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Discovery about DNA repair could lead to improved cancer treatments

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Medical researchers at the University of Alberta have made a basic science discovery that advances the understanding of how DNA repairs itself. When DNA becomes too damaged it ultimately leads to cancer.

Faculty of Medicine & Dentistry researcher Mark Glover and his colleagues published their findings in the peer-reviewed journal, *Structure* (Cell Press), earlier this summer. For years, scientists thought two key proteins involved in DNA repair operated in exactly the same way. Glover's team discovered how the proteins operate and communicate is vastly different—information that could lead to improved cancer treatments.

Glover explains that a protein known as BRCA1 acts like a hallway monitor—constantly scanning DNA for damage. At the first sign of problems, this protein figures out what kind of help is needed, and "radios" in a cleanup crew of other proteins.

A second protein, known as TopBP1, ensures that DNA can copy itself when needed. When this process stalls due to DNA damage, this protein also calls in a cleanup crew. But Glover likens its method of communication to tweets, rather than radio.

"The two proteins may be related and look very similar, but their roles and the way they communicate are in fact very different, which was surprising to us," Glover says. "Each protein plays a role in recognizing damaged regions of DNA, but the problem they each solve is different.

"The question now is how can we use this information to try to improve cancer therapies? Could we temporarily knock out cancer DNA's ability to repair itself from radiation damage? Could we administer radiation at a point that prevents cancer DNA from copying itself? Could we inhibit the activity of proteins that are normally trying to run around and fix the damage?

"Maybe some of these ideas could ultimately translate into less radiation or chemotherapy needed for patients, if the treatment can be more targeted," says Glover, who works in the Department of Biochemistry.

His team is continuing its research in this area, and wants to learn more about the role of the TopBP1 protein and why it favours communicating with a specific protein. They also want to conduct tests in their lab to see if the use of certain medications could alter the way these proteins work in a way that could result in new or improved cancer treatments.

Glover's lab members make 3-D images of proteins, making it easier to understand and see how proteins work.

Provided by University of Alberta Faculty of Medicine & Dentistry

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