FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Ketan J. Patel

MRC Laboratory of Molecular Biology, Cambridge, UK

Tuesday, 10 October 2017, 09:00 – 09:30

Alcohol, Metabolism and Endogenous DNA damage

I shall talk about the identification of reactive of aldehydes as a major source of endogenous DNA damage. I will begin by describing with the human cancer prone illness Fanconi Anaemia, such individuals lack a pathway to repair DNA crosslinks. However until recently we did not know what factors caused such DNA crosslinks, our research showed that the aldehydes formaldehyde and acetaldehyde are such factors that cause DNA crosslinks. I will show how a two tier protection system in mammals prevents such aldehydes from causing lethal DNA damage. I will finish my talk with new work that identifies the source of endogenous formaldehyde and how the body may utilise this molecule to make DNA.

References

Barragan G, Witt N, Dingler F, Mulderrig L, Pontel L, Rosado I, Brewer T, Chang C, and Patel K.J (2017) 'Mammals divert endogenous genotoxic formaldehyde into one carbon metabolism' Nature (article) 548, 549- 554.

Garaycochea J, Crossan G, Langevin F, Mulderrig L, Gibuad G, Gomes S, Yang Y, Roerink S, Nik-Zainal S, Stratton M, and Patel K.J (2017) 'Alcohol and endogenous aldehydes rearrange chromosomes and mutate stem cell genomes' Nature (article) in press

Biography

Dr KJ Patel trained in medicine but also has spent his research career at the MRC Laboratory of Molecular Biology, Cambridge one of the premier research institutes in the world. His work focuses on the molecular basis of inherited genomic instability and the role it plays in the biology of stem cells.
His research has led to new insights into how toxic molecules released from metabolism can damage the DNA of stem cells, particularly in those that produce blood. Studies carried out by his laboratory have uncovered how the body defends itself against these toxic metabolites through a dual protection mechanism that involves degradation of these metabolites and a specific form of DNA repair, the Fanconi anaemia DNA repair pathway. An important aspect of this work has also shown how the toxic by-product of alcohol metabolism, acetaldehyde, damages DNA and may contribute to diseases associated with ethanol exposure, such as fetal alcohol syndrome, bone marrow dysfunction and certain cancers.
He has received prestigious awards and prizes for his work. He is also a Fellow of the Royal Society (FRS), a member of EMBO and a Fellow of the Academy of Medical Sciences UK (FMedSci).

http://www2.mrc-lmb.cam.ac.uk/group-leaders/n-to-s/kj-patel/

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Stephen West

2007 Louis-Jeantet Prize winner

The Francis Crick Institute, London, UK

Tuesday, 10 October 2017, 09:30 – 10:00

Unresolved recombination intermediates as a source of DNA breaks and chromosome aberrations

DNA repair promoted by homologous recombination leads to the formation of recombination intermediates that physically link sister chromatids. Removal of these recombination intermediates is essential for the equal segregation of DNA to daughter cells at mitosis, and requires the MUS81-EME1 and GEN1 endonucleases. MUS81-EME1 is activated at prometaphase by formation of the SMX tri-nuclease containing three DNA repair structure-selective endonucleases: SLX1-SLX4, MUS81-EME1 and XPF-ERCC1. Within SMX, SLX4 co-ordinates the SLX1 and MUS81-EME1 nucleases for Holliday junction resolution, in a reaction stimulated by XPF-ERCC1. Cell cycle-dependent formation of this repair tri-nuclease complex provides an unparalleled mechanism by which human cells utilize existing resources to ensure chromosome segregation. To further understand their genetic interactions and functions, resolvase-defective knock out human cell lines were generated. Although the GEN1 k/o showed little cellular defect, the additional depletion of MUS81 induced massive cell death and severe cell cycle delay. This phenotype occurs in undamaged cells showing that the resolvases are essential for cell survival. The MUS81/GEN1-deficient cells displayed an elevated frequency of lagging chromosomes and DNA ultra-fine bridges (UFBs), that were distinct from previously described replication stress-induced UFBs and centromeric UFBs. The anaphase bridges are broken at cell division, leading to activation of the DNA damage response and aberrant chromosome fusions. These studies show that SMX and GEN1 promote a critical role in the resolution of recombination intermediates, and that their loss of function leads to a failure in chromosome segregation, resulting in DNA damage and genome instability.

