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Singapore: 'Non-coding' genes known as microRNAs play a big role in cancer through their mechanical regulation of other genes. In a three-year study, researchers at Garvan Institute of Medical Research have identified one microRNA, in particular, that is strongly associated with prostate cancer prognosis.

This was an inventive piece of detective work that involved identifying the hundreds of microRNAs that changed expression in prostate cancer, and narrowing that list down through extensive analysis to the greatest culprit. The gene in question, miRNA-205, was 'silenced' in prostate cancers, particularly in aggressive or metastatic cancers.

The function of miRNAs can best be understood by the other genes they 'target', or regulate. In this case, miRNA-205 was shown to target the MED1 gene, known to affect proliferation. In normal prostate cells, miRNA-205 keeps MED1 at bay, helping to maintain the normal balance of the cell and prevent proliferation. In cancerous prostate cells, miRNA-205 levels are reduced, permitting MED1 levels to increase. This has the flow-on effect of allowing cells to proliferate and spread.

After identifying miRNA-205 as a potentially significant biomarker in the lab, Dr Toby Hulf and Professor Susan Clark from Sydney's Garvan Institute of Medical Research looked at tumor samples from prostate cancer patients in collaboration with Garvan colleagues Professor Rob Sutherland and Clinical Associate Professor Lisa Horvath, dividing them into those with good or poor prognosis. They showed clearly that epigenetic methylation of miRNA-205 was associated with metastatic disease in prostate cancer. Their results are published in *Oncogene*, now online.

"We are excited, because this is the first study to investigate this class of microRNAs at the epigenetic level in prostate cancer," said Professor Susan Clark.

"The epigenome is a constantly changing set of biochemical modifications that directly impact upon gene expression - and in this case we showed extensive methylation of at least 10 microRNAs involved in prostate cancer, especially miRNA-205."

"Methylation has the effect of silencing a gene, and in this study hypermethylation of miRNA-205 was directly associated with poor prognosis for prostate cancer patients."

"This is a novel finding and we now aim to use this potential translational biomarker to screen a much larger clinical cohort, investigating how it might be used in the management of prostate cancer."