Lay summary:

My lab is working on medulloblastoma, a very aggressive pediatric brain tumour. There are at least 4 different kinds of medulloblastoma, all of which have very different clinical outcomes. One of these groups, called Sonic Hedgehog (SHH) medulloblastoma, is very high risk, as some patients survive while many others unfortunately die as a consequence of recurring disease and drug resistance. Thus, one of our goals is to identify new drugs to treat SHH medulloblastomas.

Researchers have identified cells within SHH medulloblastoma tumours that are responsible for drug resistance called "brain tumuor stem cells" and are at the "root" of the disease. We recently discovered a marker on the surface of SHH medulloblastoma tumours that is associated with these stem cells. We have also found that cells bearing this marker, known as CD271, can be specifically targeted and killed with a drug named selumetinib. This is exciting as selumetinib crosses the blood brain barrier, meaning that it can actually get to the tumour, and is currently in clinical trials for the treatment of other pediatric brain cancers. Although this appears to be a promising new strategy to fight SHH medulloblastoma, we need to further increase the efficiency of selumetinib by combining it with other cancer fighting drugs. With the fellowship provided to Dr. Brent Guppy and the 3 operating grants I have received (CIHR, Rally Foundation for Childhood Cancer Research, and the CancerCare Manitoba Foundation) to support the continual operating costs of this project, we have made substantial progress over the past year. Our preliminary data have identified genes and pathways that could potentially be compensating for selumetinib treatment in mouse models that have SHH medulloblastoma tumours. Our extensive preliminary data suggest that targeting the "JAK/STAT3" pathway in combination with selumetinib may further enhance survival in our preclinical models. JAK/STAT3 inhibition is currently being investigated for treatment of leukaemia, and as such safety studies are nearing completion (NCT00674479, NCT02723994).

We have validated our preliminary findings using multiple cell models in a dish and found that selumetinib, along with drugs targeting JAK/STAT3, significantly enhance the effects on stem cell growth, cell death and cell movement which is quite exciting. We have now moved into animal trials where we have optimized the concentration of drugs utilized that can get through to the tumour but are also not toxic. The anticipated completion date for these studies is April 2020. We are currently putting together the figures and manuscript that outline our findings for summer 2020 submission. As Dr. Guppy has now left the lab, I have another postdoctoral fellow, Dr. Jamie Zagozewski working on the project to completion. She is an outstanding trainee who currently has another paper under review at Nature Communications on highly aggressive Group 3 medulloblastoma tumours. The project is in excellent hands! Moreover, we have 2 potential MSc students who would like to continue working on the project in September 2020.