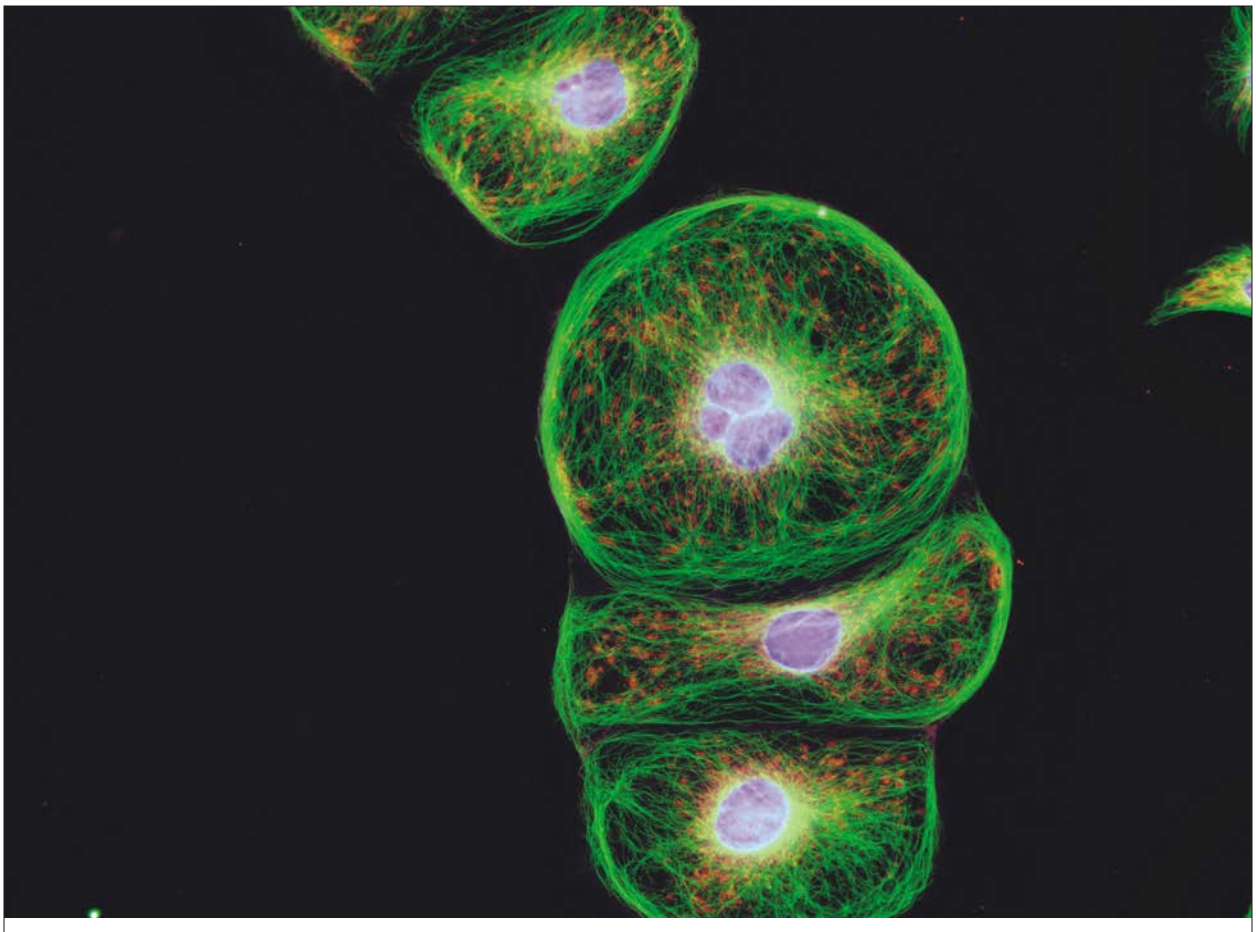

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Roundworm Unlocks Pancreatic Cancer Pathway

The National Cancer Institute estimates that more than 43,000 Americans were diagnosed with pancreatic cancer last year and more than 36,000 died from the disease. Despite advances in genetic science showing that the Ras oncogene is mutated in virtually all pancreatic cancers, scientists have been frustrated by the complexity of the signaling pathways in humans, which make it difficult to pinpoint potential therapeutic targets.

In a study published January 19 in the journal Developmental Cell, a team of researchers led by Channing Der, PhD, Distinguished Professor of Pharmacology at UNC-Chapel Hill, took a step back to a simpler organism -- a common roundworm -- and made a discovery about how the Ras oncogene chooses a signaling pathway and how the consequences of that choice play out in cellular development -- a key issue in cancer, which is characterized by uncontrolled cell growth.

Der, who is also a member of UNC Lineberger Comprehensive Cancer Center, explains, "In humans the cell signaling pathways are very complex; there are more than 20 different downstream partners beyond the two proteins we study -- Raf and RalGEF -- that Ras can choose to interact with. In *C. elegans*, there is only one of each protein. That made it easier for us to identify how Ras chooses a partner to 'dance' with and what are the critical events in the subsequent cell development that promote cancer."

"We found an elegant mechanism by which Ras switches partners and showed that the choice leads to very different fates for the cell. Now we can go back to the human pancreatic cancer cell and ask whether similar mechanisms are at work in determining how Ras causes pancreatic cancer," he adds.

Scientists often study simpler organisms to tease out genetic and cellular activity that might be almost impossible to map in humans. "Worms' cells actually share a great deal of functional overlap with human cells. However, while there may be one mechanism in a simple organism like a worm, there are multiple mechanisms at work in humans. It's a great thing for us as people, because there is a great deal of redundancy in our biological systems that helps them self-repair and function better, but it makes it a lot harder to study what's going on at a basic level," Der notes.

"If this signaling works in a similar way in humans, the *C. elegans* model may be very powerful for helping us find new therapeutic targets for pancreatic cancer," he concludes.

In addition to Der, the team included graduate student Tanya Zand, and Assistant Professor David Reiner, PhD, both of UNC's Department of Pharmacology.

The project was supported by the National Institutes of Health.

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