Biography

Stephen West received his PhD in biochemistry from Newcastle University, England in 1977, and carried out his post-doctoral work with Paul Howard-Flanders at Yale University. Steve moved back to the UK in 1985 and is now Senior Group Leader at the Francis Crick Institute in London. Steve's work focuses on the mechanisms of DNA repair by homologous recombination, and the links between repair defects, genome instability and cancer. Steve has received numerous awards for his scientific achievements: he is a Fellow of the Royal Society (UK) and a Foreign Associate of the National Academy of Sciences (USA). He was awarded the Louis-Jeantet Prize for Medicine in 2007.

https://www.crick.ac.uk/stephen-west

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Titia de Lange

Rockefeller University, New York, USA

Tuesday, 10 October 2017, 10:00 – 10:30

Telomeres and genome instability in cancer - How shelterin solves the telomere end-protection problem

Telomeres serve to protect chromosome ends from DSB repair (HR and NHEJ) and the ATM and ATR DNA damage signaling pathways. This so-called end-protection problem is solved through the agency of shelterin, a six-subunit telomere specific protein complex. Shelterin is composed of the ds telomeric DNA binding proteins, TRF1 and TRF2, and contains a ss telomeric DNA binding factor, POT1 (POT1a and POT1b in mice). These three DNA binding proteins interact with three additional shelterin subunits (Rap1, TIN2 and TPP1) to form a stable telomeric DNA binding unit. Shelterin is functionally compartmentalized such that different subunits are dedicated to separate DNA damage response (DDR) pathways. For instance, TRF2 represses the ATM kinase and NHEJ whereas POT1 prevents activation ATR signaling and contributes to repression of HR. Current work is focused on the mechanisms by which the shelterin subunits accomplish their tasks. Specifically, we showed that TRF2 promotes the formation of the t-loop structure, which provides an architectural solution to the end-protection problem by hiding the telomere end from the end-loading factors that initiate ATM signaling and NHEJ. We will present additional experiments testing this model and new data on how TRF2 uses a branched DNA binding to protect the t-loop structure from Holliday Junction resolvases. We have proposed that the mechanism by which POT1 protects telomeres involves competition with RPA for the single-stranded telomeric DNA, thus preventing the RPA dependent activation of ATR signaling. An important aspect of this model is that POT1, being tethered to the rest of shelterin has an advantage over RPA in retaining its association with telomeric DNA. A prediction of this model is that tethering of a different ss DNA binding domain in place of POT1 would also repress RPA binding and thus ATR activation, which is indeed the case.

Biography

Dr. de Lange earned a Ph.D. in biochemistry at the Dutch Cancer Center working with Piet Borst and did postdoctoral with Harold Varmus at UCSF. She joined Rockefeller University in 1990 where she is the Leon Hess Professor in Cell Biology and Genetics and directs the Anderson Center for Cancer Research. She received the Breakthrough Prize in Life Sciences, the Canada Gairdner International Award, the Vilcek Prize and the Dr. H. P. Heineken Prize and has been elected to the U.S. National Academies of Sciences and the Medicine, the American Academy of Arts and Sciences, EMBO, and the two Dutch Royal Academies.

delangelab.org

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Thanos Halazonetis

University of Geneva, Geneva, Switzerland

Tuesday, 10 October 2017, 11:00 – 11:30

Mechanisms of oncogene-induced DNA replication stress

Genomic instability is one of the most important factors driving cancer progression and resistance to therapy. Oncogenes, by inducing DNA replication stress, are a critical factor underlying genomic instability in cancer, but the mechanisms by which oncogenes cause DNA replication stress have remained largely elusive. A major impediment has been mapping DNA replication initiation sites in the human genome, which is a prerequisite for understanding how oncogenes affect DNA replication. In this study, using a sensitive assay to monitor nascent DNA synthesis in early S phase, we identified thousands of replication initiation sites in cells before and after induction of the oncogenes CCNE1 or MYC. Remarkably, both oncogenes induced the firing of many novel, overlapping DNA replication origins that mapped within highly transcribed genes. These ectopic origins were normally suppressed by transcription during G1, but precocious entry into S phase due to oncogene activation allowed origin firing within genic regions that had not yet been transcribed. Forks from oncogene-induced origins were prone to collapse, as a result of conflicts between replication and transcription, and were associated with DNA double-strand break formation and chromosomal rearrangement breakpoints both in our experimental system and in a large cohort of human cancers. Thus, firing of ectopic origins caused by premature S phase entry represents a mechanism of oncogene-induced DNA replication stress that is relevant for genomic instability in human cancer.

