

P019 PDZ-binding peptides in neurodegeneration
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Excitotoxicity has been linked to neurodegenerative disorders such as cerebral ischaemia, epilepsy, brain trauma, Huntington's Disease, Parkinson's Disease and Alzheimer's Disease making excitotoxicity an attractive therapeutic target. Here, PDZ-binding peptides were synthesised analogous to Ca²⁺-ATPase-2 (PMCA2) and the NR2B glutamate receptor subunit which are known to have an affinity to PSD-95. Ruth 2 was synthesised as a cyclic peptide in the SGUL Neurodegeneration Unit to mimic the carboxy-terminus of PMCA2. Hannah 2 was synthesised as a cyclic peptide to mimic the C-terminus of NR2B. Immunohistochemistry was used to investigate the internalisation of these peptides and their affinity to PSD-95. MTT assays were also performed to measure the effects of Ruth 2 and Hannah 2 on excitotoxic cell death. 200µM and 2mM Kainic acid (KA) and 200µM L-Glutamic Acid (GA) failed to produce measurable cell death, whereas 2mM GA and 50µM Amyloid Beta (Aβ)-42 succeeded in producing extensive cell death. The PDZ-binding peptides were able to protect against GA induced cell death but not against Aβ induced cell death therefore suggesting another mechanism of cell death in Aβ treated cells. Ruth 2 A stands out as the most capable of all the agents, with stronger staining and a significant decrease (p= 0.002) in cell death in the 2mM GA condition. However both Ruth 2 E and Hannah 2 also showed protection against excitotoxicity.