Osteoporosis drug may treat breast and liver cancers

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(Medical Xpress)—A drug used to prevent and treat osteoporosis in post-menopausal women may also be able to treat some breast and liver cancers, according to a new study from Oregon State University.

Although clinical trials on patients are still needed, in lab tests researchers found that the drug raloxifene, which is marketed under the brand name Evista by Eli Lilly and Co., killed human breast cancer cells that are "triple-negative" as well as liver cancer cells.

Triple-negative breast cancers represent about 15-20 percent of all breast cancers in the United States and are more common in younger and African-American women, according to a factsheet from the Susan G. Komen organization. Chemotherapy, radiation and surgery are the preferred treatments because triple-negative breast cancers don't respond to typical medications like tamoxifen or trastuzumab. That's because their cells lack receptors for estrogen, progesterone and a protein known as human epidermal growth factor receptor 2.

Receptors, which are proteins in or on cells, are like a lock. Hormones act like keys to these receptors to unlock different cellular functions. For example, estrogen causes uncontrolled proliferation of breast cancer cells by binding to a receptor. It's known that raloxifene blocks estrogen from binding to its receptor and thus keeps breast cancer cells from multiplying.

But what OSU researchers discovered is that raloxifene also binds with a

protein called the aryl hydrocarbon receptor (AhR) and kills cancer cells that do not have receptors for estrogen, said Ed O'Donnell, a postdoctoral scholar at OSU who conducted the research.

O'Donnell also analyzed survival data on women who had breast cancers that didn't require hormones to fuel the proliferation of the tumor cells. He found an increased survival rate in the women whose breast cancers had higher levels of the AhR protein.

"Our findings are exciting for two reasons," said OSU cancer researcher Siva Kolluri, who led the research, which was published in the journal *Cell Death and Disease*. "No. 1, our research revealed that we can target a specific protein, the AhR, to potentially develop new drugs for liver cancer and a subset of stubborn breast cancers. That's a major goal of our lab. No. 2, we discovered that raloxifene, a known drug, could potentially be repurposed to treat two distinct types of cancers."

The U.S. Food and Drug Administration approved raloxifene for use in bone loss prevention in post-menopausal women in 1997. In 1999, it was approved for treating postmenopausal women with osteoporosis. In 2007, the agency approved the use of raloxifene for reducing the risk of invasive breast cancer in post-menopausal women with osteoporosis and in post-menopausal women at high risk for invasive breast cancer, which spreads outside the lobules or milk ducts into surrounding breast tissue.

Raloxifene again hit the news in January when the federal government announced that most health insurance plans will be required to offer the prescription medicine at no cost to women who have an increased risk of developing breast cancer.

More information: "The aryl hydrocarbon receptor mediates raloxifene-induced apoptosis in estrogen receptor-negative hepatoma and breast cancer cells." O'Donnell EF, Koch DC, Bisson WH, Jang HS,

Kolluri SK. *Cell Death Dis.* 2014 Jan 30;5:e1038. DOI: 10.1038/cddis.2013.549.