

Retinoblastoma dysfunction promotes pancreatic cancer cell growth

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Indiana University cancer researchers have discovered that a protein that normally suppresses tumors actually promotes the growth and spread of pancreatic cancer.

Murray Korc, M.D., the Myles Brand Professor of Cancer Research at the Indiana University School of Medicine and a researcher at the Indiana University Melvin and Bren Simon Cancer Center, and colleagues have shown that the retinoblastoma protein, a tumor suppressor, often malfunctions in [pancreatic cancer](#). That dysfunction enables an inhibitory protein to promote pancreatic cancer growth.

The research was published online today in the *Journal of Clinical Investigation*.

As a result of the dysfunctional retinoblastoma protein, pancreatic cancer cells lose their ability to be inhibited by transforming growth factor-beta, or TGF- β , which is a key negative regulator of cell proliferation, according to Dr. Korc. Instead, the cells become stimulated by TGF- β due to activation of abnormal downstream signals known as non-canonical pathways.

The researchers also showed that TGF- β induces the expression of a growth-stimulating molecule called Wnt7b, which is not usually found in a normal adult pancreas. This combination allows TGF- β to directly enhance pancreatic cancer [cell proliferation](#) and survival.

Dr. Korc explained the combination of TGF- β and Wnt7b actions: "You have a cancer in which the accelerator is stuck to the floor and the brake is broken. But because of the malfunctioning retinoblastoma [protein](#), the combined actions of TGF- β and Wnt7b convert the broken brake into a second accelerator."

Because the abnormal pathways activated by TGF- β and Wnt7b can be disrupted with drugs, Dr. Korc

suggested that the findings open up a new avenue for exploring novel therapeutic combinations in pancreatic cancer.

However, Dr. Korc cautioned that more work remains to be done to determine how to best restore the regulatory functions of the [retinoblastoma protein](#) and prevent the harmful actions of TGF- β .

"We have to figure out how to target these important pathways and to prevent bypass pathways from being activated," he said.

Provided by Indiana University

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