

Study points to possible treatment target for aggressive liver cancer in kids

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A protein in the cell nucleus already targeted therapeutically for several types of cancer has now been linked to an aggressive form of pediatric liver cancer called hepatoblastoma (HBL), according to a study published in the *Nature* journal *Communications Biology*.

Scientists at Cincinnati Children's Hospital Medical Center conducted extensive biological and genetic tests on donated HBL tumor samples and found highly elevated levels of the protein PARP1 in patients with this cancer. PARP1 modifies chromatin structure in the [cell nucleus](#) to drive the chemotherapy-resistant form of liver cancer, according to the study's lead investigator, Nikolai Timchenko, Ph.D., head of the Liver Tumor Biology, Liver Tumor Program.

An FDA-approved drug called Olaparib that blocks PARP1 is already used to treat other types of cancer. In their tests on human liver [tumor cells](#), Timchenko and colleagues learned that PARP1 binds to DNA regions within many cancer-related genes and activates their expression in (HBL) to drive the disease. When the researchers pharmacologically blocked PARP1 in the tumor cells, this slowed or stopped cancer progression.

"Our findings provide a strong rationale for testing PARP1 inhibitors to treat aggressive pediatric liver cancer, but additional research is needed before we can verify this and recommend that it be tried in patients," Timchenko said. "This includes testing inhibitors in laboratory mouse models of hepatoblastoma to see if they work in a living organism."

The researchers also caution that findings in laboratory models often are not effective in the clinical treatment of patients.

Most Common Pediatric Liver Cancer

HBL is the most common type of pediatric [liver](#)

cancer and affects children during the first three years of life. Although overall survival rates for these patients have improved over the years, substantial numbers of them see their cancer spread, or they face aggressive, therapy-resistant tumors that cannot be removed surgically.

Children with the classic form of HBL have reduced levels of [tumor suppressor proteins](#) (TSPs). The researchers report that patients with aggressive disease have elevated levels of TSPs which undergo modifications and display cancer-promoting (oncogenic) activities. PARP1 is the molecule that causes elevation of the oncogenic forms of the TSPs in aggressive hepatoblastoma as well as activation of other [cancer](#)-related pathways such as beta-catenin.

More information: Leila Valanejad et al, PARP1 activation increases expression of modified tumor suppressors and pathways underlying development of aggressive hepatoblastoma, *Communications Biology* (2018). DOI: [10.1038/s42003-018-0077-8](https://doi.org/10.1038/s42003-018-0077-8)

Provided by Cincinnati Children's Hospital Medical Center

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