

Molecular super enhancers: A new key for targeted therapy of brain cancer in children

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Ependymoma refers to a heterogeneous group of cancers that can occur at any age, and is one of the most common types of brain cancer in children. The genetic causes for its development are largely unknown and there are no targeted treatments to date. Scientists from the Hopp Children's Cancer Center at the NCT Heidelberg (KiTZ), in collaboration with colleagues from the U.S. and Canada, have now developed a molecular approach that opens new treatment prospects.

Targeted therapies in cancer medicine are often based on [tumor](#) genome sequencing—a technique that makes it possible to identify targets for precision drugs. However, in some cancer types, these structures have not been found to date. This includes ependymoma, a group of brain tumors that are considered to be largely resistant to chemotherapy. Therefore, it would be crucial to find new options for treating them. Ependymoma can affect children as well as adults. In children, it is one of the most frequent types of [brain cancer](#).

In the quest for novel therapeutic approaches in the treatment of ependymoma, the scientists have now taken a circuitous route. Testing an alternative approach, they took a closer look at so-called enhancers, regions of the genome that regulate the activity of genes, for example, by serving as docking sites for regulatory proteins (transcription factors). Groups of enhancers with strong enhancer potential for key cellular processes are also called super-enhancers. These have already been linked to tumor development in other [cancer types](#).

"Using various genetic and epigenetic analysis methods to examine 42 ependymoma samples, we were able to identify almost 1700 super-enhancers and assign them to specific molecular groups of ependymoma," said Marcel Kool, who is a [group leader](#) at the Pediatric Neurooncology Division of the German Cancer Research Center (DKFZ) and also works at the KiTZ. "We subsequently demonstrated that many of these super-enhancers influence the activity of genes that are implicated in the development of [cancer](#)."

The researchers then took a closer look at the 15 most frequent super-enhancers. They were able to demonstrate that these enhancer elements regulate molecules that are involved in key cellular processes and may therefore be used as targets for targeted therapies. "We have thus identified whole new regulatory circuits controlling tumors development in ependymoma. We were able to interrupt these regulatory circuits using specific agents. As a result, the ependymoma cells slowed down their growth and finally died," said Kristian Pajtler, who is a group leader at DKFZ's Pediatric Neurooncology Division and a scientist at the KiTZ.

Stefan Pfister, DKFZ department head and senior physician at Heidelberg University Hospital, says, "The research results open prospects of completely new treatment options for children with [ependymoma](#), a group of tumors for which we have lacked good drug-based [treatment](#) approaches so far."

More information: Stephen C. Mack et al, Therapeutic targeting of ependymoma as informed by oncogenic enhancer profiling, *Nature* (2017). [DOI: 10.1038/nature25169](https://doi.org/10.1038/nature25169)

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