Section 2: Executive Summary

Diffuse intrinsic pontine glioma are high grade glial tumours arising in the brainstem with a median survival of 9-12 months, and a distinct biology compared to similar looking tumours arising in the cerebral hemispheres in children and adults. A major challenge to improve outcomes for these tumours is their extensive intratumoral heterogeneity, reflected by differing cellular morphologies and genomic imbalances present within an individual sample. We sought to define the subclonal diversity of DIPG with a view to better understanding the evolutionary dynamics underlying this variation.

In the first year of this grant, generously funded by the Abbie's Army and the DIPG Collaborative, we have made substantial progress in ascertaining the subclonal architecture of DIPG using next-generating sequencing of single, multi-region and longitudinal samples. We have additionally developed methodology to isolate DIPG subclones *in vitro* in order to determine how distinct genotypes link to function within the tumour mass. As highlighted in the original application, we are now requesting a second year of funding to more fully explore the interactions between subclonal populations of DIPG cells, and to assess the possibilities of disrupting communication between subclones as a novel therapeutic strategy.

Total requested: $99,470