NEUROPARIN (C3) PROTECTS SH-SY5Y NEUROBLASTOMA CELLS FROM CASPASE-DEPENDENT APOPTOSIS INDUCED BY CHEMOTHERAPEUTIC AGENTS AND H$_2$O$_2$ OXIDATIVE STRESS

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Introduction: Previous studies revealed that glycosaminoglycans (GAGs) exhibit neuroprotective properties. We have previously shown that a low molecular weight GAG, neuroparin (C3), attenuates β-amyloid-induced abnormal tau-2 immunoreactivity and reduces AF64A-induced cholinergic lesions in the rat brain, possibly via regulating apoptotic processes. However, the mechanism of this action has not been elucidated.

Aims: We investigated the mechanism of the putative neuroprotective properties of neuroparin on human neuroblastoma cells subjected to different apoptotic signals.

Methods: Neuroblastoma SH-SY5Y cells were subjected to Etoposide-, Vincristine-, Cisplatin-, Staurosporine- and H$_2$O$_2$-induced toxicity. The neuroprotective properties of neuroparin were tested by pre-incubating the cells with different concentrations of neuroparin (0.01 mM to 0.1 mM) for 6 hours. The cell viability was then assessed using MTT ((3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) cell proliferation assay. Under similar experimental conditions, the activity of caspase-3 was analyzed using the fluorogenic substrate, DEVD-AFC (Asp-Glu-Val-Asp-7-amino-4-trifluoromethyl coumarin).

Results: Pre-incubation with neuroparin yielded concentration-dependent protection against Etoposide-, Vincristine-, Cisplatin-, Staurosporine- and H$_2$O$_2$-induced toxicity. Neuroparin also inhibited caspase-3 dependent activation mediated by these insults in a dose-dependent manner.

Conclusion: Our results suggest that neuroparin exhibits neuroprotective effects on neuroblastoma cells by modulating apoptotic processes. Further signal transduction studies, utilizing apoptosis inhibitors, protein expression and assessment of mitochondria functions are currently underway in our laboratory to reveal the exact mechanism behind the neuroprotective role of neuroparin.