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New study provides important insight into how tumors metastasize

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Research has shown that the growth of cancerous tumours is affected by transforming growth factor (TGFβ) in the body's cells; TGFβ both suppresses and stimulates tumour development. But it has not been understood how this happens. A new study being published in the journal *Science Signaling* reveals important details behind this process.

"Our hope is that these findings will make it possible to discover a way to selectively inhibit the TGFβ signals that stimulate tumour development without knocking out the signals that inhibit tumour development, and that this can eventually be used in the fight against cancer," says Eleftheria Vasilaki, Postdoctoral Researcher at Ludwig Institute for Cancer Research at Uppsala University and lead author of the study.

The transforming growth factor β (TGFβ) regulates cell growth and specialisation, in particular during foetal development. In the context of tumour development, TGFβ has a complicated role. Initially, TGFβ inhibits tumour formation because it inhibits cell division and stimulates cell death. At a late stage of tumour development, however, TGFβ stimulates proliferation and metastasis of tumour cells and thereby accelerates tumour formation.

TGFβ's signalling mechanisms and role in tumour development have been studied at the Ludwig Institute for Cancer Research at Uppsala University for the past 30 years. Recent discoveries at the Institute, which are now being published in the current study in *Science Signaling*,

explain part of the mechanism by which TGFβ switches from suppressing to enhancing tumour development.

Uppsala researchers, in collaboration with a Japanese research team, discovered that TGFβ, along with the oncoprotein Ras, which is often activated in tumours, affects members of the p53 family. The p53 protein plays a key role in regulating tumour development and is often altered - mutated - in tumours. TGFβ and Ras suppress the effect of mutated p53, thereby enhancing the effect of another member of the p53 family, namely ΔNp63, which in turn stimulates tumour development and metastasis.

Provided by Uppsala University