Chemical advance supports treatment Alzheimer's disease

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Researchers at the University of Liverpool and Victoria University of Wellington have made a significant step forward in the search for a treatment for Alzheimer's disease.

The research teams have discovered a novel way to create sugar-based molecules for controlling the process that leads to proteins, called

amyloid plaques, building up in the brain. These proteins disrupt the normal function of cells leading to the progressive memory loss that is characteristic of Alzheimer's disease.

Current treatments for dementia can help with symptoms, but there are no drugs available that can slow or stop the underlying disease.

New approach

The team has previously synthesised a type of complex sugar for the same purpose, which involved a challenging 55 step process. The new approach reduces the number of reaction steps by half.

Liverpool biochemists, Professor Jeremy Turnbull and Dr Scott Guimond, worked with chemists, Dr Zubkova and Professor Peter Tyler, from the Ferrier Institute in Wellington to construct new molecules and screen their abilities to inhibit the activity of a brain enzyme called beta-secretase. This enzyme catalyses the first step in the generation of amyloid plaques in Alzheimer's.

Professor Turnbull, from the University's Institute of Integrative Biology, said: "This provides a highly desirable class of compounds that could be used in the development of new treatments, with real potential for targeting one of the underlying causes of Alzheimer's disease.

"These novel chemicals also unlock potential for a number of additional drug discovery applications in the future including cancer and diabetes."

Targeted and simplified

The team prepared a large collection of molecules, including 11 final products as pure single-entity chemicals. The cluster compounds are

much less complex and have the ability to target specific proteins.

"We wanted to simplify the synthesis without losing potency, which is quite challenging," says chemistry project leader Dr Olga Zubkova. "The new products will be easier and cheaper to make, and allow us to prepare larger amounts for testing."

The team designed a more simplified core for the molecules by replacing fragments with smaller and cheaper carbon versions. This resulted in structures that retained significant amounts of bioactivity.

More information: "Single-Entity Heparan Sulfate Glycomimetic Clusters for Therapeutic Applications." *Angew. Chem. Int. Ed.*, 54: 2718–2723. doi: 10.1002/anie.201410251

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