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# Scientists find DNA 'molecular scissors' are vital in preventing cancers

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A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

Scientists at the University of Dundee have discovered that "molecular scissors" that repair damaged and abnormal DNA are critical for keeping cancers at bay.

The laboratory of Professor John Rouse at the University's Medical Research Council Protein Phosphorylation and Ubiquitlation Unit (MRC-PPU) first discovered that a protein called FAN1 was important for cutting and repairing damaged DNA in our cells in 2010.

Recent work carried out by Dr Christophe Lachaud under the direction of Professor Rouse have shown that FAN1 carries out another important task separate from repairing DNA, but which is vitally important for preventing cancers.

The team showed that FAN1 plays an important role during the copying of chromosomes that occurs whenever cells divide. In particular, the ability of FAN1 to recognise and cut special types of abnormal structures inside cells during the copying of DNA is important for preventing cancers, particularly of the lungs, liver and pancreas. Moreover, it appears that certain cancers may be caused by failure of FAN1 to cut DNA in the way it is supposed to.

"The DNA in our cells is like an instruction manual for the proper working of each cell," explained Professor Rouse. "Every time cells divide they need to make a perfect copy of all of their chromosomes, collectively called the genome, so that the next generation of cells also have a proper instruction manual.

"In the process of copying DNA, the machinery responsible for doing this often encounters roadblocks – obstacles that stop the progression of the copying machinery and result in abnormal, potentially toxic DNA structures.

"We showed that Fan1 can recognise these dangerous structures, and uses its cutting activity to makes them less toxic. We found that when we switch off the ability of Fan1 to cut these structures, the genome starts to become abnormal and breaks apart which means the instruction manual has become corrupted. Switching off the cutting ability of FAN1 leads to cancers, such as liver cancer and lung cancer.

"Other scientists have reported that Fan1 is mutated in pancreatic cancers, and we showed that in these cancers Fan1 is not able to recognise the abnormal structures that need to be cut. This leads the genome of these cells to become abnormal accounting for the cancers."

As the findings have implications for treating cancers, Professor Rouse and his team will now try to discover the 'Achilles heel' of cancers in which FAN1 doesn't work properly. If they are able to find a drug which is only toxic to cells that are defective in Fan1, these drugs might be effective in killing the cancer cells caused by mutations in Fan1 without affecting the normal cells.

Provided by University of Dundee