

Primary driver of stomach cancer development identified

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In a discovery that could lead to the development of new treatments for gastric cancer, scientists at the Melbourne Branch of the international Ludwig Institute for Cancer Research (LICR) have discovered what appears to be the primary driver of tumor development in the stomach. Results published today on-line in the *Journal of Clinical Investigation* show that inhibiting the signaling cascade initiated by the IL-11 protein prevented the development of inflammation, hyperplasia (an abnormal increase in the number of cells) and tumor formation in pre-clinical models of gastric cancer.

Gastric cancer is the second most common cause of cancer-related deaths around the world, and has been shown previously to be correlated with chronic inflammation. Persistent activation of the Stat3 protein, which is known to play roles in inflammation-associated carcinogenesis, is commonly found in gastric and many other types of cancer.

Until now, however, the underlying cause of hyperactive Stat3 was unknown. The current study demonstrates that IL-11 promotes chronic inflammation and associated tumorigenesis in the stomach by inducing excessive activation of Stat3. The study used both genetic and pharmacologic inhibitors to show that blocking this signaling pathway prevented or reduced tumorigenesis in a mouse model of inflammation-dependent human gastric cancer.

“Although we made this discovery in a mouse model, we expect it to be highly relevant to the clinic because of the striking similarity in gastric

tumour development and appearance between mice and men,” says the lead author of the study, Professor Matthias Ernst from the LICR Melbourne Branch. “The clear link between inhibition of IL-11/Stat3 activity and suppression of gastric tumorigenesis that we identified supports the further development of pharmacologic agents that target these molecules for the treatment of gastric and potentially other cancers. We believe that we have a very relevant model in our hand for the preclinical assessment of such compounds as well as for the identification of potential markers that may ultimately help in the early detection of disease.

Source: Ludwig Institute for Cancer Research

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