

Faculty of Medicine, Chinese University of Hong Kong

Turning scientific advances into innovative clinical practices

Established in 1981, the Faculty of Medicine at the Chinese University of Hong Kong (CUHK) now has 19 schools and departments, with over 250 academic staff members. The faculty's expertise in cutting-edge translational cancer and genomic research is essential to its mission to improve human health through scientific advances.

The Faculty of Medicine, CUHK has established multiple research centres and institutes with a special focus on translational cancer and genomic research, three examples include:

- **Li Ka Shing Institute of Health Sciences (LiHS):** A key translational medicine research institute in Hong Kong, the LiHS opened in 2007 and currently has over 300 researchers. Its key focus area is translational genomics, particularly in the area of non-invasive prenatal testing and cancer.
- **Sir Y. K. Pao Cancer Centre:** Opened in 1994, the centre is the first dedicated facility in Hong Kong for cancer research and clinical services. It houses the State Key Laboratory in Oncology in South China, which focuses on cancers common in Hong Kong, such as liver, lung and nasopharyngeal cancers.

Both the LiHS and the Sir Y. K. Pao Cancer Centre are located in the Prince of Wales Hospital, the main teaching hospital of the Faculty of Medicine, CUHK.

- **School of Biomedical Sciences (SBS):** The SBS was created in 2009 through the unification of the Departments of Anatomy, Biochemistry (Medicine), Pharmacology and Physiology. The 42 professorial staff members at the SBS conduct research that falls under five thematic research programmes: (1) cancer and inflammation; (2) neuro-degeneration, -development and

repair; (3) reproduction, development and endocrinology; (4) stem cell and regeneration; and (5) vascular and metabolic biology. With its recent relocation to a new state-of-the-art facility in 2012, the school is reaching new heights of excellence in biomedical research.

The Faculty of Medicine at the CUHK has established numerous international ties, winning regional and international recognition for its work in translational genomic research. Highlights of this research include:

Circulating cell-free nucleic acid diagnostics

The detection of circulating nucleic acids — DNA and RNA molecules released from the cells of multiple body tissues into the blood — provides an opportunity to develop non-invasive blood-based diagnostics for a variety of conditions. The circulating nucleic acids laboratory at the CUHK, led by Dennis Lo and Rossa Chiu, is dedicated to the development of novel molecular diagnostics for the assessment and monitoring of human diseases and pathologies.

Lo and Chiu's team contributed to the development of non-invasive DNA-based approaches for the prenatal diagnosis of fetal chromosomal and genetic diseases by demonstrating the presence of fetal DNA in the circulation of pregnant women. Together with King's College Hospital in London and the VU University Medical Centre in the Netherlands, the CUHK group pioneered an approach based on massively parallel sequencing of cell-free DNA molecules in maternal blood that is effective for the detection of fetal Down syndrome. Soon after, the test became available for clinical use and is now offered in over 100 countries. The CUHK

team was also the first to achieve the direct determination of the fetal genome through the analysis of maternal blood, which has paved the way for non-invasive diagnosis of fetal single-gene diseases. The team has collaborated extensively with Charles Cantor at Sequenom to bring this technology to the clinic.

The CUHK team was also the first to show that genetic and genomic changes of solid cancers can be detected in a genome-wide fashion by massively parallel sequencing analysis of cell-free DNA in blood. This non-invasive molecular scan is able to detect genomic changes associated with a range of malignancies, including cancers of the liver, lung, colon, breast and nasopharynx. The team's work has been widely published in high-impact journals and has been awarded multiple international honours, including election to the Royal Society and the US National Academy of Sciences.

Liver Cancer Genome Project

Liver cancer is a highly aggressive cancer that is prevalent in China and Southeast Asia. In 2011, Nathalie Wong and her research team received a HK\$45 million grant from the Hong Kong Research Grants Council to undertake a 'Liver Cancer Genome Project'. The project is a collaboration between clinicians and basic researchers from the CUHK, the University of Hong Kong, the Hong Kong University of Science and Technology and the Beijing Genomics Institute in Shenzhen that aims to comprehensively delineate whole genome and whole-transcriptome somatic variations in liver cancer.

