Notch1 and osteoblasts play role in bone cancer initiation

September 8 2014

(Medical Xpress)—A new mouse model of osteogenic sarcoma, a potentially deadly form of bone cancer, shows that high levels of Notch1, a gene that helps determine cell fate, can drive osteoblasts (cells that normally lead to bone formation) to become cancerous, said researchers from Baylor College of Medicine in a report in the journal *Cancer Cell*.

"This is the first example of Notch1 driving this type of cancer," said Dr. Brendan Lee, professor and interim chair of molecular and human genetics at Baylor and corresponding author of the report. "Our study supports the hypothesis that Notch activating mutations can act as a common triggering mechanism in cells of mesenchymal origin such as committed osteoblasts." (Cells of mesenchymal origin are precursors of bone, cartilage and other skeletal cells.)

"This is an unusual cancer that affects mainly the young and adults over 40," said Lee. Treatment, once the disease has metastasized (spread beyond the primary tumor in bone), is only about 50 percent successful, said Lee, who is also the director of the Rolanette and Berdon Lawrence Bone Disease Program of Texas and a Howard Hughes Medical Institute investigator.

Determining what drives the disease at the molecular level can help identify targets that could improve treatment, he said.

In their studies with the mouse model of the disease, in which tumors

display important features of human osteogenic sarcoma, Lee and his colleagues found that when Notch is activated and a tumor suppressor called p53 is lost, the development of the bone cancer is speeded up.

Their studies in the mouse found that osteoblasts, the precursors to the formation of bone and other bone-related cells, can be cells in which osteogenic sarcoma starts, said Lee.

Lee holds the Robert and Janice McNair Endowed Chair in Molecular and Human Genetics at Baylor.

More information: *Cancer Cell*, www.cell.com/cancer-cell/abstr … 1535-6108(14)00311-0

Provided by Baylor College of Medicine