

Harnessing the Ubiquitin-Proteasome System in the Brain: Implications for Dementia

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United Kingdom

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Harnessing the Ubiquitin-Proteasome System in the Brain: Implications for Dementia

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1

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Research Abstract

All cells within our body need to discard waste material such as damaged or no longer wanted proteins. This process, which conceptually is similar to the recycling of household waste, is key to ensure that cells remain healthy and functional. This is particularly important in neurons as failure to deal with waste leads to the accumulation of toxic proteins and aggregates in the form of extracellular plaques and intracellular tangles. The protein ubiquitin functions as a cellular tag labelling no-longer needed proteins for recycling, in a timely and highly specific manner. A mutant form of ubiquitin (UBB+1) is found in brains of patients with Alzheimer's disease (AD). In contrast to normal ubiquitin, UBB+1 cannot be used to tag other proteins and it is therefore

unable to carry out its housekeeping task. However normal ubiquitin molecules can still get tagged onto UBB+1 in a process called polyubiquitylation. In neurons polyubiquitylated UBB+1 triggers the collapse of cellular recycling centres, which leads to neuronal cell death and neurodegeneration. This project will focus on defining the role of a novel enzyme in UBB+1 polyubiquitylation and this provides new and exciting avenues for the identification of future therapeutic targets for AD.

Further information available at:

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