The project focuses on large-scale genome-wide analyses to define genetic events that distinguish tumours from cirrhosis and progression to metastatic disease. Using next-generation sequencing, Wong's team recently illustrated the mutagenic effects of hepatitis B virus (HBV) integration in the development of liver cancer. Through transcriptome sequencing, the team also demonstrated the presence of viral-human chimeric transcripts from the site of genome integrations and helped to elucidate the oncogenic effect of viral insertion. The project has thus provided a foundation for future research into effective control strategies for the disease.

Nasopharyngeal cancer research

Nasopharyngeal carcinoma (NPC), a distinct type of head and neck cancer, is a major healthcare problem in Hong Kong and South China. For the past two decades, a team led by Kwok-Wai Lo, an international leader in NPC genome research, has sought to decipher the molecular basis of NPC and identify novel targets for this deadly disease. The group collaborates with the Dana-Faber Cancer Institute in the US and the ILCHUN Genomic Medicine Institute in South Korea, and works closely with other internationally renowned research groups. Their pioneering work has provided significant insight into the molecular biology of NPC development.

Recently, Lo and his team discovered a novel recurrent transforming fusion gene in a subset of patients — the first evidence to support the role of gene rearrangement in the genesis of NPC. To offer a molecular basis for the development of



promising disease control strategies for NPC, Lo's group has initiated a new project to uncover vital genetic changes through large-scale whole genome sequencing and bioinformatic analysis. The team plans to systematically define the driver mutations, identify key molecular targets and elucidate underlying biological mechanisms to pinpoint novel biomarkers and therapeutic targets. The project is expected to contribute to the development of personalized treatment strategies for NPC patients.

Clinical cancer research

The State Key Laboratory of Oncology in South China is built on the CUHK's long-established partnership with Sun Yat-sen University, Guangzhou, in cancer research, as well as its long tradition of cancer research and care in the local community. Led by Anthony TC Chan and Tony SK Mok, the laboratory has established current standards of care in the management of locoregionally advanced NPC and lung cancer.

Mok's team focuses on biomarker and molecular targeted therapy in lung cancer. With the discovery of epidermal growth factor receptor mutation, Mok designed and led the IPASS (Iressa Pan-Asia Study), which confirmed the role of this mutation as a predictive biomarker and demonstrated the superiority of targeted monotherapy over doublet chemotherapy. Mok has also led a number of other multinational clinical trials that have contributed to the current standard of practice for the management of advanced-stage lung cancer.

Focusing on locoregionally advanced NPC, Chan and his team reported the first prospective randomized study in one

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endemic area to establish concurrent cisplatin-radiotherapy as the current standard of care. Collaborating with Cancer Research UK, they developed a therapeutic Epstein-Barr virus (EBV) vaccine to boost *in vivo* T cell responses to EBV proteins expressed by tumour cells. The pilot study established the safety and immunogenicity of the EBV vaccine. A multinational phase 2 efficacy study is ongoing.

Digestive diseases and gastrointestinal cancer studies

The Institute of Digestive Disease (IDD), established in 2006 by Joseph JY Sung, seeks to improve the diagnosis and treatment of digestive diseases through basic, translational and clinical research. Comprising a multidisciplinary group of investigators from a wide range of internationally recognized academic fields, IDD's ultimate goal is to improve patient survival through the early detection and treatment of gastrointestinal cancers.

