

Early phase oncology trials at CUHK

Since the opening of the Chinese University of Hong Kong Phase I Clinical Trial Centre (CUHK P1CTC) in late 2013, the Department of Clinical Oncology has worked closely with the Faculty's Clinical Research Management Office in the development of the P1CTC. A key milestone was the successful accreditation of the CUHK P1CTC by the China Food Drug and Administration (CFDA) in August 2016.

The Department is collaborating with the Department of Anatomical and Cellular Pathology to establish a Patient Derived Xenograft (PDX) model laboratory at the Sir YK Pao Cancer Centre. Once established, the CUHK PDX laboratory plans to work with pharmaceutical companies in the evaluation of novel anti-cancer compounds in PDX models of nasopharyngeal cancer. The long-term goal is to develop a seamless platform at CUHK for generating proof-of-concept studies and phase 1 clinical testing in Asian-prevalent cancers.



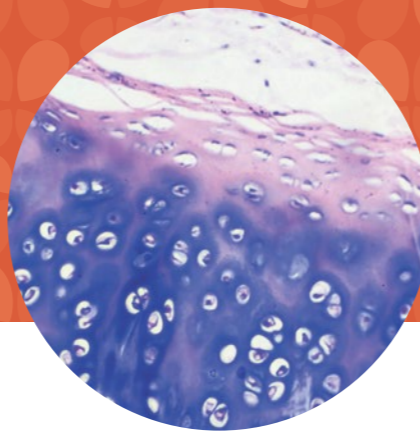
The Department of Clinical Oncology continues to expand its phase I programme and is currently conducting a wide spectrum of phase I clinical trials, ranging from signalling inhibitors and cell cycle inhibitors to immune checkpoint inhibitors in solid tumours. Our strong presence in the academic arena is reflected in the number of abstract presentations, journal articles and consultancies at the advisory board meetings of major pharmaceutical companies. We have also made oral presentations of several early phase clinical trials in nasopharyngeal cancer and lung cancer at the Annual Scientific meeting of the American Association of Cancer Research (AACR, Washington DC 2017) and the European Society of Medical Oncology Asia (ESMO, Singapore, December 2016), as well as the Japan-Taiwan Oncology Phase I Trial Conference (JTOPIC) in 2017. Moreover, our members were invited to deliver the keynote lecture on the phase I development of immunotherapy in oncology at the official opening of the newly-expanded phase I clinical trial centre at Seoul National University Hospital, South Korea, in 2017.

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Epigenetics Lab

Qian Tao's group is focused on cancer epigenomics, mainly the CpG methylome study of tumours, including the identification and functional/mechanistic characterisation of novel tumour suppressor genes (TSGs), the development of epigenetic biomarkers and epigenetic therapeutics, and EBV-induced aberrant epigenetic programming in virus-associated tumorigenesis. His group has established the CpG methylomes of common tumours in Hong Kong, including NPC, oesophageal, lung and digestive cancers, and lymphomas, identified multiple new TSGs (e.g. PCDH10, RASAL1, ZNF382, BLU, ZNF545, BCL6B, JPH3, DLEC1), and characterised their functions in cell signalling and tumorigenesis. He has also developed promising epigenetic biomarkers and therapeutics. For their epigenetic research work, his group has won international recognition in prestigious scientific journals (citations: 8001, h-index: 55) and four textbook chapters. Qian Tao has won several researcher awards in Hong Kong and mainland China and has been the Vice-President of the international Epigenetics Society since 2008.

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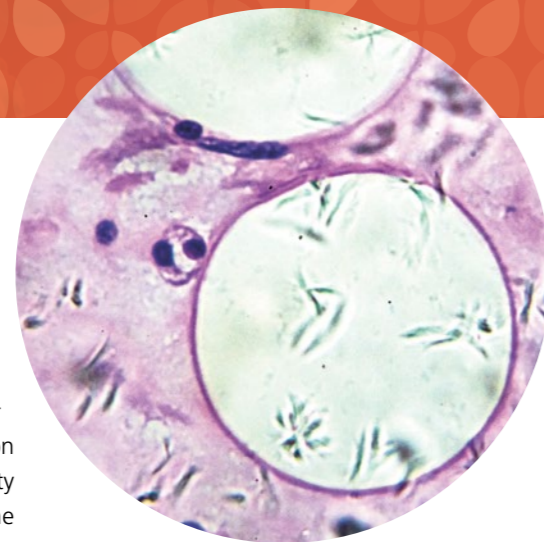


