MEDIA RELEASE

Centenary Institute life saving research
Cancer. Inflammation. Cardiovascular.

Major breakthrough on gene control in all cells in the body offers possible improvement for cancer treatment

Our DNA contains information, packaged as genes, to instruct all cells in our body to develop and function properly. Our DNA is like an “encyclopedia” and genes are the “paragraphs”. Like paragraphs, which are separated by spaces, our genes also contain “spacer DNA” known scientifically as “introns”. In addition, there are “punctuation marks” introduced by the chemical modification to the DNA. All of these features are important to ensure that messages are conveyed accurately in our cells.

Researchers from the Centenary Institute have discovered that naturally occurring chemical modification to the DNA, known scientifically as DNA methylation, can change the way information in genes are read. The research team from the Gene and Stem Cell Therapy Program led by Professor John Rasko and Dr. Justin Wong found when these “punctuation marks” are put at the wrong place, the ”spacer DNA” is present at inappropriate sections of the gene. Consequently, the information is “whited out” because the sentences in the “paragraphs” no longer make sense.

This work was performed using sophisticated gene sequencing and computational analysis by bioinformaticians, Drs William Ritchie and Dadi Gao. The team uncovered naturally occurring patterns of DNA methylation changes that alter the inclusion of “spacer DNA” in cell types including blood, brain, muscles and embryonic stem cells. By changing the DNA methylation patterns, Dr. Wong and co-lead author, Mr. Trung Nguyen then confirmed its direct effect on the positioning of “spacer DNA” or introns. The findings have been published today in the respected journal *Nature Communication*.

Of crucial importance, this discovery may have a significant impact on cancer treatment. “Punctuation marks” like DNA methylation can also switch genes on and off. In cancer, these punctuations marks are often wrongly located. A drug that can remove DNA methylation called *azacytidine* is approved for the treatment of pre-leukaemic blood diseases. This drug is also in clinical trials in combination with other drugs for leukaemia and many other cancers. The aim of this drug is to reactivate silenced genes and thereby improve anti-cancer therapies.

This new discovery that DNA methylation can alter positioning of “spacer DNA” indicates that drugs like *azacytidine* can help fight cancers but many may also result in the abnormal inclusion of “spacer DNA”. Dr Justin Wong says “It is as yet unknown whether we are switching off certain cancer preventing genes by introducing these spacer DNA while trying to switch on other genes to combat cancer. Alternatively, these spacer DNA can be beneficial if they are introduced into cancer causing genes to switch them off.”

Most clinical trials have not taken the inclusion of “spacer DNA” into account, so it is currently unclear side-effects are being inadvertently introduced while trying to treat cancers with these drugs. Revelations from this study have the potential to change the way particular cancers are treated and further studies are needed to assess how possible negative effects could be avoided to produce the best outcome for patients. “It may be crucial for clinical trials to consider whether “spacer DNA” is wrongly introduced by drugs like *azacytidine.* Ultimately a targeted approach to switch off cancer promoting genes, including the introduction of spacer DNA into these genes, is the way forward for cancer therapeutics. ” says Professor Rasko.

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