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Nuclear research reveals piece in the Parkinson's puzzle

New nuclear-based research from ANSTO[1] has focused on a protein called Alpha-Synuclein, which plays a role in the development of Parkinson's disease when it behaves abnormally. This behaviour can be stopped or even reversed using a man-made polymer called a dendrimer, also known as a 'dense star' polymer.

This fundamental research adds another piece in the puzzle to develop better treatments for Parkinson's disease, which affects around one in 250 Australians.

ANSTO Researcher, Dr Agata Rekas, said that past research had shown the dendrimer – called a PAMAM[2] dendrimer and made by Dendirtech® Inc - had positively affected a peptide involved in Alzheimer's disease (ABeta) and a prion peptide. So Dr Rekas and Dr Seok Il Yun, an ANSTO Post Doctoral fellow, decided to see if it had a similar effect on the Parkinson's disease.

"As all these diseases affect the brain and neuronal pathways in the body we anticipated the dendrimer's effect would be similar, and we were right," she said.

"The Alpha-Synuclein protein is a natural protein in the body but when it aggregates into fibrils, long insoluble strings of protein molecules stuck together, it affects transmissions to the brain, resulting in Parkinson's disease," Dr Rekas explained. "No one is sure of the protein's normal role but we believe it assists cognitive function.

"It is thought that the aggregation is triggered by a dopamine[3] deficiency and causes deposits in the brain to occur, however this could be just a factor, not the complete cause, of the disease," she said. "There is still much to find out, but it's all part of the puzzle. The exciting part of our results is that it most definitely provides further information as to how this dendrimer can contribute to developing better therapeutics for Parkinson's disease," she said.

Dr Rekas explained that a dendrimer is spherical in shape and contains chemical groups similar to those of proteins, which start branching out in the middle so the dendrimer increased in size as each layer was added, similar to the branch-like structures seen in snow flakes.

"The more layers in the dendrimer the more effective it was due to the larger surface area. In the experiments we put certain amounts of these dendrimers and a control, with no dendrimers, into a protein solution for over 120 hours and stimulated aggregation with heat and shaking," she explained. "The control measured a lot of fibrils and different dendrimers reduced this fibrillar growth to various extents.

"We used an electron microscope to look at what was physically happening and verified the results using small angle neutron scattering, where a neutron beam passes through the sample onto a detector giving information as to what's occurring at the molecular level, "she said. "The neutron experiments were conducted by Dr Yun.

"The results clearly showed that the larger dendrimer inhibited the abnormal activity of the protein best. This information can now be used by drug companies focussed on treating Parkinson's so the next stage would be for such companies to develop this research further," she concluded.

For more information and to arrange an interview with ANSTO staff please contact:
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[1] ANSTO is the Australian Nuclear Science and Technology Organisation, the country's national nuclear research and development organisation and the centre of Australian nuclear expertise – over 80 per cent of all radioisotopes used in Australian nuclear medicine are made in ANSTO's reactor.

[2] PAMAM stands for poly(amidoamine). Poly means many, and amidoamines are a type of chemical compound used to help synthesise surfactants which can be used in personal care products such as soaps, shampoos and cosmetics.

[3] Dopamine is a neurotransmitter – a chemical that passes the signal between the ends of two neurone