Stopping the spread of a deadly childhood bone cancer

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Many children with the bone cancer, osteosarcoma, die after the tumor spreads to their lungs. In a critical step toward finding a way to stop metastasis, researchers at Georgetown Lombardi Comprehensive Cancer Center say they have discovered an agent that prevents this type of cancer from spreading to the lungs in mice with the disease.

The new agent stops or inhibits "ezrin," a protein vital to the spread of osteosarcoma, say the researchers who presented their findings today at the American Association for Cancer Research (AACR) Annual Meeting 2012. If proven effective in human studies, their ezrin inhibitor might potentially treat adults whose cancers are fueled by over-expression of this protein, and could be a life-saver for children with bone tumors.

"If we can prevent metastatic disease in osteosarcoma, we will significantly improve survival and quality of life for these patients," says the study's senior investigator, Aykut Üren, M.D., an associate professor of oncology, and of biochemistry and molecular & cellular biology at Georgetown Lombardi Comprehensive Cancer Center.

The molecule they discovered represents the first-in-class ezrin inhibitor, he says. "In addition to its potential clinical application, an ezrin inhibitor will be an extremely valuable tool in the laboratory as we work to better understand how ezrin works."

Ezrin is present in many types of cells in the body including cancer cells.

It controls how the cell interacts with its environment, how the cell moves and how it survives in new locations.

In osteosarcoma, the tumor cells that produce high levels of ezrin are more aggressively invasive, Üren says. "Ezrin also helps cancer cells survive when they reach the lungs. If an osteosarcoma cell with no ezrin spreads to the lung, it can't grow there. Having too much ezrin makes it easier for cancer cells to move to the lungs and, once there, it gives these cells a growth advantage."

Osteosarcoma most commonly develops around knee and shoulder joints in children and is "relatively easy to treat the tumor on the limbs, but when the lungs are involved, patients usually die due to pulmonary insufficiency," he says.

If successfully developed, an ezrin inhibitor may be useful in preventing the spread of other tumors, too. Breast cancers, colon cancers, melanoma, ovarian carcinoma, brain tumors, and soft tissue sarcomas all show evidence that too much ezrin may mean poor survival outcomes for the patient, says Üren.

Üren and his research team are currently testing several novel compounds in other disease models, including rhabdomyorsarcoma (tumors of the skeletal muscles). They also are making derivatives of several compounds to further increase effectiveness. Some of these new derivatives are also presented the same annual meeting of the AACR today.

"Although we feel we have made a great discovery towards establishing a novel targeted therapy, we are far from our ultimate goal of using this in humans," Üren says.

Other investigators on this work include Jared T. Murdoch, Sung-Hyeok

Hong, Gulay Bulut, George W. Kosturko, Lauren E. Drebing, and Jeffrey A. Toretsky, all of Georgetown Lombardi. The authors also wish to thank Milton Brown and Mikell A. Paige for their contributions.

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Üren, Bulut, Kosturko, Toretsky, Brown and Paige are named as co-inventors on a patent application that has been filed by Georgetown University related to technology described in this abstract.

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