NOVEL THERAPY TARGETS FOR DIPG

At present, there are no effective therapy options for patients with diffuse intrinsic pontine glioma (DIPG), one of the most devastating of pediatric malignancies.

One of the barriers to effective treatment is the lack of understanding of what distinguishes DIPG from other pediatric tumors and from high-grade gliomas in adults. Researchers at the Hospital for Sick Children have addressed this by performing a genetic analysis of 11 DIPG samples and 11 pediatric supartentorial high-grade astrocytoma samples using a single nucleotide polymorphism platform; Cynthia Hawkins commented "Our intention was to identify potential biology-based therapeutic targets for future clinical trials with the hope that this would be a more successful approach to treating these patients."

Recurrent changes in the DIPG samples were observed that, crucially, were distinct from the supratentorial high-grade astrocytomas, highlighting the distinct genetic characteristics of DIPG.

The researchers identified gene copy number gains of the platelet-derived growth factor receptor α (*PDGFRA*) in approximately a third of the samples. Furthermore, strong PDGFR-α protein expression was observed in two-thirds of the tumors. Hawkins considers this particularly important because "this points to PDGFR inhibitors as potential novel therapeutic agents for use in pediatric DIPG."

In three DIPG samples, low-level gains in poly (ADP-ribose) polymerase (*PARP*)-1 were observed. The coupling of gains in this DNA-damage sensor with defects in other DNA repair pathways indicated that PARP inhibition might be another novel therapeutic target for pediatric DIPGs.

These biological data may guide the design of future clinical trials and the group are currently "expanding [their] analysis to include expression data" in order to build on this knowledge.

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Original article Zarghooni, M. *et al*. Whole-genome profiling of pediatric diffuse intrinsic pontine gliomas highlights platelet-derived growth factor receptor α and poly (ADP-ribose) polymerase as potential therapeutic targets. *J. Clin. Oncol.* **28**, 1337–1344 (2010)