

Molecular Networks of Childhood Diffused Pontine Gliomas

Diffuse intrinsic pontine glioma (DIPG), the most lethal childhood cancer, accounts for about 20% of pediatric brain tumors. Despite three decades of clinical trials (chemotherapy, radiotherapy), the survival rate for DIPG remains under 10%, emphasizing a critical need for the identification of new therapeutic targets. The slow progress in understanding the molecular mechanisms of this disease is mainly due to a lack of fresh frozen biopsy specimens of DIPG for use in molecular studies. As such, the only DIPG specimens available to study are formalin fixed paraffin embedded postmortem tumor samples from autopsy. However, due to the heavy fixation process, these samples have been difficult to use because of the inability to extract DNA, RNA and protein that is suitable for molecular analysis.

With the advancement of new technologies, such as protein profiling (proteomics), which has made it possible to evaluate thousands of proteins simultaneously from a single individual's tumor, we set our aim in producing reliable protein profiles of DIPG. We hypothesized that a comparison of the protein profile between normal brainstem and DIPG tumor samples will reveal proteins that are specific to DIPG (biomarkers), which could then be targeted for future drug development. During that past two years, we have investigated various methodologies to accomplish this goal and have recently published the first molecular characterization of DIPG, using a novel technique of proteomic profiling of fixed autopsy tissues (Nazarian et al., 2008). We have now refined these methods and will soon analyze an additional number of DIPG autopsy samples in hand. Our immediate goal is to further expand this cohort of samples by requesting the donation of autopsy DIPG specimens from collaborating institutions so that we may validate our initial molecular characterization of pediatric brainstem gliomas and identify molecules that are responsible for DIPG formation, progression and resistance to current therapy. Indeed only through the generous support provided by foundations such as the Childhood Brain Tumor Foundation could our groundbreaking achievements have been possible.

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