

Researchers discover novel mechanism to stop the spread of breast cancer

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A team of researchers from the Cancer Science Institute of Singapore (CSI Singapore) at the National University of Singapore (NUS) has found that controlling the levels of the TIP60 protein, which is a tumour suppressor, could potentially prevent the spread of breast cancer cells.

Specifically, the research team that is led by Assistant Professor Sudhakar Jha from CSI Singapore discovered that TIP60 interacts with two other proteins called DNMT1 and SNAIL2, to inhibit the spread of cancer cells. This is the first study which reports the novel function of TIP60 in regulating DNMT1-SNAIL2 axis, and subsequently inhibiting metastasis, which is the spread of cancer cells to other parts of the body.

"In this study, we found that the absence of TIP60 raises the levels of DNMT1, resulting in the activation of SNAIL-2 function. When this molecular program is turned on, epithelial cells - which protect or enclose organs - acquire migratory and invasive properties. This leads to the spreading of cancer cells. Understanding this mechanism holds the important key to suppressing the migration of [cancer cells](#)," explained Mr Zhang Yanzhou, a final year PhD student from CSI Singapore's Graduate Programme in Cancer Biology, and first author of the study.

This is an important discovery for [breast cancer](#) patients with poor Overall Survival (OS) and Disease-Free Survival (DFS) prognoses, as it was previously found that TIP60 levels in these patients are low, thus reducing their defence against cancer cell metastasis.

The team's discovery may have important implications for other cancers as patients with colon and cervical cancers have also been found to have irregular TIP60 levels. Hence, the direction of this study may open doors to potential treatment of different types of cancers in the future.

"This study provides important evidence that TIP60 levels could possibly serve as prognostic marker of breast cancer progression, and the stabilisation of TIP60 could be a promising strategy to treat cancers. We are currently developing inhibitors which can increase TIP60 levels and in turn, prevent the spread of cancer. Moving forward, we are also looking into collaborating with clinician scientists from the National University Health System to initiate clinical trials using DNMT1 inhibitors to treat [breast cancer patients](#) and decrease metastasis by targeting cells that have lower levels of TIP60 as these cells are more likely to be invasive," said Asst Prof Jha.

The findings of the study were published in the *Journal of Molecular Cell Biology* in September 2016.

More information: Yanzhou Zhang et al. TIP60 inhibits metastasis by ablating DNMT1–SNAIL2-driven epithelial-mesenchymal transition program, *Journal of Molecular Cell Biology* (2016). [DOI: 10.1093/jmcb/mjw038](#)

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