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Enzyme discovery sheds light on vitamin D

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Surprising findings by Queen's University researchers have shed new light on how the "sunshine vitamin" D – increasingly used to treat and prevent cancer and other diseases – is broken down by our bodies.

"The effectiveness of vitamin D therapy is partly dependent on how quickly it will be broken down," says Biochemistry Professor Glenville Jones, an expert in the field of vitamin D metabolism. "By studying the enzyme responsible for breaking down the vitamin, we hope to develop a way to prevent this from happening by blocking that response."

First observed in Dr. Jones's lab by undergraduate Biochemistry student Brendan O'Leary, the discovery reveals that changing a single amino acid in the hydroxylase enzyme will cause it to take a completely different pathway. Although scientists have known for 25 years that the enzyme is capable of taking two different pathways, until now they could not explain why this occurs.

The team's findings are published on-line in the journal *Proceedings of the National Academy of Sciences*. Other members include: research associate David Prosser, PhD student Martin Kaufmann, and research technician Valarie Byford.

Earlier study of the enzyme had shown that its pathway pattern is species specific. Some species, including humans and rats, favour one pathway, while others – most notably the opossum – favour the other pathway.

Using a technique called liquid chromatography mass spectrometry, the

researchers studied cells from animals in both categories. They changed the human enzyme in certain key places to see if this would affect its pathway pattern.

Surprisingly, they discovered that altering a single amino acid completely changes the enzyme from a human pattern to an opossum pattern. This change can be flicked back and forth “like a light switch,” says Dr. Jones, adding: “It’s remarkable. In biochemistry you rarely see that kind of predictive work from modeling molecules and enzymes.”

The Queen’s researchers believe the hydroxylase enzyme plays an important role in human cell functions. When vitamin D drugs are used in an attempt to arrest certain types of cancer, for example, the tumour responds by making more of this enzyme. “If we can block the tumour response, we should be able to successfully treat some tumours with vitamin D compounds,” says Dr. Jones, whose research is supported by the Canadian Institutes of Health Research.

Vitamin D deficiency has also been correlated with other diseases, including multiple sclerosis, muscle weakness, and bone-related disorders, he notes.

Source: Queen's University