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Researchers investigate protein's role in cell division

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In a paper published recently in the journal *eLife*, Mayo Clinic scientists take a step toward translating the protein BubR1's function into a potential therapy for cancer.

"I'd argue no one wants to age, and nobody wants to decline slowly, right?" says Jan van Deursen, Ph.D., a scientist at Mayo Clinic. "But, if you get fatal cancer, then you don't worry about aging anymore."

"Cancer really becomes the top priority," adds Robbyn Weaver, a Mayo Graduate School student in Dr. van Deursen's lab and first author on the paper.

Previous work by Dr. van Deursen's lab and others have used the BubR1 animal model to investigate aging. This paper instead examines how BubR1 strengthens the quality control checkpoints within cells, ensuring they divide properly."All cancer cells have this phenomenon of having an abnormal chromosome number," explains Dr. van Deursen. "So, what we really wanted to do in this paper is find out how BubR1 prevents cells from getting an abnormal number.

"In general, BubR1 works during mitosis, the process that allows cells to divide into identical copies. BubR1 sends out a signal that delays cell division until all chromosomes are correctly attached to the cellular structures that will pull them apart. The authors examined different mutations of BubR1 to determine how changes to each component of the protein affect this normal function.

"We wanted to correlate what we know about the normal functions of BubR1 in cells to cancer protection in mice," explains Weaver. "So, going in, we used cells to start looking at things like how well each different mutant prevent errors from occurring."

The authors report that, of the mutant proteins tested, two were able to prevent cancer in the mouse models: high levels of the entire protein and high levels of the protein missing an internal binding domain to Cdc20, a binding partner that activates the anaphase-promoting complex, which allows mitosis to proceed to the next stage of the cell cycle.

The high levels, while artificial, also point to BubR1's uniqueness. It is the only mitotic protein known that can be overexpressed without causing problems with the division of the cell. Dr. van Deursen explains that, while it's nothing that would happen in a normal person's life, "It's neat, because if you know how BubR1 does that, you can exploit it for therapeutic purposes. From a cancer perspective, where there's virtually nothing that will counteract this process of abnormal chromosome segregation, I think it would be good to look a bit further."

By controlling the shuffling of genetic information, cancer cells could, in theory, lose a powerful way to develop resistance to cancer therapies. With this paper, Weaver and her co-authors begin the process of understanding how components of the BubR1 protein work to see if there's one particular component that would be easier to manipulate into a cancer therapy.

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