Common cancers highjack powerhouses of cells

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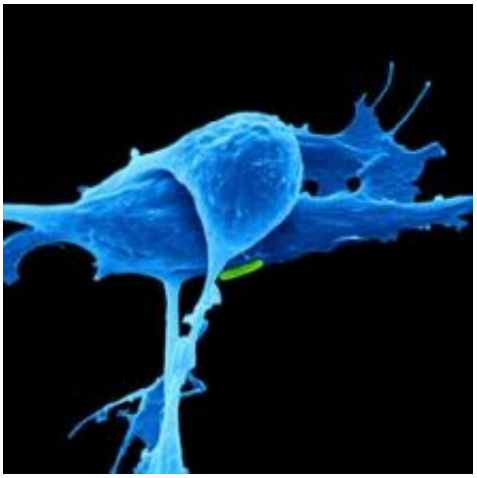

In a breakthrough in the understanding of how cancer does its deadly work, researchers at the University of Virginia School of Medicine have shown that many cancers - including nearly all pancreatic cancers - enslave and deform mitochondria, the powerhouses of cells, to create an environment more conducive to tumor growth.

In such cases, the researchers have shown, the mitochondria are being forced to divide unnaturally, to lose their normal shape and collapse around the cell's nucleus. The end result is an environment more hospitable to cancer. By blocking this process, doctors one day may be able to block the growth of such tumors.

"Perhaps in combination with other inhibitors, we can target this process of mitochondrial division, mitochondrial fission," said UVA researcher David Kashatus, PhD, of the Department of Microbiology, Immunology and Cancer Biology. "Hopefully we can make a difference in some of these cancers."

The work looked at tumors caused by mutations in the gene Ras, which is mutated in up to 30 percent of all cancers. Ras activates a cellular signaling pathway, the MAP kinase pathway, that was discovered years ago by UVA researchers Michael J. Weber, PhD, and Thomas W. Sturgill, MD, PhD. That cellular communication, Kashatus determined, is prompting mitochondria to act very strangely, to divide with a frequency they normally wouldn't.

While mitochondria are popularly thought to resemble beans floating in the cellular cytoplasm, recent research has shown they're actually long, stringy interconnected networks that constantly fuse and divide. Ras appears to send that division process into overdrive, both in mouse models and in cell lines created from human pancreatic cancer samples. "We made a similar finding in both: If we knocked down these cells' ability to divide their mitochondria, we blocked tumor growth," Kashatus said.

That finding points to a promising new target for developing cancer drugs. "Over the years, the scientific community has identified vulnerabilities in some of the pathways activated by Ras, targets we can drug that can inhibit tumor growth for a short time," Kashatus said. "The problem is, the tumors always find a way to come back. We need additional targets. And what this new finding may provide is an additional target in Ras- and MAP kinase-driven cancers."

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