Blocking Cancer Spread By Tissue Scarring

What to fear most if faced by a cancer diagnosis is the spread of the cancer to other parts of the body. This process accounts for over 90 percent of cancer patient deaths and is a strong focus for cancer researchers. Researchers at BRIC, University of Copenhagen have shown that the enzyme Lysyl Oxidase (LOX) can create a “scarred” microenvironment that enhances cancer spreading. By blocking activity of the LOX enzyme, the researchers succeeded in significantly decreasing metastasis in a model of breast cancer.

'When we inhibit the activity of LOX in our cancer models, we show a dramatic reduction in metastasis. This suggests that therapeutic targeting of LOX can keep the tumor microenvironment “healthy” and thereby decrease metastasis, says Associate Professor Janine Erler from BRIC, who has headed the research. In humans, LOX is an enzyme that is produced in response to tissue injury or chronic inflammation in our organs.

It reacts to damage signals and “glues” collagen molecules together to form the scar-like structure. The result can be a fibrotic environment. The new findings from Janine Erler’s research group show that persistent injury to lung and liver results in a fibrotic microenvironment that supports the growth of new tumors, and thereby enhances metastasis of breast cancer cells to these organs. Blocking LOX prevents the formation of this fibrotic microenvironment, thereby preventing enhanced metastasis to these organs.

'It is well-known that signals from fibrotic tissues can enhance tumor progression and metastasis, but the underlying mechanisms have remained unclear - our new results provide insight into the link between fibrosis and cancer progression. Such a biological understanding is crucial if we are to develop effective therapies preventing tumour metastasis", says PostDoc Thomas Cox from Janine Erler’s laboratory, who undertook the experimental investigation.

Currently, LOX-targeting therapies are under development for use in the clinic against cancer, as it has been known for some while that metastatic tumors express increased amounts of LOX. Yet, the new results from Janine Erler’s group are the first to show that LOX promotes distant metastasis through structural changes in the organ microenvironments in response to persistent injury. The next step for the researchers is to dig deeper into the mechanisms underlying the relationship between fibrosis and cancer metastasis, and also to test their findings in other cancer models such as gastric and colon cancer.

'Further, our study indicates that LOX-targeting therapy can be relevant not only for cancer patients, but also to prevent fibrosis in patients with chronic inflammation or patients who have been exposed to persistent organ injury. This opens up for an even wider applicability of our biological findings, which strongly motivates the basic research in my laboratory, says Janine Erler. The results have just been

published in the international journal *Cancer Research*.

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