

Professor Tak Mak Tak-wah

Honorary Professor, Department of Pathology, School of Clinical Medicine, Li Ka-shing  
Faculty of Medicine

麥德華教授

李嘉誠醫學院臨床醫學學院病理學系名譽教授

Tak W Mak is internationally known for his work on the genetics and molecular biology of cancer and the immune system. He has been a major figure in the fields of immunology and molecular and cellular biology for almost 40 years, and is a world leader in basic and translational research into the genetics of immunity and cancer. In 1984, he led the group that cloned the gene encoding a chain of the human T cell receptor, this discovery laid the ground work for our understanding of much of T cell biology and heralded the CAR-T technologies now approved for the treatment of leukemias and lymphomas. Prof Mak's lab was also a pioneer in the genetic modification of mouse strains ("knockout mice") to identify factors associated with susceptibility to immune disorders or various cancers. The Mak team used these mutant animals to elucidate the functions of numerous molecules involved in immune responses, programmed cell death, and tumorigenesis, including the important tumour suppressors p53 and PTEN, and the breast cancer-related genes BRCA1 and BRCA2. Notably, in 1995, his group used mutant mice to show that CTLA4 is a negative regulator of T cell activation, paving the way for the development of T cell checkpoint inhibitor regulators as immunotherapeutic agents. Prof Mak's laboratory continues to develop novel approaches for designing and producing TCRs that are specific for antigens appearing on the surfaces of cancer cells. In a different vein of investigation, his team recently showed that the brain communicates with the immune system via T and B cells producing acetylcholine, a finding with implications for future treatments of cancer and autoimmune or neurodegenerative diseases. The Mak group continues to uncover immune cell subsets that can synthesise this prototypical neurotransmitter, and is delving into the novel functions of this molecule outside neurotransmission.

In addition to this academic success, Prof Mak has made significant contributions on the biotech front, in particular co-founding Agios Pharmaceuticals and Treadwell Therapeutics. These companies specialise in delineating metabolic vulnerabilities in tumour cells that can be exploited as novel cancer therapies. Several first-in-class small-molecule compounds are now in clinical trials for the treatment of cancer and certain genetic disorders. This strategy has produced two IDH inhibitors that are now FDA-

approved for the treatment of acute myeloblastic leukemias, as well as another first-in-class agent for the treatment of anaemia. Two novel agents targeting the aneuploid cancer cells common in advanced solid tumours are now in phase II clinical trials.

Prof Mak is a member of the Royal Society of Canada, Royal Society of London, US National Academy of Sciences (USA), American Academy of Arts and Sciences (USA), and American Association for Cancer Research (USA). His copious accomplishments have been recognised by the scientific community through many prestigious awards and honours, including the Gairdner Foundation International Award (Canada), Emil von Behring Prize (Germany), McLaughlin Medal (Canada), King Faisal International Prize for Medicine (Saudi Arabia), Sloan Prize of the GM Cancer Foundation (USA), Paul Ehrlich and Ludwig Darmstaedter Prize (Germany), Novartis Immunology Prize (Switzerland), Gold Leaf Prize for Discovery (Canada), Albert Szent-Györgyi Prize for Cancer Research (USA) and the 2023 Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research. Prof Mak holds a dozen honorary degrees from numerous universities in North America and abroad, and serves on the boards of many top-ranked scientific journals and biotechnology companies.

麥德華教授以癌症遺傳學、分子生物學和免疫系統研究而在學術界享負盛名。他在免疫學和分子及細胞生物學領域中擔當重要角色達 40 年之久，亦是免疫和癌症遺傳學基礎和轉譯研究的世界領袖。於 1984 年，他領導的團隊複製了人類 T 細胞受體鏈 (TCR) 的基因，這項發現為我們理解 T 細胞生物學奠定基礎，預示了現在已獲批用於治療白血病和淋巴瘤的 CAR-T 技術出現。麥教授的實驗室也是基因工程小鼠模型 (基因敲除小鼠) 的先驅，以識別各種與免疫疾病或癌症相關的遺傳易感因素。麥教授的團隊利用這些突變動物來闡明各種與分子相關的免疫反應、程序性細胞死亡和腫瘤發生的機制，包括重要的腫瘤抑制基因 p53 和 PTEN，以及與乳腺癌相關的 BRCA1 和 BRCA2 基因。尤其在 1995 年，他的團隊利用基因敲除小鼠表明 CTLA4 是 T 細胞活化的負調節因子，為開發 T 細胞檢查點抑制劑作為免疫治療劑奠定了基礎。麥教授的實驗室繼續開發新方法來設計和生產專門靶向癌細胞表面抗原的 TCRs。他的團隊最近於另一範疇研究中表明，大腦透過 T 細胞和 B 細胞來與免疫系統通信時會產生乙醯膽鹼，對未來癌症和自身免疫或神經退行性疾病的治療具有重要意義。麥教授的團隊繼續揭示可以合成這種典型神經傳遞物質的免疫細胞亞群，並正深入研究這種分子在神經傳遞以外的新功能。

除學術成就外，麥德華教授在生物科技領域也作出巨大貢獻，特別是共同創立 Agios Pharmaceuticals 和 Treadwell Therapeutics。這些公司專門研究腫瘤細胞的代謝弱點，以作為癌症治療的新手段。數項首創用於治療癌症和某些遺傳性疾病的小分子化合物現在進行臨床試驗，當中已生產出兩種 IDH 抑制劑，一種為用於治療急性骨髓母細胞白血病，另一種則為治療貧血症，兩款藥物均已獲 FDA 批准使用。目前，另有兩種針對晚期實體腫瘤中常見的異染色體癌細胞的新型藥物，正在進行二期臨床試驗。

麥德華教授是加拿大皇家學會、英國皇家學會、美國國家科學院、美國藝術與科學會以及美國癌症研究協會的成員。他的眾多成就獲得了科學界的認可，包括加拿大蓋爾德納國際獎、德國 Emil von Behring 獎、加拿大勞克林獎章、沙特阿拉伯費薩爾國王國際醫學獎、美國 GM 癌症基金會斯隆獎、德國保羅·埃爾利希和路德維希·達姆施泰特獎、瑞士 Novartis 免疫學獎、加拿大 Gold Leaf 發現獎、美國聖·喬奇癌症研究創新成就獎以及 2023 年 Pezcoller 基金會—AACR 國際癌症研究傑出成就獎。麥德華教授擁有多個北美和國外大學頒發的榮譽學位，並擔任多家世界知名的科學期刊和生物技術公司的董事會成員。