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Researchers identify a potential molecular trigger for invasiveness in prostate cancer cells

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A small protein modification can trigger the aggressive migratory and invasive properties of prostate cancer cells, according to new research published on the cover of *Oncotarget*. The findings give greater insight into how cancers can move from one location in the body to another, and could help develop more effective therapies in the future.

When cells break free from the original tumor and migrate to another location through the bloodstream, they become metastatic. The emergence of secondary tumors is often correlated with a poor prognosis.

The cellular process that allows these cells to migrate is known as epithelial-to-mesenchymal transition (EMT). One of the proteins thought to activate EMT is called transforming growth factor β (TGFβ), which exerts its effects by activating several other proteins, including one called Snail1. While the activation of Snail1 is recognized as an important event in EMT, how it happens has remained unclear. Revealing this mechanism could give scientists a way to target EMT, thus preventing cancer metastasis.

The Oncotarget study, carried out by researchers from two Swedish universities, Umeå University and Uppsala University, now reveals a key step in Snail1 modification. The team found that modifying a single amino acid - the building block that makes up proteins - can alter Snail1

and make cancer cells grown in the lab more invasive. This modification, called 'sumoylation,' involves the attachment of other small proteins, which change the structure and function of Snail1. Importantly, the researchers found that preventing the sumoylation of Snail1 by genetic modification abolished the migratory and invasive properties in human prostate cancer cells.

The team also found that modified Snail1 regulated the expression of specific genes and proteins involved in EMT. Furthermore, the researchers identified that in prostate cancer cells, sumoylated-Snail1 can further enhance TGFβ signaling and EMT in prostate cancer. Lastly, when they compared the levels of proteins involved in EMT in prostate cancer tissues and normal tissues, they found levels of several proteins including Snail1 were elevated in the cancer.

"These results suggest that sumoylation of Snail1 might be a marker for prostate cancer progression," said Professor Marene Landström. "As sumoylation inhibitors are currently being tested to combat the development of breast cancer tumors, it would be interesting to see the effects of targeting Snail1 sumoylation in prostate cancer."

Future studies in different cancers is necessary to understand whether sumoylated-Snail1 is a universal trigger for cancer cell invasiveness.

More information: Shyam Kumar Gudey et al, Pro-invasive properties of Snail1 are regulated by sumoylation in response to TGFβ stimulation in cancer, *Oncotarget* (2017). DOI: 10.18632/oncotarget.20097

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