

BC EXTRA | PRECLINICAL NEWS

SALK STUDY UNVEILS LIF'S MECHANISM IN FORM OF PANCREATIC CANCER

BY LAUREN MARTZ, ASSOCIATE EDITOR

A new study from Salk Institute for Biological Studies pinpoints new mechanistic details about how LIF promotes pancreatic cancer, providing preclinical support for Northern Biologics' lead candidate.

In a *Nature* paper published Wednesday, Salk's Tony Hunter and colleagues showed that LIF is secreted by pancreatic stellate cells (PSCs) to drive pancreatic ductal adenocarcinoma (PDAC) progression and chemoresistance.

Hunter is professor of molecular and cell biology at Salk. Northern Biologics Inc. (Toronto, Ontario) started a Phase I trial of its anti-LIF mAb MSC-1 in solid tumors last year.

LIF was previously identified as a target for cancer based on its immunosuppressive functions in the tumor microenvironment and its role in cancer stem cell biology, and the new data pointing to a specific pathogenic role in pancreatic cancer adds to Northern Biologics' case that the cytokine makes a good target (see "**Two Leases on LIF**").

Northern Biologics CBO Fred Sweeney told BioCentury, "it's quite a nice complementary approach and provides a strong hypothesis on the role of LIF in resistance in pancreatic cancer."

The Salk researchers identified LIF as a key factor in the communication between activated PSCs and pancreatic cancer cells, which is known to enhance progression and metastasis. They showed that PSC-secreted LIF activates STAT3 in the cancer cells, driving proliferation.

In a mouse model of PDAC, knockout of LIF receptor LIFR expressed on pancreatic cancer cells increased survival, which was further extended by combination treatment with gemcitabine chemotherapy. A LIF-neutralizing mAb produced similar results in the same model.

The team tied LIF levels to disease progression in mice and humans. In mice, LIF levels were elevated during the earliest stages of tumorigenesis, and increased during progression. LIF was also higher in tissues from 77 PDAC patients than in tissues from healthy controls.

In blood samples from PDAC patients, LIF levels correlated with response to chemotherapies, suggesting the target could also serve as a marker to monitor drug response.

CEO Philip Vickers told BioCentury that LIF is among the biomarkers Northern Biologics is evaluating in its clinical trial.

According to BioCentury's BCIQ database, Northern Biologics is the only company targeting LIF. Northern Biologics has not licensed IP involving LIF from Salk.

Celgene Corp. (NASDAQ:CELG) has an option to acquire MSC-1.

Targets: LIF - leukemia inhibitory factor; LIFR (CD118) - leukemia inhibitory factor receptor α ; STAT3 - signal transducer and activator of transcription 3