New Hope for Deadly Childhood Bone Cancer

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(PhysOrg.com) -- Researchers at Huntsman Cancer Institute (HCI) at the University of Utah have shed new light on Ewing's sarcoma, an often deadly bone cancer that typically afflicts children and young adults. Their research shows that patients with poor outcomes have tumors with high levels of a protein known as GSTM4, which may suppress the effects of chemotherapy. The research is published online today in the journal *Oncogene*.

"Doctors and researchers have long known that certain Ewing's sarcoma patients respond to chemotherapy, but others don't even though they have the same form of cancer," says HCI Investigator Stephen Lessnick, M.D., Ph.D. "Our research shows that GSTM4 is found in high levels among those patients where chemotherapy doesn't seem to work. It's found in low levels in patients where chemotherapy is having a more positive effect."

The research could lead to drugs that can suppress GSTM4 in certain patients. It also could lead to a screening test that could reveal which therapies will be most effective for patients. "GSTM4 doesn't seem to suppress the benefits of all chemotherapy drugs, just certain ones. A GSTM4-based test could help to identify the best therapy for each individual patient," Lessnick says.

Ewing's sarcoma is the second most common bone cancer in children and adolescents. The five-year survival rate is considered poor at about 30 percent if the cancer has spread by the time it is diagnosed, and there is an even poorer prognosis for patients who have suffered a relapse.

For this study, researchers focused on an abnormal protein known as EWS-FLI, which is found in most Ewing's sarcoma tumors. What they discovered is that EWS-FLI causes increased amounts of the GSTM4 gene - and the protein it produces - to be expressed in tumors, a previously unknown effect that led them to make the connection between poor outcomes and high levels of GSTM4. The discovery was made by focusing on repetitive DNA sequences called microsatellites. Microsatellites are sometimes referred to as "junk DNA" because they are not thought to have a normal role in the genome. By examining how EWS-FLI interacts with certain microsatellites, Lessnick and his team were able to identify GSTM4.

Lessnick says the next step in research is to focus on testing and treatments that may lead to better survival rates in patients. "Personalized medicine is the next frontier in the battle against cancer," he says. "We now know all cancers are not the same. By focusing on how these proteins are expressed in individual tumors, we may soon be able to offer the treatment that will work best for each patient, and that could lead to higher cure rates," he says.

Lessnick is director of HCI's Center for Children's Cancer Research, and is a Jon and Karen Huntsman Presidential Professor in Cancer Research. This research was supported by funds from the Terri Anna Perine Sarcoma Fund, the Liddy Shriver Sarcoma Initiative, the Sunbeam Foundation, the Huntsman Cancer Foundation, and Alex's Lemonade Stand Foundation.

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