

**P057** Cell cycle-related signalling in Alzheimer's disease type neurodegeneration

**Kevin F. Gallagher\*** and **Helen C. Gallagher<sup>†</sup>**

*Applied Neurotherapeutics Group\* Department of Pathology†  
Conway Institute, University College Dublin, Ireland.*

Expression of proteins associated with the early cell cycle in Alzheimer's disease suggests that these proteins may provide new therapeutic targets for its treatment. Therefore, study of the role of these proteins in neuronal proliferation, differentiation and death may increase understanding of their pathophysiological relevance.

To this end, we have profiled the expression of cell cycle-related proteins in the G1-phase of neuro-2A neuroblastoma synchronised by mitotic selection. D-type cyclin expression did not change throughout the G1-phase. Conversely, phosphorylated retinoblastoma protein expression increased in the mid- to late-G1 phase, suggesting that this is a requirement for S-phase entry.

Previously we have shown that cyclin D3 levels increase in cells induced to differentiate with valproate [J. Neurochem. (2002)83, 12-19]. We investigated if a similar upregulation would be observed in dibutyryl cAMP (2mM) differentiated neuro-2A. In parallel with neurite outgrowth, cyclin D3 expression was significantly increased at 24 and 48h. Further study showed this increase in cyclin D3 to be time-dependent, but not dose-dependent.

An apoptotic model has been established using time-lapse video microscopy and caspase-3 cleavage to confirm apoptosis following serum starvation. The expression of 200 cell cycle-related proteins will be analysed using proteomic methods in this and a  $\beta$ -amyloid toxicity model.