Six2 homeoprotein allows breast cancer cells to detach and metastasize

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In results presented at the AACR Annual Meeting 2013, researchers from the University of Colorado Cancer Center show that the Six2 homeoprotein, while not involved in primary tumor growth, allows cells to detach from substrate and survive their transition through the bloodstream to faraway sites of metastasis.

"Here we show for the first time that Six2 causes breast cancer progression. It's this metastasis, especially to the lung, that can eventually be deadly and so perhaps even more so than affecting the size of the primary tumor, we are especially excited to present this new information about metastasis," says first author Chu-An Wang, PhD, postdoc in the lab of CU Cancer Center investigator Heide Ford, PhD, the paper's senior author.

The Six2 gene codes for a transcription factor that regulates cell growth – needed in developing kidney tissues, but then silenced in the healthy, adult body. Some breast cancer cells have discovered a way to reactivate this Six2 gene, which allows them to survive detachment from their tissue of origin and the programmed cell death known as anoikis that makes most wandering cells self-destruct.

Wang and colleagues knocked down Six2 expression in breast cancer cells and showed that the cells' ability to metastasize in mouse models was much reduced. Interestingly, Six2 knockdown did nothing for the cells' ability to grow at the site of origin. Corroborating the claim of Six2's role in metastasis is its correlation with poor prognosis in human

breast cancer tissues – of 1881 samples examined from the GOBO database, the breast cancer tissues higher in Six2 were simply more aggressively metastatic.

"We're now working to discover Six2's target genes," Wang says. "For example, we hypothesize an effect on the expression of E-Cadherin, whose loss has been implicated in the metastatic potential of many cancers."

Provided by University of Colorado Denver

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