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Dormant prostate cancer cells may be reawakened by factors produced in inflammatory cells

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Researchers in the Cedars-Sinai Samuel Oschin Comprehensive Cancer Institute discovered in pre-clinical models that dormant prostate cancer cells found in bone tissue can be reawakened, causing metastasis to other parts of the body. Understanding this mechanism of action may allow researchers to intervene prior to disease progression.

"Understanding how and why dormant cells in bone tissue metastasize will aid us in preventing the spread of disease, prolonging survival and improving overall quality of life," said Chia-Yi "Gina" Chu, PhD, a researcher and postdoctoral fellow in the Uro-Oncology Research Program and lead author of the study published in the journal *Endocrine-Related Cancer*.

In the study, investigators found that cancerous cells in the bone were reawakened after exposure to RANKL, a signaling molecule commonly produced by inflammatory cells. Researchers then genetically engineered cells to overproduce RANKL and found that these cells could significantly alter the gene expression of surrounding dormant cells in lab studies and in laboratory mice, causing them to transform into aggressive cancer cells.

Researchers then injected these engineered RANKL cells directly into the blood circulation of laboratory mice, which caused dormant cells within the skeleton to reawaken, creating tumors within the bone. When

the RANKL receptor or its downstream targets were blocked, tumors did not form.

"After examination, these engineered tumors were found to contain both RANKL-producing prostate cancer cells and dormant cells, which had been transformed to become cancerous," said Chu. "However, the transformed cells displayed aggressive traits that would metastasize to bone and become resistant to standard hormone therapies used to treat the disease."

Though findings are preliminary, researchers plan to identify other cells known to produce RANKL that may also recruit and reprogram dormant cells to colonize bone tissue. Investigators plan to embark into clinical research with human patients in collaboration with leading Cedars-Sinai researchers, including Edwin Posadas, MD, medical director of the Urologic Oncology Program.

"Though more work must be done to understand how RANKL reprograms dormant cells to become cancerous, we look forward to examining its influence on promoting metastasis and secondary tumors, as well as the possibility of 'deprogramming' metastatic cancer cells," said Leland Chung, PhD, director of the Uro-Oncology Research Program.

More information: *Endocrine-Related Cancer*. 2014 January: RANK- and c-Met-mediated signal network promotes prostate cancer metastatic colonization.

Provided by Cedars-Sinai Medical Center

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