THE VICTOR CHANG
CARDIAC RESEARCH INSTITUTE

MEDIA RELEASE

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Putting the brakes on gene expression

Scientists have found that gene expression is controlled much like a car by tiny brakes called microRNA.

These tiny brakes are central to the mechanism of embryo development, including heart formation, and their failure could contribute to human disease including heart defects and cancer.

The study, published today in the science journal *Proceedings of the National Academy of Sciences USA,* was led by Dr Thomas Preiss from the Victor Chang Cardiac Research Institute. Dr Preiss is also, this week, presenting his findings at the 6th Peter Mac Cancer Symposium in Melbourne.

"Humans have roughly 30 thousand genes in each of their trillion cells. The genes are a blue-print of how we are built, and their complex workings are controlled and regulated to allow for proper body development and maintenance, as well as to prevent or fight disease," Dr Preiss said.

By understanding how genes are controlled Dr Preiss and his team aim to shed light on the development of disease and how it might be stopped, reversed and cured.

"Genes give all their information to large molecules, called messenger RNA (mRNA), which oversee the synthesis of proteins that in turn go to work and build specialised cells, tissues and organs," Dr Preiss said.

"Surprisingly, cells express too many mRNA molecules for many genes and then need to restrict the usage of the mRNA during protein synthesis. It's a bit like driving your car at full-throttle while applying the brakes to hold the speed limit.

"Cells use tiny brakes, called microRNAs, to slow gene expression. These tiny brakes had largely been overlooked until about five years ago, but now hundreds of distinct microRNAs are known. It is clear that if left unchecked, cells go on a collision course if some or all of their tiny brakes are out of whack. In some cases this can result in unrestricted cell growth, such as in cancer.

"We are only scratching the surface in terms of the biomedical importance of microRNAs, but already they have been shown to be essential for stem cell differentiation and heart development, and are major players in cancer," Dr Preiss said.

Just how microRNAs go about controlling protein synthesis in animal cells has until now been a mystery. "Although we've known for a while that microRNAs have the ability to control the rate of gene expression in animal cells by blocking the process of protein synthesis, no one knew exactly how. We set out to discover this.

"We found that the microRNAs blocked the functions of the *cap* and *tail* components of the mRNA, and we were further able to demonstrate a role for the cap-binding factor eIF4E. We now understand the process a lot better. Rather like having gone from knowing that a car has brakes to locating them at the wheels and working out that they are disk brakes," Dr Preiss said."
This is a significant find for biomedical sciences as it gives a better understanding of how a major class of gene regulators functions. It is hoped that this work will help researchers move closer to unlocking the complexity of, and ultimately finding a cure for heart disease and cancer.

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