

PBX1 identified as a new pioneer factor underlying progression in breast cancer

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The presence of a new pioneer factor, known as PBX1, can guide the response to estrogen in breast cancer cells according to researchers at Dartmouth-Hitchcock Norris Cotton Cancer Center in results published on November 17 in the open-access journal *PLoS Genetics*. This research reveals that PBX1 alone can determine the risk of the spread of cancer in patients with estrogen receptor alpha (ER α)-positive breast cancer, which accounts for about two-thirds of all breast cancers diagnosed in North America.

Pioneer factors are an emerging class of chromatin remodelers with the capacity to modulate cellular identity as they set the stage by defining the genomic regions accessible for transcription factors. "Since cancer is characterized by a loss of cell-fate identity, it is not surprising that other pioneer factors have already been characterized as oncogenic factors in breast cancer, but PBX1 is one that discriminates progression," said Dr. Mathieu Lupien, assistant professor of genetics, Norris Cotton Cancer Center, Dartmouth Medical School, who served as principal investigator for the study. Specifically, this research demonstrates that PBX1 directly modulates chromatin compaction at discrete genomic regions to promote the recruitment of the transcription factor $ER\alpha$, driving the proliferative response to estrogen in <u>breast cancer cells</u>.

"Unfortunately, numerous $ER\alpha$ -positive patients with breast cancer progress to more advanced stages of the disease as they develop resistance to endocrine therapies, which directly target $ER\alpha$." said lead author Dr. Luca Magnani, post-doctoral scientist.



"This work may rapidly translate to the clinic because PBX1 could likely serve as a prognostic marker for ER α -positive breast cancer progression. It also highlights the potential therapeutic benefit of developing means to antagonize pioneer factors such as PBX1 to prevent <u>breast cancer</u> progression" said Dr. Lupien.

More information: Magnani L, Ballantyne EB, Zhang X, Lupien M (2011) PBX1 Genomic Pioneer Function Drives ERa Signaling Underlying Progression in Breast Cancer. *PLoS Genet* 7(11): e1002368. doi:10.1371/journal.pgen.1002368

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