EFFECT OF ALUMINUM ON MANGANESE SUPEROXIDE DISMUTASE (MnSOD) EXPRESSION

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Aluminum is a neurotoxic metal which has been implicated in various neurological diseases as Alzheimer's disease. However, despite numerous studies on aluminum-treated animals and cells in culture, the sites at which aluminum is bound within cells still remains unclear.

We have recently shown, by electrophoretic mobility shifft assay on nuclear extraits of HeLa cells, that various concentrations of aluminum sulfate led to a decrease of SP1 DNA binding activity. Yet, the MnSOD gene expression is under control of an SP1-containing and TATA-less promotor.

So, we hypothesis that aluminum could act on MnSOD expression at the initiation of transcription level, by a mechanism which involves SP1 sites.

To verify this hypothesis, we used a plasmid containing human MnSOD promoter –210/+37 (pMnSOD Luc) link to luciferase gene as a reporter. HeLa cells are transfected with the reporter plamid, using calcium-phosphate methods, and stimulated during 3 and 24 hours by various concentrations of aluminum sulfate. The reporter gene activity is measured by a luciferase base assay system (Promega).

We reported that aluminum sulfate decrease luciferase activity from the reporter construct as a dose dependant manner.

These date support the hypothesis that one of the delerious effect of aluminum may be to decrease the level of the antioxidant enzymes MnSOD throught an interaction with DNA SP1 sites and thereby alter the ability of cells to be effectively protect from an oxidative stress. Moreover this effect of aluminum could be link to abnormalities in the cellular regulation and expression of antioxidant enzymes described in Alzheimer disease.