First Croucher Summer Course in

Precision Genome Engineering by CRISPR: Applications in Biology and Medicine

Date: August 10-15, 2018
Venue: Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong

Program

August 10, 2018

Introduction to CRISPR

09:00 Opening remarks (Prof. Dong-Yan Jin and Prof. Ben Berkhout)
09:15 Introduction to CRISPR (Dr. Bo Gao)
10:30 Cutting-edge CRISPR technologies (Dr. Alan Wong)
11:45 Bioinformatics of gRNA design (Prof. Qi Liu)

13:00 Lunch

14:30 Practical session 1: 1) Practical briefing. 2) gRNA design. 3) Transfection of CRISPR plasmids into HEK293 cells (Dr. Sam Yuen)

August 11, 2018

CRISPR in model systems

09:00 Genome-editing in preimplantation embryos and in EPSCs (Prof. Pengtao Liu)
10:30 Organoids as a model system and their tools for genetic manipulation (Dr. Bon-Kyoung Koo)

12:20 Lunch

14:30 Practical Session 2: 1) Cloning of CRISPR construct. 2) Introduction to CRISPR library construction (Dr. Sam Yuen)

August 12, 2018

Mechanism of CRISPR

09:00 Crystallography and HF-AFM of CRISPR-Cas9 (Prof. Osamu Nureki)
10:30 Workshop (Prof. Ben Berkhout and all invited speakers)

12:20 Lunch

14:30 Practical Session 3: 1) Harvest of genomic DNA. 2) PCR verification of CRISPR editing (Dr. Sam Yuen)

August 13, 2018

One-Day Symposium on Precision Genome Engineering

08:30 Opening remarks (HKU representatives)
08:45 Bioinformatics of CRISPR editing (Dr. Qi Liu)
09:30 Molecular mechanism of CRISPR-Cas and structure-guided development of genome-editing tools towards medical applications (Prof. Osamu Nureki)
10:25 Genome-editing in preimplantation embryos and in EPSCs (Prof. Pengtao Liu)
11:10 CRISPR/Cas-assisted genetics in intestinal organoids (Dr. Bon-Kyoung Koo)
11:55 CRISPR-based genetic screens (Dr. Kosuke Yusa)

12:40 Lunch

14:00 Gene editing of the functional cancer genome (Dr. Sidi Chen)
14:45 The use of large scale fuctional genomic screens for the identification of novel drug targets and effective combination therapies (Dr. Roderick Beijersbergen)
15:40 CRISPR-Cas9 screening to identify cancer dependencies (Dr. Andrew Aguirre)
16:25 CRISPR-Cas genome editing technologies for therapeutics (Dr. Shengdar Tsai)
17:10 Anti-HIV CRISPR (Prof. Ben Berkhout)

August 14, 2018

09:00 CRISPR-based genetic screens (Dr. Kosuke Yusa)
10:15 CRISPR screens in vivo (Dr. Sidi Chen)
11:30 Development and application of CRISPR/CAS9 technologies for large scale pooled screening (Dr. Roderick Beijersbergen)

12:45 Lunch

14:15 Free afternoon
16:15 Hiking in Lamma Island (if weather permits)

August 15, 2018

09:00 Antiviral CRISPR (Prof. Ben Berkhout)
10:15 Discovery of therapeutic targets and drug resistance mechanisms by functional genetic screening (Dr. Andrew Aguirre)
11:30 Defining the genome-wide activity of CRISPR-Cas nucleases for therapeutics (Dr. Shengdar Tsai)

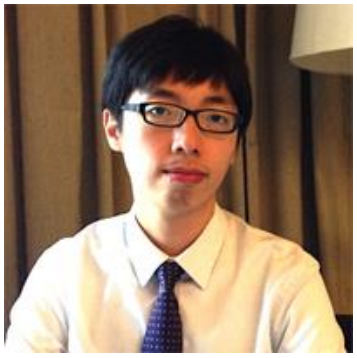
12:45 Lunch

14:25 Practical Session 4: 1) PCR verification and data analysis. 2) Single cell isolation. 3) Cell sorting demonstration.
16:55 Concluding remarks (Prof. Dong-Yan Jin and Prof. Ben Berkhout)

