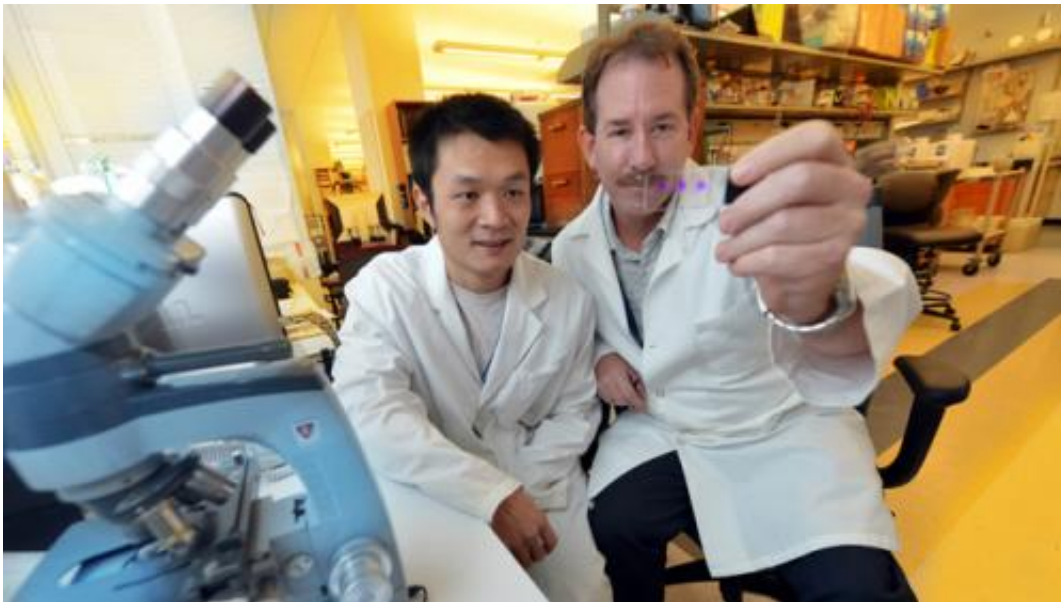


Erectile dysfunction drugs may prevent colon cancer

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This is a photograph cancer researcher, Dr. Darren Browning. Credit: Phil Jones

Erectile dysfunction drugs may be able to help prevent or even treat colon cancer, researchers say.

They are studying three drugs, including Viagra, that appear to protect the lining of the colon from inflammation and other damage resulting from the relentless onslaught of food, drink, and bacteria that we consume. They say the drugs work by protecting the integrity of the colon's natural barrier and reducing excessive and risky [cell proliferation](#)

"We've found a way of activating a tumor suppressive pathway in the gut using drugs already in use for [erectile dysfunction](#)," said Dr. Darren Browning, cancer researcher at the Georgia Regents University Cancer Center and a faculty member at the Medical College of Georgia.

Browning just received a \$1.8 million National Cancer Institute grant to further explore how and how well the drugs work to prevent [colon cancer](#).

As with most things, a healthy colon is about balance, in this case tight regulation of the process of [cells](#) dying and new cells forming and differentiating in the dynamic, caustic environment. "It's basically the inside of your body exposed to the outside world," Browning said of the colon, or large intestines.

The colon is lined with a sheet of mucus on top of a single layer of tightly knit epithelial cells that is peppered with tiny pits, or crypts. To deal with the naturally high turnover of cells in this tough environment, the crypts hold stem cells which produce proliferating cells that ultimately rise up and differentiate into new cells to help maintain important functions such as mucus production and nutrient absorption. Mucus reciprocates by continually oozing out of the crypts to keep foreign object from venturing inside.

"They replace the whole lining every few days," Browning said. If the renewal process gets out of balance, the protective barrier of [mucus](#) and endothelial cells can break down, exposing underlying tissue to gut contents, causing inflammation and setting the stage for cancer.

Browning had discovered that an enzyme called type 2 protein kinase G, or PKG2, has an important role in protecting the cells that make up the

barrier and slowing down cell proliferation in the colon. His research team set about looking for ways to increase PKG activation in the colon as a way to reduce cancer risk and help patients with inflammatory bowel disease.

"We became interested in the erectile dysfunction drugs because they are known to increase the levels of a chemical called cyclicGMP, which can activate PKG," Browning said.

In the penis, the drugs' activation of PKG relaxes the smooth, circular muscles around blood vessels so they can fill with blood. The drugs essentially work the same way to reduce pulmonary hypertension in premature babies.

The three drugs Browning is using in the colon inhibit phosphodiesterase, an enzyme that breaks bonds, in this case, cleaving cyclicGMP so that it does essentially nothing. Inside the colon, Browning found that the drugs activate PKG2.

He has two mouse models, one with a genetic predisposition for colon cancer and another with a more common, inflammation-driven disease. They'll be giving the drugs by mouth to both models to see if they can prevent or dramatically reduce the incidence of colon cancer. They also want to know which [drug](#) works best and to double check that PKG2 is a central point of action that results in barrier protection and cancer prevention.

Browning also is pursuing the drugs' effectiveness in colitis, a painful inflammation of the colon and a major risk factor for colon cancer, in which the balance of cell death and differentiation also is lost.

"If the drugs continue to work as our studies to date have indicated, the next stage is clinical trials because these drugs are in the clinic already,"

Browning said.

Provided by Medical College of Georgia

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