

Scientists discover first 'DNA ambulance'

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U of T researchers have discovered how severely damaged DNA is transported within a cell and how it is repaired.

It's a discovery that could unlock secrets into how cancer operates—a disease that two in five Canadians will develop in their lifetime.

"Scientists knew that severely injured DNA was taken to specialized 'hospitals' in the cell to be repaired, but the big mystery was how it got there," said Karim Mekhail, a Professor in the Faculty of Medicine's Department of Laboratory Medicine and Pathobiology. "We've now discovered the DNA 'ambulance' and the road it takes."

Mekhail discovered this DNA ambulance, which is a motor protein complex, by using <u>yeast cells</u>. His research was recently published in *Nature Communications*.

Mekhail's team also found that the DNA hospital, also known as the <u>nuclear pore complex</u>, repairs damaged DNA inaccurately.

This inaccurate fix is important because DNA contains the instructions for all our genetic information. While the repaired DNA can still replicate, it has irregular cell instructions—a scenario that could cause cancer.

"This process allows cells to survive an injury, but at a great cost," said Mekhail. "The cell has a compromised genome, but it's stable and can be replicated, and that's usually a recipe for disaster."



Co-author Daniel Durocher, Senior Investigator at Mount Sinai's Lunenfeld-Tanenbaum Research Institute, helped the team track the damaged DNA in living cells by using advanced microscopy. The tracking showed that this DNA ambulance is necessary for damaged DNA to efficiently change location within the nucleus.

"Cancer often occurs when our chromosomes break and are misrepaired," said Durocher. "This work teaches us that the location of the break within the cell's nucleus has a big impact on the efficiency of repair."

The implications of the research could extend to a large number of developmental and disease settings.

"The processes we're studying are fundamental to the basic survival of a cell," said graduate student and first author Daniel Chung. "Almost every aspect of disease can be linked to problems with DNA."

Now Mekhail's team is searching for more DNA ambulances and roads while conducting a study to see what role they might play in causing cancer. "We expect that this may allow us to identify targets for a new class of anti-cancer drugs."

"Scientists have been searching for this DNA <u>ambulance</u> for a long time and now we suspect there may be more than one," said Mekhail. "It's exciting because it's a whole new area of research."

Provided by University of Toronto

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