Professor Ben Berkhout, University of Amsterdam

Prof. Ben Berkhout is Professor and Head of the Laboratory of Experimental Virology at the Academic Medical Center of the University of Amsterdam, the Netherlands. In the late 1980s, he was instrumental in changing the paradigm of thinking on gene regulation. At a time when the focus in eukaryotic transcription was on DNA-enhancers and DNA-binding proteins, he emerged to propose HIV-1 TAR RNA and the viral Tat protein as prototypes of RNA and RNA-binding protein mediated mammalian gene regulation. That novel insight, focusing on TAR as RNA rather than DNA, subsequently directed efforts toward the cloning of additional TAR RNA-binding proteins, such as the human TRBP protein, which is now recognized to play a critical role in interferon signaling, RNA interference and micro-RNA biogenesis. Professor Berkhout's research on RNA has provided additional important building blocks for many other aspects of our current knowledge on HIV-1 replication. He has employed a multi-disciplinary approach to research, combining methods from molecular biology, biochemistry and most importantly, virology. His research has extended our insights into the mechanisms of transcription, reverse transcription, drug-resistance, RNA interference and CRISPR.

Website: https://www.amc.nl/web/research/who-is-who-in-research/who-is-who-in-research.htm?p=61



Dr. Alan Wong, The University of Hong Kong

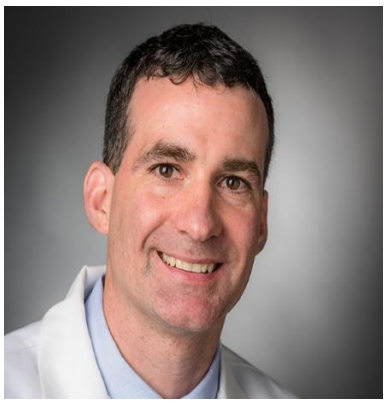
Dr. Alan Wong's research topics focus on developing and applying cutting-edge technologies for studying complex disease biology and devise new therapeutic strategies. Many human diseases are caused by multigenic perturbations. His research takes an integrative approach leveraging on various techniques in synthetic biology, CRISPR-based genome engineering, high-throughput sequencing, molecular biology, and genetics to decode the complex genetic bases of human diseases including cancers and neurodegenerative disorders. His laboratory aims to develop and apply new technologies to interrogate and understand the complex biological systems, and rationally design and engineer genetic circuits for providing new biomedical and biotechnological solutions.

Website: http://www.sbms.hku.hk/research/aslw/index.html

Professor Pengtao Liu, The University of Hong Kong

Prof. Pengtao Liu graduated from Henan Normal University and earned his Master of Science degree from Chinese Academy of Sciences/University of Science and Technology of China. He received his PhD from Baylor College of Medicine under the guidance of Professor Allan Bradley, and completed his postdoctoral training at National Cancer Institute (USA) in the laboratories of Dr. Neal Copeland and Dr. Nancy Jenkins. Dr. Liu joined the Wellcome Trust Sanger Institute in September 2003. He initiated the high-throughput recombineering for the large-scale mouse mutagenesis programme at the Sanger Institute. Dr. Liu's laboratory has identified the critical roles of transcription factors, Bcl11a and Bcl11b, in hematopoietic stem cells, in lymphocyte development, and in mammary gland development. By mutating Bcl11b, they have discovered that T lymphocytes are reprogrammed to a new type of cancer killer cells. Dr. Liu's lab has also identified that BCL11A is an important cancer gene in triple negative breast cancer. Dr. Liu's lab also studies pluripotent stem cells, and the mechanisms of reprogramming somatic cells to iPS cells. His group is the first to demonstrate CRISPR editing in iPS cell generation.

Website: http://www.sbms.hku.hk/staff/pengtao-liu



Dr. Andrew Aguirre, Dana-Farber Cancer Institute

Dr. Aguirre is a medical oncologist and physician-scientist at Dana-Farber Cancer Institute and the Broad Institute of Harvard and MIT. He is dedicated to improving care for patients with gastrointestnal cancers, particularly pancreatic cancer. He directs a research laboratory focused on developing new diagnostic and treatment approaches for these diseases.

