

When cancer cells stop acting like cancer

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Researchers noticed that cancer cells crowded back-to-back -- high density -were less effective at invading cancer-free tissue than cells grown in a low density -- less crowded -- environment. Credit: Ghada M. Sharif/Georgetown

Cancer cells crowded tightly together suddenly surrender their desire to spread, and this change of heart is related to a cellular pathway that controls organ size. These two stunning observations are reported today by researchers at Georgetown Lombardi Comprehensive Cancer Center



in the journal Oncogene.

"What we really need in <u>cancer treatment</u> is a way to stop cancer from growing in the organ it has spread to, and we have discovered a mechanism that seems to do that," says the study's senior investigator, Anton Wellstein, MD, PhD, a professor of oncology and pharmacology at Georgetown Lombardi.

Wellstein says the initial finding was made when Ghada M. Sharif, PhD, a member of the Wellstein lab, noticed that cancer cells crowded back-toback—high density—were less effective at invading cancer-free tissue than cells grown in a low density—less crowded—environment.

It turns out that high-density cells activated the "Hippo" molecular pathway, an ancient biological mechanism that limits the size of an organ. Low-density cancer cells do not engage Hippo, which means the cells are free to grow unchecked within the organ. The trigger for activating Hippo is a single molecule called YAP.

"What was very surprising to us was that this pathway is active in cancer cells," says Wellstein.

"You can make the same cancer cells become invasive or not, depending on whether that pathway is activated—which is fascinating," he says. "Invasive and non-invasive cells are genetically the same. What's different is whether the Hippo pathway is active."

He says experiments show the mechanism is common to a variety of cancers, including breast, prostate, pancreatic and lung.

"We think <u>cancer cells</u> go wild, they just take off. They will invade and there is nothing you can do about it," he says. "But it actually turns out that crowded cells still have that memory of how good citizens—good



cells—behave, and that was a big surprise to us. That is why this finding is quite significant."

Because many cancers metastasize early in their development, a drug based on the Hippo pathway could be used to limit their spread within the organs the cancer spreads to, he says.

"We have figured out a mechanism that is crucial for cancer cell invasion and metastasis, and we have found the driver of that mechanism, but there is still much work to do," Wellstein says.

Provided by Georgetown University Medical Center

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