Biology and Diagnostic Applications of Plasma DNA

We have achieved international acclaim in this area, especially for our work on the use of plasma DNA for non-invasive prenatal testing (NIPT) and liquid biopsies for cancer. Our research has been supported by a UGC Areas of Excellence Grant and three RGC Theme-Based Research Scheme Grants. NIPT is now available in dozens of countries, where millions of pregnant women are benefiting from this technology each year.

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Nasopharyngeal Carcinoma

We are conducting a large-scale prospective cancer screening project aiming to detect early nasopharyngeal carcinoma (NPC), a disease that is prevalent in South China. Its prognosis depends on the stage of the disease at the time of diagnosis. Patients with early stage disease (Stages I and II) have a much better survival rate than those who are in a more advanced stage (Stages III and IV). However, over 70% of NPC patients diagnosed are in the advanced stage of the disease. Our Department has pioneered the development of plasma Epstein-Barr virus (EBV) DNA as a tumour marker for NPC. In this screening study, over 20,000 apparently healthy males age 40 to 60 years have been screened for NPC using plasma EBV DNA analysis. This study has demonstrated the usefulness of NPC screening in early detection to enhance survival, the results of which were published in the *New England Journal of Medicine* in August 2017.

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Chemical Pathology

Chemical Pathology focuses on the study of molecular, biochemical and immunological changes that occur as part of a disease process. Established in 1983, our Department is one of the few independent departments of Chemical Pathology in the world. Its mission is to advance the science and practice of chemical pathology through education, research and clinical service.

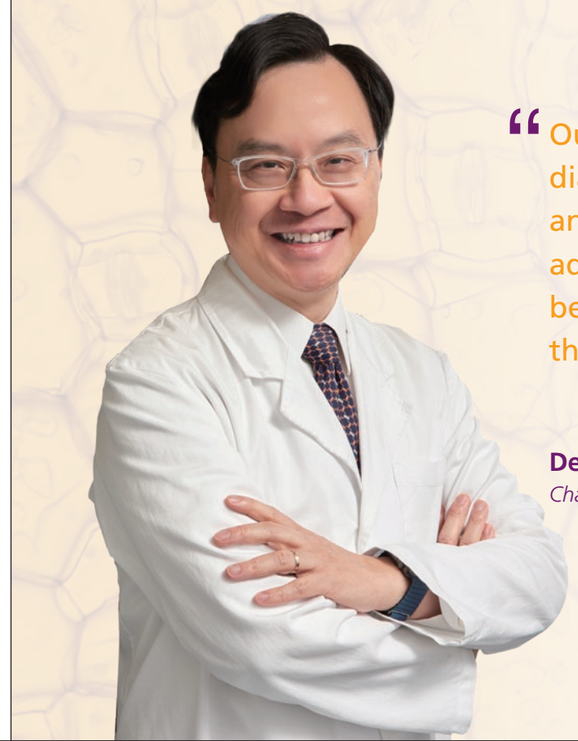
The Department of Chemical Pathology has academic interests in several fields of study. In particular, it has a world-leading programme in plasma DNA-based molecular diagnostics, especially for non-invasive prenatal testing and cancer detection. Other areas of interest include diagnostic applications of next-generation DNA sequencing, allergic diseases, inborn errors of metabolism, and bioinformatics, as well as stem cells and regeneration.

Many pioneering discoveries made by the Department have led to clinical applications and sparked multidisciplinary research with national and international collaborations. Examples include a widely used non-invasive prenatal test for Down syndrome and screening for nasopharyngeal cancer using plasma EBV DNA.

The Department is well funded and has a track record of support by the most competitive research funding in Hong Kong, namely the University Grants Committee (UGC) Areas of Excellence programme and the Research Grants Council (RGC) Theme-based Research Scheme. It is well equipped with state-of-the-art research equipment, including next-generation sequencers, digital polymerase chain reaction platforms, flow cytometers, and bioinformatics and stem cell research facilities. Inventions made by the Department have created an extensive and valuable patent portfolio owned by The Chinese University of Hong Kong.

DEPARTMENT OF

CHEMICAL PATHOLOGY



"Our goal is to solve unmet needs in diagnostic medicine. By combining ingenuity and cutting-edge technologies, we deliver advances in clinical laboratory science that benefit patients and have put Hong Kong on the global biotechnology map."

Dennis LO
Chairman

Genetics of Complex Traits

Nelson Tang is the principal investigator of the Laboratory for Genetics of Disease Susceptibility. With specialties in the genetics of complex traits and genetic statistics, he and his team conduct research in genetic association, expression quantitative traits and genome-wide association (GWAS) analysis. In the big data era, his team is further involved in the analysis of various big datasets generated by high-throughput sequencing such as RNA-seq. He also teaches a bioinformatics course in the Faculty of Engineering.