Website: http://www.dana-farber.org/find-a-doctor/andrew-aguirre/

Professor Qi Liu, Tongji University

Prof. Qi Liu earned his Ph.D. from a joint program between Zhejiang University and University of Georgia in 2008. He then received postdoctoral training in Hong Kong University of Science and Technology. He is a biocomputational biologist with interest in precision medicine and drug informatics, RNAi and gene editing analysis, siRNA and sgRNA in-silico design as well as clinical data analysis and related disease mechanism. His research aims at using various statistical learning and machine learning techniques to address the bioinformatics and chemo-informatics problems.

Website: http://bm2.runyoo.com

Professor Osamu Nureki

Prof. Nureki is a structural biologist who has published numerous articles on prestigious scientific journals in the CRISPR field (e.g. Cell, 2014, 2015 & 2016). Prof. Nureki has a long-lasting collaboration relationship with Prof. Feng Zhang at Broad Institute, one of the key discoverers of CRISPR technology. Prof. Nureki and Prof. Zhang co-publish many scientific papers and co-file key critical patents on CRISPR and gene editing technologies. Prof. Nureki receives his PhD from University of Tokyo. He is currently a Professor at Department of Biological Sciences, Graduate School of Science in the University of Tokyo.

He was awarded the JSPS PRIZE in 2008, the Mochida Memorial Research Prize in 2009 and the Inoue Prize in 2011 for his research into “the genetic code translation and the definition of protein synthesis mechanism”, and was awarded the Uehara Prize and Takeda Medical Prize in 2014 for his research into “molecular mechanism of membrane transport.”

Website: http://www.nurekilab.net/index.php/en?FrontPage

Dr. Sidi Chen, Yale University

Dr. Chen earned his PhD from The University of Chicago, and performed postdoctoral studies at MIT and the Broad Institute. His research focuses on global understanding of biological systems. He has led studies on identifying and characterizing genes of new origin in eukaryotic genomes, essential function of new genes in animal development and tumorigenesis, microRNA regulation of hypoxia and angiogenesis, in vivo modeling of lung cancer and liver cancer using gene editing, and genome-wide in vivo screens. His research team is interested in developing and applying novel tools for next generation cancer genetics, genomics and systems biology, and tackle problems in cancer initiation, progression, metastasis, immunity, and therapeutic responses.

Website: https://medicine.yale.edu/genetics/people/sidi_chen.profile

Dr. Shengdar Tsai, St. Jude Children's Research Hospital

Dr. Tsai got his BS degree from University of Michigan and his MS and PhD degrees from North Carolina State University. He then received postdoctoral training from Harvard Medical School and Massachusetts General Hospital. His research interest is in genome engineering and hematology. Particularly, he is trying to improve genomic methods to define and measure gene editing "off-target" effects, to make use of CRISPR-Cas nucleases for precise gene correction and to understand regulation of DNA damage repair choice between error-prone non-homologous end-joining and precise homology-directed repair. He is also interested in genome-scale CRISPR-Cas screening for novel effectors of hematological diseases and the development of novel strategies for allele-specific editing of genetic mutations that cause sickle cell disease and other hematological disorders.

Website: https://www.stjude.org/directory/t/shengdar-tsai.html

Dr. Roderick Beijersberge, Netherlands Cancer insitute

Dr. Roderick Beijersbergen did his doctoral research in the lab of René Bernards at the Netherlands Cancer Institute in Amsterdam where he studied the control of the cell cycle by the retinoblastoma gene family. He received his Ph.D from the University of Utrecht in 1995. He then joined the group of Robert Weinberg at the Whitehead Institute in Cambridge, USA for his postdoctoral training. He was involved in the identification of the catalytic component of telomerase, hTERT, in human cells and studied the role and regulation of hTERT expression in the transformation of normal cells to tumor cells. In 1999 he returned to the Netherlands Cancer Institute as an AvL fellow where he continued to work on the regulation of the expression of hTERT.

Over the last years he has focused on the generation of tools to perform functional genetic screens with special emphasis on loss-of-function cell based screens. To facilitate loss of function genetic screens he has developed large collections of shRNA knockdown vectors, targeting large numbers of both human and mouse genes. The development of these technologies has opened up the possibility to perform large scale mammalian somatic genetics.