Radiotherapy

The five linear accelerators in the Department offer radiotherapy at different levels of sophistication, according to the tumour types treated. Advanced treatment options are readily available, including Intensity Modulated Radiation Therapy (IMRT), Volumetric Modulated Arc Therapy (VMAT), Image-guided Radiation Therapy (IGRT), Stereotactic Radiosurgery (SRS), Stereotactic Body Radiation Therapy (SBRT), and Gated-VMAT. TrueBeam, our latest linear accelerator, provides high dose-rate delivery, advanced imaging and motion management capabilities. It has created a new paradigm of advanced treatment techniques, which are particularly useful for moving targets such as lung and liver cancer, tumours adjacent to critical normal organs such as the head and neck, and spinal tumours.

Our team is also involved in clinical research in collaboration with local hospitals as well as overseas organisations, including NRG Oncology, Stanford and Shantou University. At present, we are currently conducting clinical trials on nasopharyngeal, head and neck, prostate, lung and breast cancer. We aim to enhance global knowledge transfer with other institutions, ultimately providing quality healthcare for our cancer patients.

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Clinical Oncology

The integrated University Department and the Hospital Authority Department of Clinical Oncology bring together medical oncologists, haematological oncologists, radiation oncologists, and palliative medicine specialists to conduct quality research. This multidisciplinary team approach covers a full range of research areas, from cancer prevention, screening, diagnosis and active treatment to palliative and psychosocial care.

Accredited by the China FDA in 2006 as an oncology study site in Hong Kong, our Department is a Partner State Key Laboratory of Oncology in South China. We also have experience conducting US National Cancer Institute-funded studies, particularly in Asian cancers. In 2009, we joined as a Sister Institution of the US MD Anderson Cancer Center's Global Academic Programs (MDACC GAP). Additionally, we participate in regional clinical trial groups such as those organised by the Cancer Therapeutics Research Group (CTRG), Asian Breast Cancer Cooperative Group, Asian Oncology Early Phase 1 Consortium (Asia One), and Asian Thoracic Oncology Research Group ("ATORG").

Our professors are editorial members of international journals and chairmen of local, regional and international professional bodies. The annual international conference we co-organise with The Hong Kong Cancer Institute has become a local flagship event with high attendance.

DEPARTMENT OF CLINICAL ONCOLOGY



“Cancer is a genomic disease, thus we must tackle cancer at the molecular level. The Department of Clinical Oncology leads and works with multiple international collaborators in the development of biomarker and novel therapeutics that target specific cancer genes. Through our work, we have changed the paradigm of cancer therapy.”

Tony MOK
Chairman

Lung Cancer

With the discovery of the EGFR mutation in 2004, precision medicine has become the standard management approach as it has greatly enhanced the survival rates of patients. Tony Mok and his team have led the world in demonstrating the first-line EGFR tyrosine kinase inhibitor (TKI) as superior to standard chemotherapy in biomarker selected populations. Since then, the team has established the efficacy of the combination of chemotherapy and EGFR TKI, the principle of TKI treatment beyond progression, plasma-based detection of EGFR mutation, and management of the resistant T790M mutation. In addition to their work on EGFR mutation, they have published two *New England Journal of Medicine* (NEJM) papers that define first line targeted therapy for ALK positive lung cancer.



EGFR mutation studies

IPASS study (NEJM 2009): In this first randomised study of gefitinib, we showed the superiority of this drug over chemotherapy in patients with EGFR mutation, and also confirmed EGFR mutation as the predictive biomarker. The study has changed the management paradigm and confirmed that all patients with adenocarcinoma should know their EGFR mutation status prior to treatment.

FASTACT 2 (*Journal of Clinical Oncology* 2012): This randomised phase III study demonstrated that the intercalated combination to be superior to chemotherapy.

ASPIRATION (*JAMA Oncology* 2016): This was the first single arm study to confirm the improvement of progression free survival by four months by allowing treatment beyond RECIST progression.

IMPRESS (*Lancet Oncology* 2016): This randomised phase III study is the first to confirm that the continuation of EGFR TKI with chemotherapy is not superior to chemotherapy alone once a patient develops clinical resistance to EGFR TKI.

