

Sugar key to cellular protein protection and viability

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A Simon Fraser University laboratory's breakthrough in understanding how a specialized sugar regulates protein levels in our cells could generate new targets for therapies to treat diseases caused by improper protein regulation. Cancer and various neurodegenerative diseases are among these diseases. In the case of Alzheimer's disease, the levels of toxic forms of two proteins build up in our brains.

Working with Dr. Yanping Zhu and other researchers in SFU's Laboratory for Chemical Biology, which he heads, SFU Chemistry and Molecular Biology and Biochemistry professor David Vocadlo has discovered that a specialized sugar gets attached to proteins as they form. The sugar protects them from being marked for premature destruction. Decreasing such sugar modification leads to destruction of newly forming [protein](#) chains and lowers levels of mature stable proteins.

"This is an exciting discovery because proteins, which are encoded by genes, pretty much perform all our cellular activities," explains Vocadlo. "Improper control of protein levels in our cells is a factor in many diseases, such as Alzheimer's. So our findings suggest that modification of proteins as they are being born by this specialized sugar may represent a common strategy used by our cells to ensure newly formed proteins are stable and functional."

The journal *Nature Chemical Biology* has just published a paper on these findings. Vocadlo, a Canada Research Chair and an E.W.R. Stacie Memorial Fellow, cautions that he and his colleagues still have a long

way to go before this new insight can be exploited to treat diseases that stem from improper regulation of [protein levels](#).

"We still have to define the repertoire of proteins that this sugar modifies during the creation of proteins and how this modification process influences the health of cells facing various stresses."

Vocadlo's previous appreciation of this specialized sugar's powerful role in Alzheimer's and cancer motivated him to investigate whether its presence and activity affects cellular protein formation and regulation.

Following on the observation that the sugar's presence is decreased in Alzheimer's disease, Vocadlo and his team had previously shown that proper levels of its modification are needed to prevent disease in neurodegeneration models.

In cancers, which are very metabolically active and take up large amounts of glucose to power their growth, the scenario is different - this sugar's modification levels are commonly elevated. Blocking this sugar modification decreases the activity of proteins involved in the metabolism of cancer cells and thus helps decrease tumour growth.

Vocadlo says understanding how this [sugar](#) modification regulates the levels of proteins in these diseases should enable appropriate tuning of its levels for therapeutic benefit.

More information: *Nature Chemical Biology*, [DOI: 10.1038/nchembio1774](#)" target="_blank">nature.com/articles/[DOI: 10.1038/nchembio1774](#)

Provided by Simon Fraser University

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