Biography

Thanos Halazonetis studied dentistry at the University of Athens. He then pursued a PhD degree at Harvard University under the guidance of Philip Leder, worked briefly at the pharmaceutical company Merck, and then joined the Wistar Institute/University of Pennsylvania as Assistant Professor. In 2006 he became Professor of Molecular Biology at the University of Geneva. His research interests focus on cancer. He worked initially on nuclear oncogenes, then on p53 and DNA damage response pathways leading to the discovery that oncogenes induce DNA replication stress. This discovery could form the basis for novel, non-toxic cancer therapies.

http://www.molbio.unige.ch/fra/research_groups/halazonetis/lab

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Jos Jonkers

Netherlands Cancer Institute, Amsterdam, The Netherlands

Tuesday, 10 October 2017, 11:30 – 12:00

Genetic dissection of tumor development, therapy response and resistance in mouse models of BRCA-deficient breast cancer

Heterozygous germline mutations in BRCA1 or BRCA2 strongly predispose to development of breast and ovarian cancer (as well as other cancer types) via loss of the remaining wildtype allele. BRCA1/2-deficient cancers are defective in DNA double-strand break (DSB) repair via homologous recombination (HR) and therefore hypersensitive to DNA-damaging agents, including platinum drugs and poly(ADP-ribose) polymerase (PARP) inhibitors. However, these treatments do not result in tumor eradication and eventually resistance develops. To maximize therapeutic efficacy of these drugs and achieve durable remissions, it is important to unravel the mechanisms by which these tumors acquire resistance to platinum drugs and PARP inhibitors, in order to develop combination therapies that prevent development of resistance or re-sensitize resistant tumors. To study therapy response and resistance in a realistic in vivo setting, we have established several genetically engineered mouse models (GEMMs) and patient-derived tumor xenograft (PDX) models for BRCA-deficient breast cancer. These mice develop mammary tumors that are characterized by genomic instability and hypersensitivity to DNA-damaging agents, including platinum drugs and PARP inhibitors (PARPi). Using cross-species oncogenomics and reverse genetics, we have identified several cancer genes including p53, MYC and RB as critical drivers in BRCA1-associated breast cancer. In addition, we have used these mammary tumor models for preclinical evaluation of therapy response and elucidation of mechanisms of acquired drug resistance. Using functional genetic screens, reverse genetics and genomic analysis of therapy-resistant tumors, we found that therapy response and resistance of BRCA1-deficient mammary tumors to cisplatin and PARPi is affected by several factors, including drug efflux transporter activity, type of BRCA1 founder mutation and restoration of HR repair via loss of 53BP1 or REV7. Also BRCA1 re-activation via genetic or epigenetic mechanisms contributes to therapy resistance in PDX models of BRCA1-deficient breast cancer. Importantly, pharmacokinetic or HR-related mechanisms underlie PARPi-resistance in only a fraction of BRCA1/2-deficient mammary tumors, indicating the existence of additional, unknown resistance mechanisms. One such mechanism involves the loss of poly(ADP-ribose) glycohydrolase (PARG), the major enzyme responsible for the catabolism of poly (ADP-ribose).

Biography

Jos Jonkers performed his PhD and postdoctoral research in the group of Dr. Anton Berns at the Netherlands Cancer Institute (NKI). Following his second postdoc in the group of Dr Allan Bradley at the Wellcome Trust Sanger Institute, he started his own research group at the NKI in 2003. He is currently a Senior Group Leader and Head of the Division of Molecular Pathology at the NKI, and Affiliate Professor of Molecular Experimental Oncogenetics and Cancer Therapeutics at Leiden University. In 2012, he was elected to membership of the European Molecular Biology Organization (EMBO).

https://www.nki.nl/divisions/molecular-pathology/jonkers-j-group

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Jiri Lukas

Novo Nordisk Foundation Center for Protein Research, Copenhagen, Denmark

Tuesday, 10 October 2017, 12:00 – 12:30

Confinement, heritability and intrinsic limitations of cellular responses to DNA replication stress

