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Research identifies potential proteins to target in osteosarcoma treatment

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New models developed at the Masonic Cancer Center, University of Minnesota reveal the genes and pathways that, when altered, can cause osteosarcoma. The information could be used to better target treatments for the often-deadly type of cancer.

The new research is published in *Nature Genetics*.

"Human osteosarcoma tumors are so genetically disordered it is nearly impossible to utilize usual methods to identify the genes associated with them," said first author Branden Moriarty, Ph.D., researcher in the Masonic Cancer Center and the University of Minnesota Medical School's Department of Pediatrics. "This model offers the first opportunity to understand and research the genetics and drivers of osteosarcoma."

Moriarty partnered with researchers in the lab of David Largaespada, Ph.D., also with the Masonic Cancer Center and UMN Medical School's Department of Pediatrics. The researchers utilized the "Sleeping Beauty" method to develop the cancer model, a technique developed by the Largaespada lab in 2005 and now used widely around the world.

The comprehensive genomic analysis uncovered several osteosarcoma genes which make proteins that could be targets for therapies in the future, such as SEMA4D and SEMA6D. SEMA4D and SEMA6D were found to be expressed at high levels in over half of all human osteosarcomas. Slowing or inhibiting the expression of SEMA4D could

help stop the growth of osteosarcoma.

"SEMA4D seems to cause many human osteosarcomas to grow out of control," said Largaespada. "We think, in the future, osteosarcomas could be targeted using monoclonal antibodies versus SEMA4D."

Targeted antibodies for SEMA4D are in clinical trials for other solid tumors. The discovery of its relationship to osteosarcoma could pave the way for future trials in patients with osteosarcoma.

More information: A Sleeping Beauty forward genetic screen identifies new genes and pathways driving osteosarcoma development and metastasis, *Nature Genetics* 47, 615–624 (2015) DOI: 10.1038/ng.3293

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