Kinome Profiling in Pediatric Brain Tumors; a New Approach for Target Discovery

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Study Design
PamChip® tyrosine kinase activity profiles of 29 pediatric brain tumors (9 ependymomas, 7 pilocytic astrocytomas, and 13 primitive neuroectodermal tumors, of which 10 medulloblastomas) were generated. From each tumor, 12 slices of 5 μm of a 5x5mm tissue block was lysed.

Key Findings
Figure 1 shows a supervised clustering of the 4 different brain tumor types. The venn diagram in figure 2 shows that 30 substrates are common for all pediatric brain tumor types. 20/30 identified peptides are potentially phosphorylated by Src family kinases. The hypothesis of Src being the common kinase, was confirmed by Phos-Tag SDS-PAGE approach (figure 3). This technique makes use of the affinity of phosphorylated proteins for the Phos-Tag ligand, resulting in retention of phosphorylated proteins, separating them from their unphosphorylated counterpart during electrophoresis. Src kinase activation in tissue samples of all three brain tumor as well as in each of 9 pediatric brain tumor cell lines was confirmed through Phos-Tag SDS-PAGE (Sikkema et al. 2009).

“Author Quote”
In this study, we successfully applied a novel high-throughput technique to generate tyrosine kinase activity profiles of pediatric brain tumors and show its usefulness in target discovery. We identified and validated Src activity as a potential target in pediatric brain tumors for therapeutic intervention.

Background
Progression in pediatric brain tumor growth is thought to be the net result of signaling through various protein kinase mediated networks driving cell proliferation. Defining new targets for treatment of human malignancies, without a priori knowledge on aberrant cell signaling activity, remains exceedingly complicated. Here, we show kinase profiling using flow-through peptide microarrays as a new concept for target discovery.

Conclusion
PamChip® PTK peptide arrays, were successfully employed as a kinase activity screening technique which allows identifying of new targets for pediatric brain tumor treatment.

References: