432o Characterization of Beta-Amyloid Toxicity of P19 Embryonal Carcinoma Stem Cell during Development

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Deposition of insoluble beta-amyloid peptides in the brain is believed to be one of most important histopathological features of Alzheimer's disease. Beta-amyloid, a ~4 kDa peptide proteolytically cleaved from amyloid precursor protein, is a ubiquitous protein in our body. The mechanism of neurotoxicity is still poorly understood. One hypothesis is that beta-amyloid association with GM1 ganglioside is important in the neurotoxic properties of peptide. In the current study, we examine the relationship between GM1 distribution and susceptibility to beta amyloid toxicity as a function of neuronal differentiation and nonneuronal differentiation of the P19 embryonal carcinoma stem cell, pluripotential cell line. The P19 cell line is induced to differentiate into neuronal and glial like cell in the presence of retinoic acid and cardiac and skeletal cells in the presence of dimethyl sulfoxide. P19 cell differentiated into neuronal cells expressed more GM1 ganglioside and more vulnerable to beta amyloid peptide. However, P19 differentiated cell into nonneuronal cells are impervious to beta amyloid peptides. These results suggest that the differentiation of P19 cell into neuronal cells increase the susceptibility of beta amyloid peptides. Understanding the mechanism of beta amyloid toxicity could lead the development of new treatment for Alzheimer's disease.