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## INHIBITION OF NEURITE OUTGROWTH AND TRANSCRIPTION FACTOR ACTIVATION BY OCHRATOXIN A IN CULTURED PC-12 CELLS

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The mycotoxin, ochratoxin A (OTA) has been known to induce microcephaly in animals and in vitro whole embryo. Cytotoxic effect and inhibition of cell differentiation were proposed as underlying mechanisms responsible for OTA-induced microcephaly. we previous found that OTA inhibited cell differentiation of a cultured rat embryonic midbrain cells, a dopaminergic nerve cells. In this study, we investigated whether OTA could inhibit cell diferentiation of PC-12 cells, a widely accepted model system for study of neuronal differentiation. Cell viability was determined by 3-(4,5-dimethyl Thiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT). Cell differentiation was assessed by measurment of neurite outgrowth. OTA decreased neurite outgrowth and cell viability in dose-dependant manners. To determined one possible toxic mechanism, generation of reactive oxygen species (ROS) was also measured by fluorescence spectrophotometer with 2',7'-dichlorofluorescin, a fluorescent intracellular dye. ROS generation was increased in a dose-dependent manner. Since transcription factors AP-1, SP-1, and NF-$\kappa$B have been implicated in cell differentiation, we next examied whether OTA could inhibit the constituted or nerve growth factor (NGF)-induced transcription factor activation. OTA inhibited NGF-induced AP-1 and SP-1 activation but not NF-$\kappa$B. These results show that AP-1/SP-1 activation may be related to neurite outgrowth of PC-12 cells. Role of ROS generation in the transcription factor activation and neurite outgrowth is under investigating.