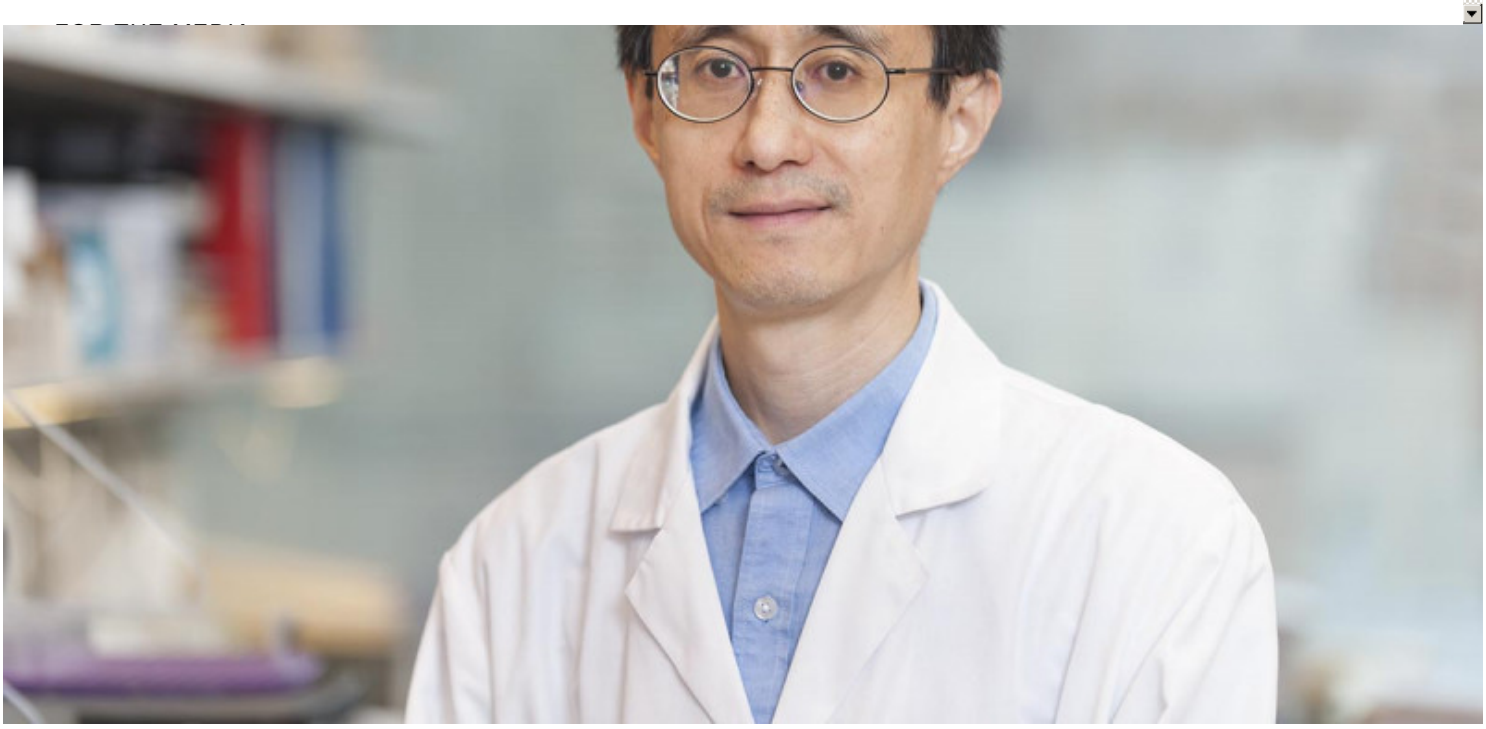

Characterization of B7-H3: A Target for Monoclonal Antibody Therapy of Human Solid Tumors

Monoclonal antibody (mAb) 8H9 radioimmunotherapy has shown promise in people with central nervous system (CNS) relapse. It is specific for cell surface glycoprotein gp58. This project was initiated with the biochemical characterization of gp58, which was purified from the extract of neuroblastoma cell line LAN-1 by 8H9-affinity chromatography and was unequivocally identified by mass spectrometry as 4Ig-B7-H3, the long and principal form of B7-H3, an immune modulator that is known to inhibit immune cell attack by natural killer (NK) and T cells. While B7-H3 transcript was ubiquitously expressed in solid tumors and normal human tissues, B7-H3 protein was detected by 8H9 only in human solid tumors but not in most normal tissues, including normal CNS tissues tested. Currently, the research focuses on two aspects. We are investigating the mechanism behind B7-H3 overexpression in solid tumors, especially the role of microRNAs in its regulation. Modulating B7-H3 protein expression may improve the therapeutic potential of mAbs like 8H9, especially for people with metastatic solid tumors. Second, we are identifying the putative B7-H3 receptors on activated NK/T cells and determining which receptors function primarily as a coinhibitory molecule. Unraveling the role of B7-H3 coinhibitory receptors may help in developing more efficient, innovative NK/T cell-based therapeutic approaches in neuroblastoma and other solid tumors.

Publications

Xu H, Cheung IY, Guo HF, Cheung NK. MicroRNA miR-29 modulates expression of immunoinhibitory molecule B7-H3: potential implications for immune based therapy of human solid tumors. Cancer Research. 2009 Aug 1;69(15):6275-81.