The IDD has made a number of important discoveries related to the treatment of digestive diseases, including a technique for the management of peptic ulcer bleeding, led by Francis KL Chan, and insight into the treatment of HBV infection, led by Henry LY Chan. In addition, the research laboratory led by Jun Yu has pioneered the use of microRNAs as novel non-invasive biomarkers for colorectal cancer, and has discovered novel tumour suppressor genes in gastric cancer and new mutation signatures in colorectal and gastric cancers. The IDD's research has been published in a number of international peer-reviewed journals, including the *New England Journal of Medicine* and *The Lancet*. Of IDD's over

Discovered at the CUHK

- **Dennis Lo and Rossa Chiu noninvasively determined the fetal genome, DNA methylome and transcriptome through maternal blood analysis.**
- **Nathalie Wong identified a novel mechanism of viral-host fusion sequence HBx-LINE1 in liver oncogenesis.**
- **KW Lo generated a high-resolution genome map of EBV-associated nasopharyngeal cancer.**
- **Anthony Chan and Tony Mok led international multi-centre anti-PDL1 immunotherapeutic studies in nasopharyngeal and lung cancers.**
- **Jun Yu discovered novel molecular events and biomarkers of gastrointestinal cancer through genome sequencing and bio-functional analyses.**
- **HC Chan discovered a novel role of cystic fibrosis transmembrane conductance regulator in insulin secretion and cystic fibrosis-related diabetes.**

1,600 publications, 300 were published in high-impact journals.

The IDD has been honoured with 42 prestigious national and international awards. Core IDD team members serve on editorial boards of major medical journals and advisory boards of major industrial partners and have secured 120 external local, national and international research grants of over HK\$350 million in the past 5 years.

In addition, The State Key Laboratory of Digestive Disease was established at the IDD in 2013, in partnership with the Fourth Military Medical University in mainland China. The IDD's strong international network, enables collaborations with key leaders in the field around the world.

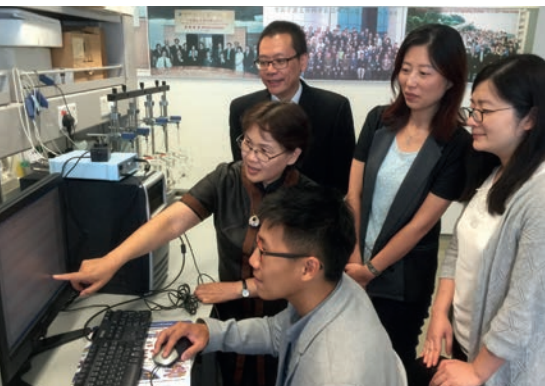
Epithelial cell biology research

Epithelial cells form a diverse group of tissues that cover or line almost all body surfaces, cavities and tubes, such as the lungs, liver, kidneys and reproductive tract. Defects in epithelial cell function are therefore associated with a wide spectrum of disorders and diseases, including hypertension, diabetes, infertility and cancer. Recognizing the importance of epithelial cells, researchers at the CUHK and the Academy of Military Medical Sciences joined forces in 1999 to establish the first and leading Epithelial Cell

Biology Research Centre (ECBRC) in China, with help and support from the National Natural Science Foundation of China.

Since its establishment, the ECBRC has built a multidisciplinary technology platform and has stayed at the forefront of epithelial cell biology research. This cross-disciplinary approach, together with a network of over 50 collaborating laboratories worldwide, have led to ECBRC's high-impact publications in leading journals, such as *Nature Medicine*. Among the ECBRC's many notable discoveries, ECBRC researchers have identified the role of epithelial ion channels in reproduction, mechano-sensing, cancer development and insulin secretion, and have illustrated the importance of defensins in sperm function and male fertility.

With a strong team led by Hsiao Chang Chan, the ECBRC is engaged in a wide variety of basic and translational research. From investigation of the ion channels in signal transduction to researching risk factors of assisted reproduction technology, the ECBRC's research has numerous potential applications in the diagnosis and treatment of infertility and other diseases. The ECBRC embraces the team spirit and is open to further collaborations, including joint ventures with the industrial sector to promote translational research. "Together, great things are possible," Chan says.



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