Our laboratory is interested in how are DNA repair proteins wired into functional pathways, how are repair reactions coordinated with cell cycle progression, how much damage a cell can handle without compromising the fidelity of repair reactions, and how malfunctions of these mechanisms impact on aetiology of cancer and other diseases marked by unstable genomes. We are particularly focused on DNA damage generated by spontaneous (and thus unavoidable) errors during two major drivers of cell cycle progression, DNA replication in S phase and chromosome segregation in mitosis, respectively. To this end, we have developed a robust single-molecule and single-cell imaging pipelines to quantitatively assess the robustness of DNA replication and to interrogate replication stress-induced DNA damage over several successive cell generations. I will use these tools to discuss our latest insight into how cells coordinate the replisome activity with autonomously oscillating metabolic cycles to supress biochemically unstable DNA intermediates such as reversed, stalled, collapsed or broken replication forks. I will also discuss what happens if such primary surveillance of a replicating genome fails and show that the resulting DNA lesions can be inherited by daughter cells, which need to build specialised nuclear compartments to mitigate potentially destructive consequences of heritable DNA damage. Finally, I will provide evidence that mitotic errors can function as primary sources of replication stress, and show that tracking such lesions can provide unexpected insights into how distinct forms of tetraploidy predispose the ensuing cell generations to genomic instability.

Biography

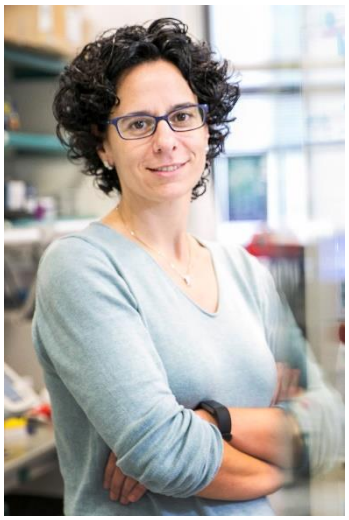
Jiri Lukas studied veterinary medicine and obtained PhD in zoology in Brno (Czech Republic). His research interests took shape during two short but defining postdoctoral visits with Paul Nurse (University of Oxford) and Giulio Draetta (EMBL Heidelberg). In early 90s, Jiri moved to Copenhagen where he has been working ever since – first at the Danish Cancer Society, and now at the Novo Nordisk Foundation Center for Protein Research. Jiri's recent discoveries include a ubiquitin driven pathway that orchestrates the assembly of repair proteins, heritability of chromosomal lesions generated by replication stress, and rate-limiting components of genome maintenance subverted in cancer.

http://www.cpr.ku.dk

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250



Nuria Lopez-Bigas

Institute for Research in Biomedicine, Barcelona, Spain

Tuesday, 10 October 2017, 13:45 – 14:15

Coding and non-coding cancer mutations

Somatic mutations are the driving force of cancer genome evolution. The rate of somatic mutations appears to be greatly variable across the genome due to variations in chromatin organization, DNA accessibility and replication timing. However, other variables that may influence the mutation rate locally are unknown. I will discuss recent findings from our lab on how DNA-binding proteins and differences in exons and introns influence mutation rate. These finding have important implications for our understanding of mutational and DNA repair processes and in the identification of cancer driver mutations. Given the evolutionary principles of cancer, one effective way to identify genomic elements involved in cancer is by tracing the signals left by the positive selection of driver mutations across tumours. We analyze thousands of tumor genomes to identify driver mutations in coding and non-coding regions of the genome.

Biography

Nuria Lopez-Bigas is an ICREA Research Professor at the Institute for Research in Biomedicine and associate professor at the University Pompeu Fabra. She leads the Biomedical Genomics lab (http://bbglab.irbbarcelona.org), focused on the study of cancer from a genomics perspective. She is particularly interested in the identification of cancer driver mutations, genes and pathways across tumor types and in the study of their targeted opportunities.

http://bbglab.irbbarcelona.org/web/

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Charles Swanton

The Francis Crick Institute and UCL Hospitals, London, UK

Tuesday, 10 October 2017, 14:15 – 14:45

Chromosomal order and chaos in lung cancer evolution and immune surveillance

Increasing evidence supports complex subclonal relationships in solid tumours, manifested as intratumour heterogeneity. Parallel evolution of subclones, with distinct somatic events occurring in the same gene, signal transduction pathway or protein complex, suggests constraints to tumour evolution that might be therapeutically exploitable. Emerging data from TRACERx, a longitudinal lung cancer evolution study will be presented. Drivers of tumour heterogeneity change during the disease course and contribute to the temporally distinct origins of lung cancer driver events. APOBEC driven mutagenesis appears to be enriched in subclones in multiple tumour types. Oncogene, tumour suppressor gene and drug induced DNA replication stress are found to drive APOBEC mutagenesis. Evidence that intratumour heterogeneity and chromosomal instability is finely tuned will be presented, to create sufficient diversity for adaptation mitigating the risks of excessive genome instability resulting in cell autonomous lethality. On-going chromosomal instability, manifested as Mirrored Subclonal Allelic Imbalance (MSAI) is found to be a major driver of intratumour heterogeneity in non-small cell lung cancer, contributing to parallel evolution and selection. The finding of subclonal driver events, evidence of ongoing selection within subclones, combined with genome instability driving cell-to-cell variation is likely to limit the efficacy of targeted monotherapies, suggesting the need for new approaches to drug development and clinical trial design and integration of cancer immunotherapeutic approaches. The clonal neo-antigenic architecture may act as a tumour vulnerability, targeting multiple clonal neo-antigens present in each tumour to mitigate resistance and treatment failure. However, evidence for the role of chromosomal instability in the initiation of escape from immune surveillance and subclonal expansions will also be presented.

Biography

Charles completed his MDPhD in 1999 and clinician scientist/medical oncology training in 2008. He combines his laboratory research at the Francis Crick Institute with clinical duties focussed on biological mechanisms of cancer drug resistance. Charles is the Chief Investigator of the CR-UK TRACERx lung cancer evolution study and co-directs the CRUK Lung Cancer Centre of Excellence. He was awarded the Royal College of Physicians Goulstonian lecture and Graham Bull Prize for Clinical Sciences in 2013 and appointed Fellow of the European Academy of Cancer Sciences in 2013 and Fellow of the Academy of Medical Sciences in 2015. Charles was awarded the Jeremy Jass Prize (2014), Stand up to Cancer Translational Cancer Research Prize (2015), Glaxo Smithkline Biochemical Society Prize in recognition of distinguished research leading to new advances in medical science and was awarded the Ellison-Cliffe Medal and Lecture, Royal Society of Medicine (2017) and the San Salvatore Prize for Cancer Research (2017). Charles was appointed Napier Professor in Cancer by the Royal Society in 2016.

https://www.crick.ac.uk/research/a-z-researchers/researchers-p-s/charles-swanton/

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Mike Stratton

2013 Louis-Jeantet Prize winner

Wellcome Trust Sanger Institute, Cambridge, UK

Tuesday, 10 October 2017, 14:45 – 15:15

Signatures of Mutational Processes

All cancers are caused by somatic mutations. However, the processes underlying the genesis of somatic mutations in human cancer are remarkably poorly understood. Recent large-scale cancer genome sequencing initiatives have provided us with new insights into these mutational processes through the mutational signatures they leave on the cancer genome. In this talk I will review the mutational signatures found across cancer and consider the underlying mutational processes that have been operative.

Biography

Mike Stratton is Director of the Wellcome Trust Sanger Institute. His primary research interests have been in the genetics of cancer. His early research focused on inherited susceptibility. He mapped and identified the major high risk breast cancer susceptibility gene BRCA2 and subsequently a series of moderate risk breast cancer and other cancer susceptibility genes.
In 2000 he initiated the Cancer Genome Project at the Wellcome Trust Sanger Institute which conducts systematic genome-wide searches for somatic mutations in human cancer. Through these studies he discovered somatic mutations of the BRAF gene in malignant melanoma and several other mutated cancer genes in lung, renal, breast and other cancers. He has described the basic patterns of somatic mutation in cancer genomes revealing underlying DNA mutational and repair processes. He is the recipient of several awards, including the 2013 Louis-Jeantet Prize for Medicine.
He is a Fellow of the Royal Society (FRS), and was Knighted by the Queen in 2013.

http://www.sanger.ac.uk

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Ian Tomlinson

Institute of Cancer and Genomic Sciences, Birmingham, UK

Tuesday, 10 October 2017, 15:45 – 16:15

Mutational and selective constraints on cancer evolution

The growth of cancers is a Darwinian evolutionary process. It is therefore ultimately constrained by the number of mutations that occur and whether those mutations confer a selective advantage on a tumour cell. Cancers can escape mutational constraints by being in a highly mutagenic environment, or by acquiring mutator phenotypes, such as specific DNA repair defects. The role of selection in tumorigenesis is usually not assessed directly, but is surmised from the presence of recurrent “driver” gene mutations that cause cancer cells to leave more offspring than their normal counterparts. In general, however, selection in cancer evolution is poorly characterised. We have performed a systematic search for driver genes and mutations the prevalence of which cannot be explained by underlying mutational processes. Although mutation can explain much of the variation in driver mutation spectra, there are also many examples of pathogenic mutations that are more readily explained by selection. Examples include KRAS, PIK3CA, APC, and IDH1 and IDH2. I shall explore the last two of these in some detail. In addition, mutator phenotypes can lead to atypical, and probably sub-optimal, driver mutation complements, suggesting that selection of cancer driver mutations is generally weak.

