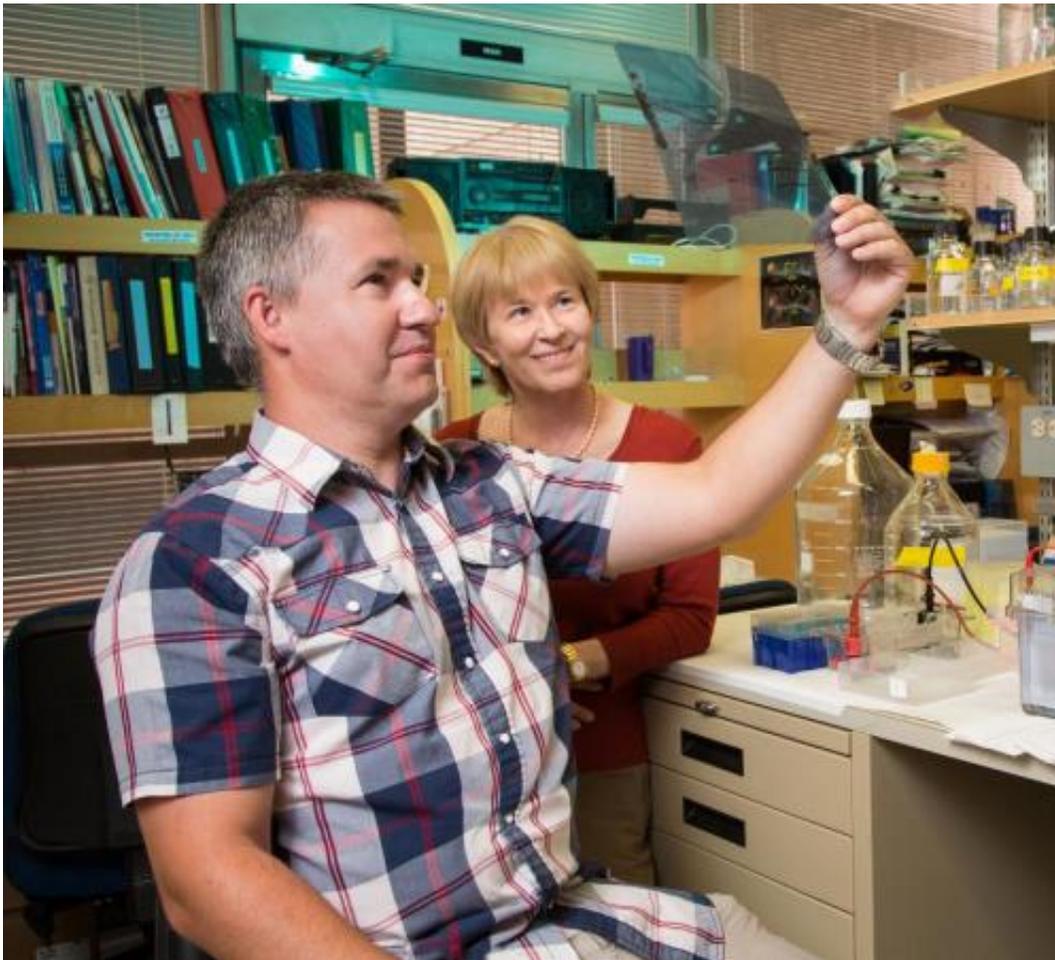


Study identifies novel regulator of key gene expression in cancer

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This image shows Michal Krawczyk and Beverly Emerson, Professor of Regulatory Biology Laboratory. Credit: Salk Institute for Biological Studies

Scientists at the Salk Institute for Biological Studies have identified a

key genetic switch linked to the development, progression and outcome of cancer, a finding that may lead to new targets for cancer therapies.

The switch, a string of nucleotides dubbed a long non-coding RNA (lncRNA), does not code for proteins like regular RNA. Instead, the scientists found, this particular lncRNA acts as an on/off switch for a key gene whose excessive activity is tied to inflammation and [cancer](#), COX-2.

The COX-2 gene mediates inflammation, which in most cases helps our bodies eliminate pathogens and damaged cells. But inflammation also has a dark side: it aids growth and spread of tumors in the early stages of cancer. By learning more about how COX-2 is affected, scientists may be able to provide a potential target for future cancer treatment.

"Deciphering the mechanism of COX-2 gene regulation is of great clinical interest," says senior author Beverly Emerson, a professor in Salk's Regulatory Biology Laboratory and holder of the Edwin K. Hunter Chair. "COX-2 is instrumental in the development of several types of cancer, including colon, breast and [prostate cancer](#). Strategies that specifically modulate COX-2 activity could be an attractive treatment approach."

The findings of the study were published April 29 in the open-access online journal [eLife](#).

The function of lncRNAs is not well understood, but evidence increasingly points to their role in regulating [gene expression](#), as they are found overexpressed in esophageal, colorectal and breast cancers.

Using human mammary epithelial cells, Emerson and Michal Krawczyk, a senior scientist in Salk's Regulatory Biology Laboratory, discovered that an lncRNA called PACER (p50-associated COX-2 extragenic RNA)

teams up with molecules that change the activity of the COX-2 gene. The scientists demonstrated that PACER kicks a molecule called p50 off of the COX-2 gene, causing COX-2 to go into overdrive. This is the first time scientists have shown that non-coding RNAs must be activated in order to squelch the activity of p50, a gene repressor. In turn, says Krawczyk, blocking p50 promotes the assembly of molecular activators of gene expression, which ramp up COX-2 activity.

The Salk scientists were also surprised to note an additional potential role for PACER-induced COX-2 activation in cancer. Early in the disease process, instead of activating the [immune system](#) to clear malignant cells from the body, COX-2 aids the growth and spread of tumors. In later stages of disease, however, Krawczyk says cancer cells often shut off COX-2 activity, as if at that stage COX-2 is no longer beneficial for tumor growth because it exposes spreading tumor cells to the immune system. That presents the opportunity to trigger COX-2 expression via PACER in late-stage cancers to aid immune system clearance of metastatic cells.

"This could be a potential treatment for late-stage cancers," says Krawczyk. "We could possibly use small molecules to reactivate COX-2 activity, or perhaps even supply PACER itself, to fight the disease."

Provided by Salk Institute

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