

RNA interference (RNAi): An experimental molecular therapeutic approach to the treatment of cancers of the cerebellum

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Medulloblastoma is the most common malignancy of the cerebellum in children. There is strong evidence that medulloblastoma results from the molecular dysregulation of pathways involved in the developing cerebellum. Implicated are members of the hedgehog (Hh) pathway, sonic hedgehog (SHh), smoothen (Smo), patched (Ptch) and the transcription factor family, Gli1-3.

The object of this study was to test the hypothesis that post-transcriptional gene silencing (RNAi) might be useful in determining the role of *hh* genes in the development of medulloblastoma and ultimately its use as a means to control this disease.

The results of these studies show that *shh* and *gli-1* siRNA specifically targeted the mRNA for both *shh* and *gli-1* genes resulting in a significant decrease (greater than 90% by 96 hours following transfection) in the levels of targeted mRNAs and 85% protein expression as measured by Western blot analysis.

The ability to silence these genes *in vitro* has laid the groundwork for murine preclinical studies reported here. The use of this technology as a therapy for patients with different types of brain cancers may lead to the development of an effective treatment that will obviate the need for current modalities which are often associated with severe side effects. In general, cancers of the brain are not uncommon in older dogs and cats. However, most cases of medulloblastoma are seen in younger animals. It is hoped that the results of the current murine study will translate into treatments for veterinary forms of this highly malignant and metastatic cancer.