leeds, UK (Speaker)
Martin B Richards is Professor of Archaeogenetics at the University of Leeds, UK. He studied genetics at the Universities of Sheffield and Manchester, moving to Oxford University and into archaeogenetic research in 1990. From there, he developed collaborative links with a small group of like-minded colleagues who spearheaded the use of network diagrams in the phylogenetic and phylogeographic analysis of human mitochondrial DNA (mtDNA). This enjoyable collaboration was to yield influential models for the settlement of both Europe and the Pacific, and for prehistoric dispersals in Africa. He subsequently moved to UCL, Huddersfield and then Leeds University, where he now teaches, amongst other topics, human evolution, molecular evolution and bioinformatics. His research in the last decade has particularly sought to apply complete mtDNA genome variation to archaeogenetic questions, such as the route taken by modern humans dispersing out of Africa and the settlement of Southeast Asia and the Pacific – most recently returning his focus to the continuing controversy over the settlement of Europe. He co-edited Mitochondrial DNA and the Evolution of Homo Sapiens (Springer-Verlag, 2006) with Hans-Jürgen Bandelt and Vincent Macaulay.

Dr Chris Tyler-Smith, The Wellcome Trust Sanger Institute, UK (Speaker)
Dr Chris Tyler-Smith is head of the Human Evolution team at The Wellcome Trust Sanger Institute. His background is in human molecular and evolutionary genetics, and from 1987 to 2003, his research concentrated on understanding the structure and function of human centromeres, responsible for proper segregation of chromosomes when the cell divides.

This work used the Y chromosome centromere as its model, and during this period he developed an interest in the use of variation on the Y chromosome to provide insights into aspects of human history and evolution.

In 2003, he moved to The Sanger Institute, and concentrated on human evolution. While his interest in the use of neutral markers such as the Y chromosome and mitochondrial DNA continues, particularly as part of the Genographic Project, the main thrust of his work is now directed towards investigating the way natural selection has shaped modern humans. In order to do this, they document the extent of genetic variation, including structural variation, in human populations. This is done as part of the Genome Structural Variation consortium and the 1000 Genomes Project. They are then particularly interested in identifying regions of the genome that have experienced recent positive selection in humans.
TBC

Sir Mark Walport FRS, The Wellcome Trust, UK (Chair)
Mark Walport is Director of the Wellcome Trust, which is a global charitable foundation dedicated to achieving extraordinary improvements in health by supporting the brightest minds. Before joining the Trust he was Professor of Medicine and Head of the Division of Medicine at Imperial College London.
He is a member of the Prime Minister's Council for Science and Technology, the India UK CEO Forum, the UK India Round Table, the advisory board of Infrastructure UK and a non-executive member of the Office for Strategic Coordination of Health Research. He is also a member of a number of international advisory bodies.
He has undertaken independent reviews for the UK Government on the use and sharing of personal information in the public and private sectors: 'Data Sharing Review' (2009) and secondary education, 'Science and Mathematics: Secondary Education for the 21st Century' (2010). He received a knighthood in the 2009 New Year Honours List for services to medical research and was elected to the Fellowship of the Royal Society in 2011.

Professor Robin Weiss FRS, University College London, UK (Speaker)
Professor Robin Weiss FRS is a Senior Research Fellow at University College London. He has made pioneering contributions to HIV and AIDS research, most notably the identification of CD4 as the HIV receptor on cells, and the neutralization of HIV by antibodies. He has worked on AIDS-associated cancers such as Kaposi's sarcoma and is currently investigating HIV vaccine development supported by the Bill & Melinda Gates Foundation. Early in his career, Professor Weiss found that retroviral genomes can be inherited as Mendelian traits in host DNA, marking the discovery of endogenous retroviruses, and he later investigated whether endogenous retroviruses of pigs could potentially be transferred to humans during xenotransplantation. From 1980 to 1990, he was Director of the Institute of Cancer Research, London. His current interests include the origins of pandemic infections. He is a past President of the Society for General Microbiology.

Professor Eske Willerslev, Centre of GeoGenetics, Natural History Museum of Denmark, Denmark (Speaker)

Eske Willerslev is director for Centre of Excellence in GeoGenetics and the National CryoBank and Sequencing Facility, situated at the National History Museum, University of Copenhagen. His research interests include: human evolution, palaeoecology, palaeontology, domestication, DNA degradation and repair, macroevolution, molecular evolution, barcoding, and genomics. He did his doctorate at University of Copenhagen and a Wellcome Trust Fellowship at Oxford University, UK. He has also been a visitor at MD Anderson Cancer Research Centre in Texas, US. His group established the fields of sedimentary ancient DNA (Science 2003), and ice core genetics (Science 2007), and were the first to sequence the complete mitochondrial DNA genome (Science 2008) and nuclear genome (Nature 2010) of ancient humans.