Researchers witness new type of cell division, use it to battle cancer

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The surprise discovery in humans of a type of human cell division previously seen only in slime molds has put a University of Wisconsin research team on a path to prevent some common and deadly cancers.

While on their way to finding a means to attack certain types of cancers, the researchers made the first observations of cytofission in humans, a type of cell division that occurs at a different time than normal division.

It started simply enough. Scientists at the UW School of Medicine and Public Health wanted to find a way to attack cancers that had too much DNA. Roughly 14 percent of breast cancers and 35 percent of pancreatic cancers have extra sets of chromosomes, compared to normal cells that have two.

"We want to find a way to destroy those cancers with a medicine," said Mark Burkard, member of the UW Carbone Cancer Center and assistant professor of hematology-oncology in the Department of Medicine. "We thought that would be a good target because the medicine would potentially destroy the cancer that had twice as much DNA but leave the healthy cells with normal amounts of DNA untouched."

To start testing, they took a culture of cells and prevented the final stage of cell division, creating cells that were tetraploid, having four sets of chromosomes instead of two sets.

The traditional process of human cell division begins by the cell

duplicating all of its components, including the DNA-containing chromosomes in the nucleus. Then during mitosis, the two sets of components are separated to opposite ends of the cell. Lastly, the original cell is cut into two daughter cells.

To make cells that mimic cancer with twice as many chromosomes, Burkard and his team blocked the cell from dividing into two, but the results weren't as straight forward as they anticipated.

"We couldn't figure it out because we found most of the cells were normal after that process. There were a few tetraploid cells so we eventually got to start our original research, but we couldn't understand why most of them seemingly hadn't undergone the process of becoming tetraploid. We started looking into it, and this whole publication came out of that."

What Burkard and his team discovered, published online in the *Proceedings of National Academy of Sciences* in July, is that human cells have a way to split that had not been seen before. The splitting occurred, unpredictably, during a delayed growth phase rather than at the end of mitosis.

The slight detour hasn't been for naught. Burkard, after observing the novel cellular splitting in late fall, already has a bead on a chemical that can block the division of tetra- and polyploid cells, effectively blocking the growth of cancer-like cells with too much DNA. He and his lab are now exploring exactly how the chemical does so, which is no small feat.

"If you think of something as simple and old-fashioned as aspirin which was discovered in the 19th century, how it works wasn't discovered until 1971," said Burkard. "We want to find out more quickly. Fortunately, we have tools that weren't available in 1971. That's what we're really focused on doing right now because we think that might impact patients

in the near term."

While study of the chemical continues to be a top priority, the unanswered riddle of how cancers begin is on the table for Burkard, too.

"There is a lot of evidence that failed cell divisions can lead to cells with extra chromosome sets which turn into cancer," said Burkard. "It is interesting that cytofission can prevent that."

He admits preventing cancer is a lofty goal, but one worth pursuing. In the recent study, 90 percent of cells resolved the issue of having extra DNA by way of cytofission. The interest for Burkard is in the remaining 10 percent of cancer-like cells.

"What exactly controls the selection of the 10 percent and the 90 percent is an interesting question," he said. "If you want to think about cancer prevention, you want to think about what controls that selection. When I proposed this to the American Cancer Society last fall, some of the reviewers said that it's very interesting, but the idea was pretty far outside the box, preventing cancer by controlling the switch."

More information: www.pnas.org/content/early/201 … 7b-a221-210f2ba6e51e.

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