Latest successes from Dr. P. Sorensen's Lab:
Date: August 25th, 2023

1. Publications:

Science Advances
Zhang H-F, Delaidelli A, Javed S, Turgu B, Morrison T, Hughes CS, Yang X, Pachva M, Lizardo MM, Singh G, Hoffman J, Huang YZ, Patel K, Shraim R, Kung SHY, Morin GB, Aparicio S, Martinez D, Maris JM, Bosse KR, Williams KC, **Sorensen PH**. A MYCN-independent mechanism mediating secretome reprogramming and metastasis in *MYCN*-amplified neuroblastoma. ***Sci Adv***. PMID: 37611092

2. Grants:

Rutledge Cancer Foundation
Title: Targeting the IL1RAP surface protein for immunotherapy in Ewing sarcoma
Team: Poul Sorensen (PI), Kevin Hay (co-I), Wei Li (collaborator), Dimiter Dimitrov (collaborator), Timothy Cripe (collaborator)
Amount: $100,000 USD for 1 year
Lay abstract: Ewing sarcoma (EwS), the 2nd most common childhood bone sarcoma, is an aggressive tumor that primarily affects children, adolescents, and young adults. When EwS tumor cells spread to other parts of the body, known as metastasis, survival is drastically diminished to only 15-20%, which has not changed for decades. Immunotherapy (IT) empowers a patient's own immune system to attack cancer, which has tremendous promise as an alternative to chemotherapies that are often toxic. However, surface proteins that suitable for IT targeting are very limited in EwS. It was first recognized nearly 100 years ago that cancer cells exploit distinct pathways to enhance their metabolism (i.e. the use of nutrients to make energy) to support their cancerous features, such as unlimited growth capacity and the ability to spread to other organs. Proteins on the cell surface that help cancer cells maintain their unique metabolic features likely represent an "Achilles heel" for these tumours, which can potentially be exploited as IT targets using antibodies and other targeting techniques. In a recent study, we searched for surface proteins that fit the criteria for promising IT targets in EwS. We identified the IL1RAP surface protein as being crucial for helping EwS cells maintain sufficient levels of cysteine, an amino acid metabolite that is critical for EwS cell survival under oxidative stress encountered in the primary tumor microenvironment, and during metastasis. Notably, only minimal IL1RAP is found in normal tissues except placenta, nominating IL1RAP as an ideal IT target with little chance of inducing toxicities in children undergoing treatment for EwS. In this grant we will seek to develop and optimize two IT strategies that enhance T cell therapeutic targeting of IL1RAP in EwS. We will build on our previous work in order to enhance the in vivo efficacy of our IL1RAP targeting CAR T cells using combination therapies, previously demonstrated by other groups to improve cell therapy outcomes. We will also generate and test so-called bispecific T cell engagers directed against IL1RAP and CD3, and incorporate them into a recombinant adeno-associated virus, a novel single-dose solution for achieving prolonged systemic BiTE

delivery in vivo. With these approaches, we will develop reagents targeting a key metabolic regulator and driver of metastasis in EwS.

The Osteosarcoma Institute
Title: Harnessing the osteosarcoma surfaceome for immunotherapy targets to block metastatic capacity
Team: Poul Sorensen (PI), Gregg Morin (co-I), Wei Li (co-I)
Amount: $500,000 USD for 2 years
Lay abstract: Osteosarcoma (OS) is the most common bone cancer of children, adolescents, and young adults. When OS tumor cells spread to other parts of the body, known as metastasis, survival is drastically reduced from ~75% to ~25%. Since metastatic disease has remained largely incurable for decades, there is a critical need to identify new treatments for patients with metastatic OS. Immunotherapy (IT) uses a patient's own immune system to attack cancer by targeting tumor-specific cell surface proteins, and has shown tremendous promise as an alternative to chemotherapies, which often have severe side effects. However, surface proteins suitable for IT are very limited in OS. We have characterized surface proteins expressed in OS cells, identifying ~70 cell surface proteins specific to OS. Two of these, TMEM119 and ROR2, are highly expressed in OS but largely absent in normal tissues, and have been implicated in metastatic disease. We will characterize the functions of TMEM119 and ROR2 in OS, and validate their immunotherapeutic potential. We will also use a high-throughput approach to identify which of the other 70 proteins are involved in OS metastasis to identify additional IT opportunities. For the proteins shown to be involved in OS metastasis, we will develop and characterize antibodies that bind those proteins, add toxic drugs to the antibodies, and test their efficacy for IT. Our program aims to validate novel IT targets that could improve outcomes for patients with metastatic OS.

3. Awards: (BC Cancer and UBC communication departments and Cynthia for BCCRC website/MO)

Poul Sorensen appointed as an ambassador of the Technical University of Munich
Lay summary:
Dr. Poul Sorensen, a UBC Professor of Pathology and a Distinguished Scientist at the BC Cancer Research Institute, has been appointed as an International Ambassador to the Technical University of Munich (TUM), in Germany. These prestigious Ambassadorships are given by TUM to renowned international researchers that have formally conducted research at TUM, and who have retained particularly close ties to the university. Global TUM ambassadors are chosen based on their research contributions to the German academic landscape, and for maintaining close collaborations with the TUM research community. TUM Ambassadors are part of an international outreach program to expand TUM's global network, spot talent worldwide, and advise young TUM scientists as they make their way into the international world of research. This is exemplified by Dr. Sorensen's continued work to identify immunotherapeutic strategies to target high-risk childhood cancers with TUM investigators.