Supervisor Name: Minna Woo

Hospital/Research Institution: Toronto General Hospital Research Institute

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Field of Research (2 keywords): molecular biology and in vivo mouse models

Department: Medicine, Division of Endocrinology

School of Graduate Studies Appointment (IMS, LMP, IHPME etc)? Yes/No: YES

If YES, please name:
IMS and Immunology

Project Title: Investigating JAK2 inhibitors for treatment or cure of liver cancer

Brief Project Description (<300 words):

With the obesity epidemic, along with increasing success in treatment of hepatitis B and C, non-alcoholic fatty liver disease (NAFLD) is an emerging leading cause of hepatocellular carcinoma (HCC). HCC is the second most deadly cancer which continues to rise in incidence without effective treatment or cure.

My lab has been investigating the role of JAK-STAT pathway in multiple tissues relevant for diabetes and related complications. JAK-STAT is a major intracellular signaling pathway that mediates actions of many hormones and cytokines. We have recently shown that mice lacking JAK2 specifically in hepatocytes are protected from development of HCC. Given that JAK2 inhibitors are already available clinically for other diseases including myeloproliferative and certain autoimmune diseases, we are excited to test whether JAK2 inhibitors can treat or cure HCC.

Experiments to be conducted by the student will involve using JAK2 inhibitors in vitro on human liver cancer cell lines and assessing the effects of JAK2 inhibition on various aspects of cancer progression, including proliferation, migration and invasion. Changes in gene and protein
expression will also be assessed. Additionally, JAK2 inhibitors will be tested *in vivo* in mice. The inhibitor will be given throughout the duration of cancer development to assess for its role in cancer prevention. Another cohort of mice will be treated with the inhibitor after the development of liver cancer to assess for its efficacy in treatment or cure.

Overall these studies will provide translational, clinically relevant discoveries towards improvement or cure of liver cancer. All of the research techniques to be learnt are generalizable and therefore will be widely applicable for other projects involving molecular biology and other disease models.