New research points to amino acid chain as possible cancer, lung disease treatment target

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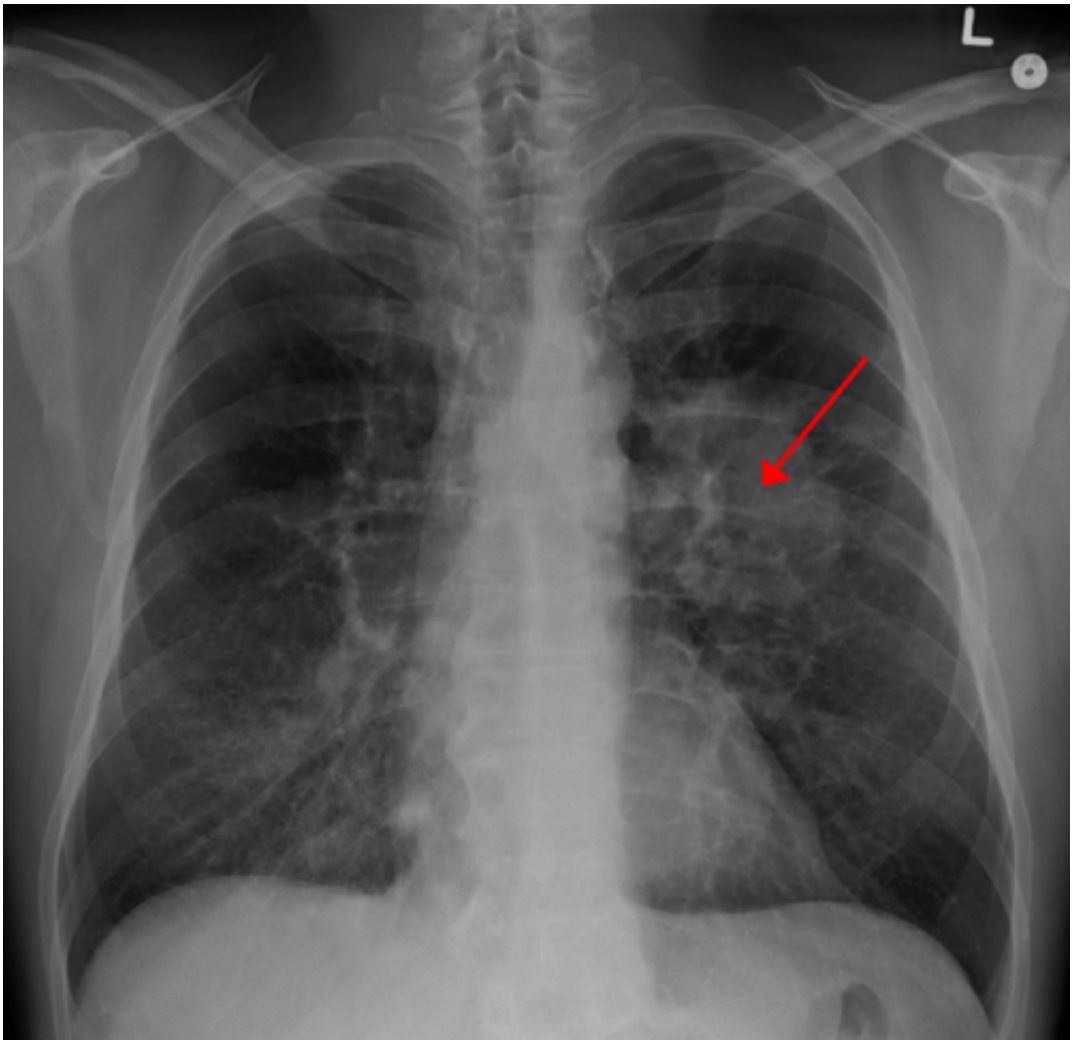

Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

An estimated 19 million new cases of cancer were diagnosed worldwide in 2020, and almost 10 million people across the globe died of the disease. This week, researchers will explore how endothelin, an amino acid chain secreted by the endothelial cells that line the blood vessels, plays a role in cancer progression and lung disease sometimes caused by cancer treatment. The researchers are meeting at the Seventeenth International Conference on Endothelin (ET-17), hosted and organized by the American Physiological Society (APS).

Endothelin (ET) is a vasoconstrictor, meaning it causes blood vessels to narrow. Too much endothelin—also called overexpression—can lead to chronic health conditions such as high blood pressure, heart disease and vascular dysfunction. Three forms of endothelin—ET-1, ET-2 and ET-3—are encoded by different genes but function in a similar fashion. Recent research suggests that ET-1 and ET-2 may play a role in cancer progression and that in some situations act in contrast to one another.

Endothelin-2 may be promising target to treat lung cancer

Lung cancer is the third most common cancer in the U.S. and tops the list of cancer deaths worldwide. Adenocarcinoma, a form of the cancer that begins in the epithelial cells of glands, is the most common type of lung cancer. Previous research has shown that ET-1 expression is high in people with lung adenocarcinoma. In a new study that explored the function of ET-1 and ET-2 in lung cancer, researchers from the Kobe Graduate School of Medicine and Kobe Pharmaceutical University in Japan found that silencing (blocking) ET-2 in human adenocarcinoma cells led to reduced proliferation, less spread and increased cell death. These results suggest that "endothelin-2 might be a promising target for lung adenocarcinoma treatment," said Ratih Paramita Suprapto, MD, first author of the study.

Blocking endothelin-1 receptor may improve ovarian cancer recurrence, survival rate

High-grade serous ovarian cancer is the most common type of ovarian cancer and carries the poorest prognosis. Researchers from the IRCCS-Regina Elena National Cancer Institute in Italy have identified a protein interaction—called the endothelin-1/ZEB1/YAP regulatory circuit—that drives tumor growth in high-grade serous ovarian cancer. The research team found that blocking the activity of endothelin-1 receptors that transmit this signaling pattern impaired tumor growth. These results "suggest that endothelin-1 receptor blockade can be exploited as a target therapeutic strategy for preventing recurrence, leading to an improvement of the survival of ovarian cancer patients," explained Rosanna Sestito, Ph.D., first author of the study.

Two forms of endothelin act differently in drug-induced lung disease

People with pulmonary (lung) fibrosis, an incurable condition in which the lung tissue becomes thick and scarred, have been found to have higher levels of ET-1. Certain medications, including bleomycin, a drug used to treat cancer, can lead to lung fibrosis in some people. Several previous studies suggested that ET-1 strongly promotes pulmonary fibrosis development. In a new study, researchers studied the effects of ET-2 on a mouse model of lung fibrosis. The research team found that mice without ET-2 in their epithelial cells had worsened the bleomycin-induced pulmonary fibrosis. In addition, mouse lung cells treated with ET-1 showed higher fibrogenic activity, while those treated with ET-2 showed less fibrogenic activity than a control group. These results lead to the intriguing discovery that "peptides with high similarity could possibly have divergent effects in certain conditions and cells," said Aristi Intan Soraya, MD, of Kobe Pharmaceutical University in Japan, first author of

the study.

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