To be able to perform large scale screens, he has set up the NKI Robotics and Screening Center (NSRC). This center facilitates the large scale and high throughput use of both genomic tools as well as compound collections. The NSRC is a resource center that provides the technology for medium to high throughput applications, provides support and expertise for automated cell and non-cell based assays and is used for the development, production and maintenance of large screening reagent collections. The NSRC has realized an automated high content screening platform with state-of-the-art image analysis software, database development and statistical analysis, integrated with bioinformatics to perform large scale complex phenotype cell based.

Website: https://www.nki.nl/divisions/molecular-carcinogenesis/beijersbergen-r-group/

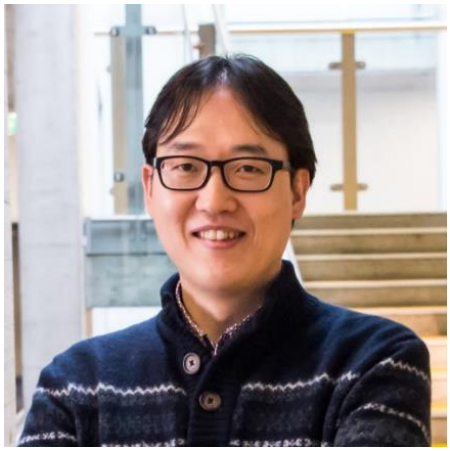
Dr. Kosuke Yusa develops and applies novel genome engineering techniques in mouse and human embryonic stem (ES) cells and induced pluripotent stem (iPS) cells to screen for disease-causing variations. His group's recent focus has been on development of genome-wide CRISPR-based genetic screening and its applications in stem cell and oncology research.

Kosuke graduated from Osaka University in 1999 with a BSc in Bioengineering and completed an MSc in Agricultural science in 2001 at the University of Tokyo. In 2005, he obtained his PhD from Osaka University under the supervision of Professor Junji Takeda and received the 'Yamamura prize' (Graduate Student of the Year). As part of his PhD, Kosuke established a novel forward genetic screening method in mouse ES cells that uses the hyper-recombination phenotype of Bloom helicase-deficient cells.

After his PhD, he was awarded a post-doctoral fellowship from the Japan Society of Promotion of Science and joined Professor Allan Bradley's team at the Sanger Institute in 2007. He has developed the hyperactive piggyBac 'jumping gene' (DNA transporter system) and used it to create a novel platform of iPS cell reprogramming. By combining this system with zinc finger nuclease technology, he has achieved highly precise genetic correction of disease-causing mutations in human iPS cells, opening the way to new clinical treatments.

In October 2012, Kosuke was appointed as a member of the Sanger Institute Faculty in the newly developed scientific programme, Cellular Genetics.

Website: https://www.sanger.ac.uk/people/directory/yusa-kosuke



Dr. Bon-Kyoung Koo, Institute for Molecular Biotechnology, Austria

Dr. Bon-Kyoung Koo is an experienced mouse geneticist actively employing the emerging organoid culture technology to study stem cell maintenance and activation in mouse and human intestinal and stomach organoid cultures. Following his PhD and first post-doctoral studies in the laboratory of Prof. Young-Yun Kong at POSTECH – Republic of Korea, Dr. Koo joined the group of Prof. Hans Clevers at the Hubrecht Institute, KNAW, Netherlands. Here he witnessed the first establishment of the Lgr5+ cell-derived intestinal organoid culture system pioneered by Dr. Toshiro Sato and Prof. Hans Clevers. In the following years Dr. Koo has utilised this novel culture system to perform sophisticated gene correction studies, to unravel the molecular regulation of adult stem cells and to proof the stem cell properties of a Troy+, quiescent reserve stem cell population in the stomach. Dr. Koo started his own group at the University of Cambridge in 2013. He has now moved his group to IMBA Institute of Molecular Biotechnology in Vienna, where he continues his work on developing novel genetic tools to further investigate how proliferating and quiescent adult epithelial stem cell populations are regulated both in homeostasis and during injury mediated repair.

Website: https://www.imba.oeaw.ac.at/research/bon-kyoung-koo/