AURA 3 (NEJM 2017): This was the first study to confirm the superiority of osimertinib, a third generation EGFR TKI, over chemotherapy in patients with resistant T790M mutation.

As a result of these studies, we confirmed that all patients who developed resistance to first line EGFR TKI should be tested for the presence of T790M mutation.

ALK translocation

PROFILE 1014 (NEJM 2014): This is the first randomised phase III study that showed the superiority of crizotinib over standard chemotherapy in patients with ALK positive lung cancer. From the study, it was determined that all patients need to be tested for ALK translocation prior to first line treatment.

ALEX (NEJM 2017): Alectinib is a second generation ALK inhibitor. In this randomised phase III study comparing alectinib with crizotinib, we showed that median progression free survival to be 25.7 and 10.1 months, respectively. The drug was also found to have greater penetration in the brain, resulting in a significant reduction of CNS progression.

From these studies, we have established a new standard for first line therapy.

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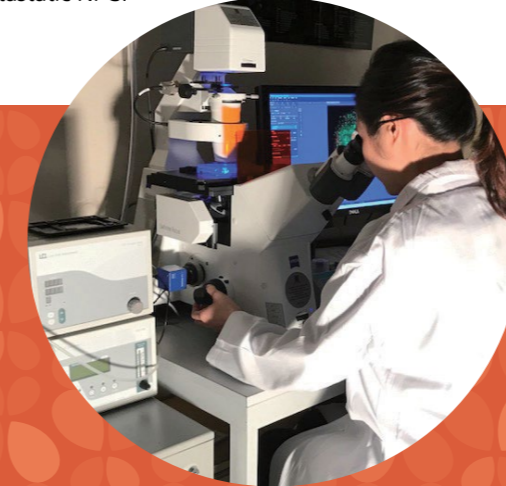
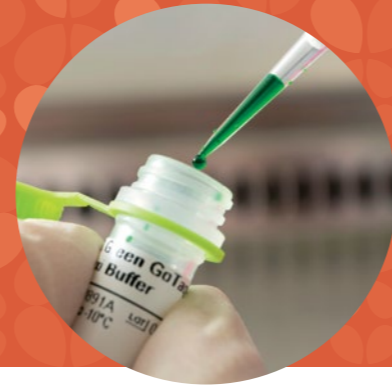
Nasopharyngeal Carcinoma

In locoregionally advanced nasopharyngeal carcinoma (NPC), Anthony Chan of the Department reported the first prospective randomised study in an endemic area that established concurrent cisplatin-radiotherapy as the current standard of care. A regional phase III randomised trial in high risk patients with elevated post-treatment Epstein-Barr Virus (EBV) DNA was completed and presented at ASCO 2017, demonstrating the prognostic significance of the marker. An NRG global study on individualising the adjunctive treatment of NPC based on EBV DNA status was also initiated.

The collaborative research efforts of CU Medicine and Cancer Research UK have led to the development of a therapeutic 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 Modified Vaccinia Ankara (MVA) EBV vaccine, and a multinational phase II efficacy study is near completion. What's more, Anthony Chan has presented multiple keynote international lectures, including "EBV as a Paradigm: From Lab to Clinic" at the 2014 American Society of Clinical Oncology 50th Anniversary Session as well as "Epstein Barr Virus and Nasopharynx Cancer" at the opening session of the 2016 ESMO Asia meeting.

Multiple clinical and translational studies on immune checkpoint inhibitors (ICPI) and other targeted therapies are ongoing, including a pivotal randomised trial of ICPI versus standard of care in metastatic NPC.

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Sarcomas

This team operates under the auspices of the Prince of Wales Hospital (PWH) Adult Sarcoma Multidisciplinary Team (Adult Sarcoma MDT), for which Herbert Loong of the Department serves as chair and convener. The PWH Adult Sarcoma MDT holds regular interdisciplinary meetings to discuss patient management issues, as well as provide a platform for research and medical education across medical disciplines.

In collaboration with the Department of Orthopaedics & Traumatology, we hosted the 1st CUHK Sarcoma Preceptorship Programme in May 2017. Akira Kawai, Head of Musculoskeletal Oncology at the National Cancer Center Japan, was the event's inaugural plenary speaker.