Research directions:

1. Genetics of Complex traits to identify prevalent genetic variants causing common diseases in Han Chinese, e.g. adolescent idiopathic scoliosis (AIS); and

2. Statistical genetics and computational statistical analysis of big genetic and biological datasets.

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Immunology

Research topics in immunology include the following: (1) elucidation of the cytokine and chemokine network and intracellular signal transductions of immune effector cells, including eosinophils, lymphocytes, mast cells, basophils and dendritic cells in inflammatory diseases, with recent emphasis on immunoregulatory cytokine and pattern recognition receptor-mediated innate immunity; (2) the immunopathological mechanisms of allergic diseases, autoimmune diseases, infectious diseases and diabetes mellitus, with interdepartmental collaboration. Results can help uncover the development of disease markers and provide a biochemical basis for the development of novel therapeutic modality; and (3) the immunomodulatory, anti-tumour and anti-allergic activities of traditional Chinese medicine.

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Stem Cells and Vascular Regeneration

This group studies cardiovascular regeneration and the pathophysiology of cardiovascular complications during diabetes, using human pluripotent stem cells (including embryonic stem cells and induced pluripotent stem cells) and chemically modified mRNA as platforms. We are especially interested in the role of adaptive immunity in cardiovascular diseases and regeneration.

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Bioinformatics

The bioinformatics team has research interests covering many areas of genomics and bioinformatics. We are focused on (1) developing integrative bioinformatics methodologies and computational tools for solving the challenges facing non-invasive cancer detection and prenatal testing using the cell-free DNA molecules; (2) investigating the fundamental aspects of the transcriptional regulations for both coding and noncoding genes using Next Generation Sequencing techniques in a variety of biological systems; and (3) integrating and mining the biological databases for discovery-driven biological research.

The research on bioinformatics is computationally driven and interdisciplinary in nature, with a complement of collaborative experimental investigations with bench scientists.

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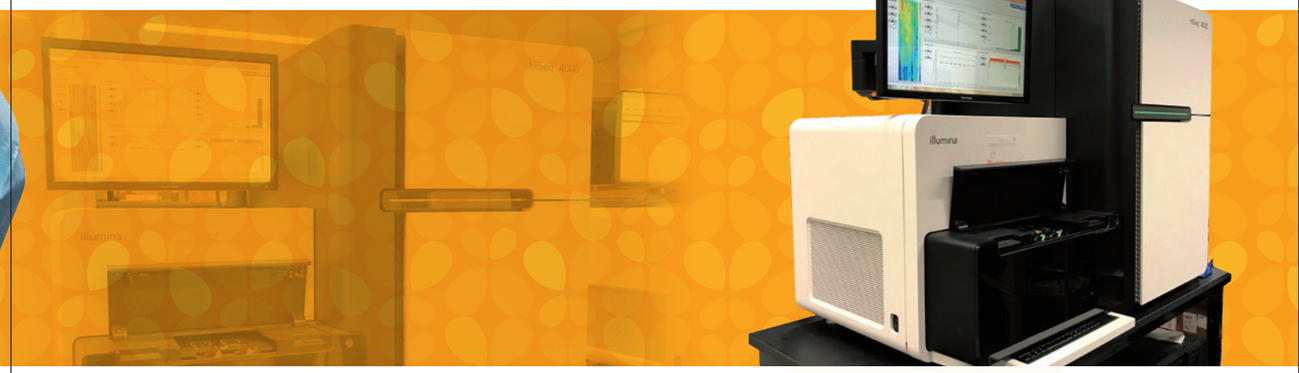

Acute Myeloid Leukaemia

We have discovered that a subtype of acute myeloid leukaemia (AML) with chromosomal rearrangement of t(9;11)(p22;q23), resulting in MLL-AF9 gene fusion, shows a favourable prognosis if BRE gene expression is up-regulated in leukaemia. Our Department has done pioneering work on BRE. We have found that the protein has antiapoptotic activity and can promote development of human hepatocellular carcinoma (a common form of liver cancer). We are particularly interested in studying how BRE favours survival of AML patients with MLL-AF9 rearrangement. Our interests are two-fold: understanding this apparently paradoxical antitumourigenic effect of BRE in AML, and identifying the potential therapeutic targets for AML, not only of the MLL-AF9 subtype, using the BRE pathway as the gateway of our exploration. For this project, we have started collaboration with the MRC Weatherall Institute of Molecular Medicine, University of Oxford, in the UK; Cincinnati Children's Hospital Medical Center at the University of Cincinnati in the US; and Pediatric Oncology/Hematology, Erasmus MC-Sophia Children's Hospital, at Erasmus University Rotterdam in the Netherlands.

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