Researchers identify protein that causes epithelial cancers to spread

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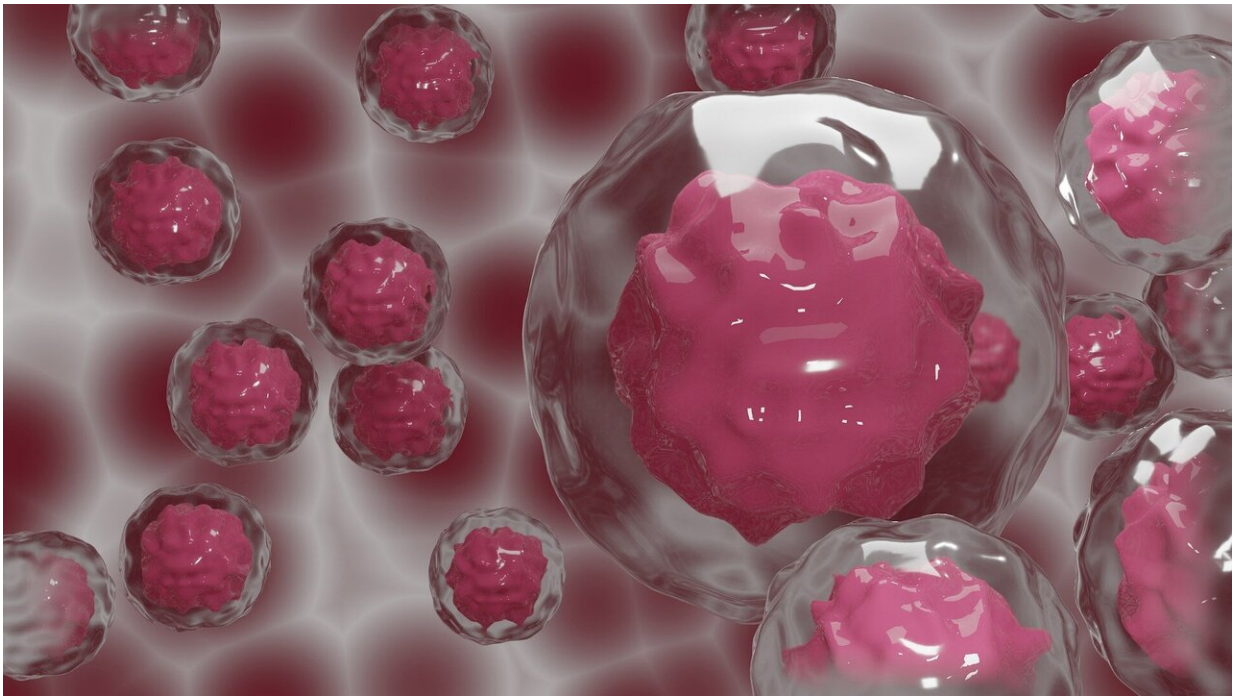

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Cancer is complex and unpredictable. Despite successful treatment or years of remission, there is always a chance that a patient's cancer can return. It usually happens in the form of metastasis, which is when remaining cancer cells in the body spread to another location and grow. Moffitt Cancer Center researchers are working to better understand what happens at the cellular level of cancer to develop new strategies to

prevent and treat metastasis. In a new article published in the July issue of *Cancer Research*, Elsa Flores, Ph.D., and her team discovered a key protein that oscillates its expression through microRNA regulation to facilitate cancer spread to distant organs. This protein is deltaNp63, a member of the p53 family of tumor suppressor genes.

The overarching goal of the Flores lab is to develop therapies for p53 mutant cancers. P53 is difficult to target therapeutically because of its wide range of important cellular functions. This work from the Flores lab expands on previous research focused on the p53 family and its role in inhibiting tumor development and growth. DeltaNp63, a protein and p53 family member, regulates the epithelial to mesenchymal (EMT) process, which in cancer can allow cells to lose contact with surrounding tumor cells, enter the blood stream and spread to other areas of the body. This protein is overexpressed in many primary tumors and metastases. The Flores lab showed that deltaNp63 must be silenced for the cancer cells to undergo EMT and enter the blood stream to spread.

To better understand the deltaNp63 protein expression and its role in cancer metastasis, the Flores lab developed mouse models to modulate deltaNp63 expression during breast cancer metastasis. They found that oscillatory, or periodic, expression of the protein is required for efficient metastasis. They also discovered a network of four microRNAs, regulated by TGFbeta;, that can target and silence deltaNp63 expression.

"This finding is important because it gives us better insight into the regulation of deltaNp63 and TGFbeta; key players in the metastatic process," said Flores, chair of the Department of Molecular Oncology and leader of the Cancer Biology and Evolution Program at Moffitt. "P53 is commonly mutated in human cancers, and we have found that deltaNp63 and p53 interact extensively in cancer. We can use this information to design personalized therapies for cancer patients with alterations in the p53/p63 pathways."

The Flores lab is developing microRNA-based therapies to keep proteins like deltaNp63 expressed at appropriate levels in the proper context in a growing cancer to block metastatic spread.

More information: Ngoc H.B. Bui et al, Spatiotemporal Regulation of ΔNp63 by TGFβ-Regulated miRNAs Is Essential for Cancer Metastasis, *Cancer Research* (2020). DOI: 10.1158/0008-5472.CAN-19-2733