In recent years, we have forged closer links with our international counterparts. We were a founding member of the Asian Sarcoma Consortium and are an active member of the Trans-Atlantic Retroperitoneal Sarcoma Working Group. Additionally, Herbert Loong is a faculty member of the Singapore Sarcoma Preceptorship Programme hosted by the National Cancer Centre Singapore and the ESMO Asia Congress Sarcoma Track. He will assume the position of Sarcoma & Melanoma Track Chair at the ESMO Asia 2018 Congress.

Herbert Loong is also an active member of the Connective Tissue Oncology Society (CTOS) as well as an individual member of the Sarcoma Alliance for Research Through Collaboration (SARC). We continue to promote collaborative efforts with like-minded counterparts across the region and the world to further advance the science and management of this complicated and heterogeneous disease.

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Immuno-Oncology Hong Kong



Neuro-Oncology

Together with the Department of Surgery, the Department of Clinical Oncology is an integral part of the CUHK Otto Wong Brain Tumour Centre at the Prince of Wales Hospital. At this tertiary referral centre for neurosurgery and brain tumours, patients are managed in a multidisciplinary fashion through the weekly Combined Neuro-oncology Clinic – the first of its kind in Hong Kong. Our centre provides care for around 50 new glioblastoma multiforme (GBM) patients yearly.

We have been involved in pivotal multinational clinical trials for glioblastoma multiforme and other forms of malignant brain tumours. With our partners in the Division of Neurosurgery and the Department of Anatomical Pathology, the Department of Clinical Oncology has strong translational and clinical research interests in this disease group. While continuing our work in the preclinical setting, we also look forward to contributing to early phase as well as registration phase clinical trials.

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Liver Cancer

Liver cancer is a prevalent and highly lethal cancer in Asia. Our team focuses on developing novel management strategies for liver cancer. The team is currently undertaking more than 10 clinical trials on testing different trans-arterial formulations and drugs for treatment of liver cancer. In particular, our team has also initiated a clinical trial to study the microbiome and immune environment during check-point immunotherapy for liver cancer. Results of this study will significantly enhance the understanding of the interaction between the cancer and the tumour environment in the liver.

Our team is also active in studying the link between inflammation and liver cancers. There have been multiple publications and ongoing research projects on the impacts of the degree of inflammation on outcomes of liver cancer. Notably, our group has identified a panel of circulating cytokines to be highly prognostic of survivals in liver cancers and developed an inflammatory prognostic score for liver cancer. Our group is currently working with the University of Newcastle on the role of inflammatory cells in the progression of liver cancer.

Internationally, our team is widely recognised as a centre of excellence in liver cancer research and patient care. For example, our research results have been published in high-impact journals, including the *Journal of Clinical Oncology*. Dr Stephen Chan has also been invited to become an overseas member of the United States Hepatobiliary Taskforce to provide opinions on research in liver cancer. In terms of patient care, our team is organising a bimonthly liver meeting with the multidisciplinary team of the Memorial Sloan Kettering Cancer Centre in the United States to share their experiences in the management of liver cancer.

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Pancreatobiliary cancer

The incidence of bile duct cancer, especially the subtype of intrahepatic cholangiocarcinoma, is increasing worldwide. The team's research interest is to find more effective ways of treating advanced bile duct cancer. Globally, the team is leading an international multi-centre phase II study to evaluate the combination of international radioembolisation with yttrium-90 and conventional chemotherapy on the treatment of intra-hepatic cholangiocarcinoma. This ongoing clinical trial will provide the first prospective clinical data in the world on this novel combination in the treatment of liver cancer. Due to the high tumour heterogeneity of biliary tract cancer, the team is also interested in developing biomarker-driven targeted therapy for bile duct cancer. In particular, the team is testing various FGFR inhibitors in early clinical trials on the treatment of bile duct cancer.

For pancreatic cancer, most of the patients present with locally advanced and metastatic disease. For locally advanced disease, the team has advocated the sequential use of chemotherapy followed by chemoradiotherapy. The group has collected the largest case series in Hong Kong on this approach for treating locally advanced tumours. For metastatic disease, the team has recently completed the preclinical evaluation of a novel arginase drug on pancreatic cancer cell lines and animal models. Translation to clinical trials in human is currently in progress.

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