

MCC-C3 Padres Pedal the Cause Spring 2018

## Natural Killer Cells for Treatment of Medulloblastoma



Dan Kaufman, MD, PhD (MCC)  
Robert Wechsler-Reya, PhD (SBP)

### Scientific Abstract:

Immunotherapy has shown promise for treatment of a variety of cancers. Most immunotherapies work by increasing the ability of cytotoxic CD8+ T cells to attack tumor cells. For a CD8+ T cell to recognize and kill a tumor cell, it must bind to MHC-I on the tumor cell surface; if tumor cells downregulate MHC-I, they cannot be recognized and killed. Using mouse models of the pediatric brain tumor medulloblastoma (MB) we recently showed that tumors with mutations in p53 do not express MHC-I on their surface. This may make them invisible to T cells and insensitive to T cell-based immunotherapies. On the other hand, tumors that lack MHC-I have been reported to be more sensitive to natural killer (NK) cells. Importantly, in preliminary studies we found that p53-mutant MB tumors are more susceptible to NK-mediated killing than WT tumors, suggesting that this approach may be effective in patients with p53- mutant MB. Here, we will use murine and human models of MB to test whether adoptive transfer of NK cells can be used to effectively target p53- mutant tumors. If these studies are successful, they will pave the way for NK- cell based therapies that can improve outcomes for patients with this devastating disease.

### Lay Abstract:

Immunotherapy is emerging as a powerful approach to treating cancer. Most immunotherapies work by increasing the activity of immune cells called T cells, but T cells can only attack tumor cells if the tumor cells display a protein on their surface called MHC-I. In our recent studies of the childhood brain tumor medulloblastoma, we discovered that tumor cells frequently shut off expression of MHC-1, and thereby become invisible to T cells. This raises the possibility that these patients may be insensitive to T cell-based immunotherapy. In contrast, a different type of immune cell called a natural killer cell is not dependent on (and is actually inhibited by) MHC-I, and thus may be better able to kill tumors that do not express MHC-I. In the proposed studies, we will test whether natural killer cells can be used to attack and kill medulloblastoma cells that lack MHC-I. If successful, these studies could markedly increase the numbers of patients who benefit from this type of cell- based immunotherapy.