Biography

Ian Tomlinson is Director of the Institute of Cancer and Genomic Sciences at the University of Birmingham, UK, having previously worked at Cancer Research UK, University of Oxford and the Institute of Cancer Research. His research interests lie in discovering and characterising cancer driver genes, especially in the germ line, and in cancer evolution. He is especially keen to integrate work across a variety of biomedical areas, including human patient cohorts, animals models of disease and biomathematics.

http://www.birmingham.ac.uk/staff/profiles/cancer-genomic/tomlinson-ian.aspx

FONDATION LOUIS-JEANTET

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250

Hans Clevers

Hubrecht Institute, Utrecht, The Netherlands

Tuesday, 10 October 2017, 16:15 – 16:45

Lgr5 Stem Cell-based Organoids in human disease

The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. We originally defined Lgr5 as a Wnt target gene, transcribed in colon cancer cells. Two knock-in alleles revealed exclusive expression of Lgr5 in cycling, columnar cells at the crypt base. Using lineage tracing experiments in adult mice, we found that these Lgr5+ve crypt base columnar cells (CBC) generated all epithelial lineages throughout life, implying that they represent the stem cell of the small intestine and colon. Lgr5 was subsequently found to represent an exquisitely specific and almost 'generic' marker for stem cells, including in hair follicles, kidney, liver, mammary gland, inner ear tongue and stomach epithelium.
Single sorted Lgr5+ve stem cells can initiate ever-expanding crypt-villus organoids, or so called 'mini-guts' in 3D culture. The technology is based on the observation that Lgr5 is the receptor for a potent stem cell growth factor, R-spondin. Similar 3D cultures systems have been developed for the Lgr5+ve stem cells of human stomach, liver, pancreas, prostate and kidney. Using CRISPR/Cas9 technology, genes can be efficiently modified in organoids of various origins.

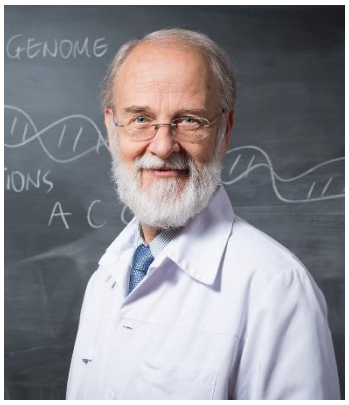
Biography

Hans Clevers obtained his MD degree in 1984 and his PhD degree in 1985 from the University Utrecht, the Netherlands. His postdoctoral work (1986-1989) was done with Cox Terhorst at the Dana-Farber Cancer Institute of the Harvard University, Boston, USA. From 1991-2002 Hans Clevers was Professor in Immunology at the University Utrecht and, since 2002, Professor in Molecular Genetics. From 2002-2012 he was director of the Hubrecht Institute in Utrecht. From 2012-2015 he was President of the Royal Netherlands Academy of Arts and Sciences (KNAW). Since June 1, 2015 he is director Research of the Princess Maxima Center for pediatric oncology. He was awarded the Louis-Jeantet Prize for Medicine in 2004.

www.hubrecht.eu

2017 LOUIS-JEANTET SYMPOSIUM

10 October 2017
Centre Medical Universitaire (CMU), Geneva
Auditorium 250



Stylianos Antonarakis

University of Geneva, Geneva, Switzerland

Tuesday, 10 October 2017, 16:45 – 17:15

Somatic mutation rate

The laboratory of Antonarakis studies the genetic basis of phenotypic variation, particularly in humans. Individual genomes vary extensively from each other; individuality, evolutionary potential, and disease phenotypic risk, all heavily depend on this genomic variability. Understanding the functional role of each nucleotide is a prerequisite in order to unravel the causes of human genetic disorders.

Biography

Stylianos Antonarakis was educated at the University of Athens (MD and DSc) and the Johns Hopkins University School of Medicine (Human Genetics). He was the President of the European Society of Human Genetics, and the President of HUGO in 2013. He is Professor and Chairman of Genetic Medicine at the University of Geneva Medical School, and founding director of the iGE3 institute of Genetics and Genomics of Geneva.

http://www.ige3.unige.ch/antonarakis.php