MB-03. FUNCTIONAL CHARACTERIZATION OF NOVEL BIOMARKERS IN SELECTING FOR SUBTYPE SPECIFIC MEDULLOBLASTOMA PHENOTYPES
Lisa Liang1, Christopher Aiken1, Robyn McClelland1, Ludvine Morrison1, Marc Remke2, Vijay Ramaswamy2, Marc Del Bigio1, Michael Taylor2, and Tamra Werbowetski-Ogilvie1; 1University of Manitoba, Winnipeg, MB, Canada; 2The Hospital for Sick Children, Toronto, ON, Canada

Major research efforts have focused on characterization of brain tumor propagating cells from a variety of cancers. Elucidating cell surface marker profiles for selective isolation of this population, which could include stem or progenitor cells, will be imperative toward development of targeted therapies. Medulloblastoma (MB) is the most common primary malignant pediatric brain cancer and consists of 4 molecular subgroups: Wnt, Shh, Group 3 and Group 4. Given the cellular heterogeneity within and between MB variants, cell surface marker profiles will likely be subtype-specific. We employed an unbiased high throughput flow cytometry screen to identify differentially expressed cell surface markers in high vs. low self-renewing Shh MB phenotypes. The top 25 differentially expressed markers were refined by evaluating levels in Shh relative to the other molecular variants in 3 transcriptome datasets representing 548 patient samples. Four markers, CD271/p75NTR, CD106/VCAM1, EGFR and CD171/NCAM-L1 showed consistent differential expression in the Shh subtype relative to the other variants and this was validated in additional cell lines. In addition, immunohistochemical staining specifically for CD271 in paraffin embedded sections of primary MB patient samples validated higher expression of CD271 in Shh MB compared to the other MB variants as well as high levels in the external granular layer of the fetal cerebellum. Further functional characterization of CD271 was performed as proof of principle to demonstrate the power this unique approach has in identifying novel markers associated with Shh MB tumorigenesis. Gain and loss of function studies performed in vitro as well as in vivo analysis suggested that CD271 selects for progenitors, as opposed to more primitive stem cell populations, and that CD271 levels are inversely correlated with expression of representative Shh pathway genes. This work highlights an integrated approach for identification and subsequent functional validation of novel cell surface markers representing diverse MB phenotypes.