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AIF translocates to the nucleus in the spinal motor neurons in a mouse model of ALS

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by selective loss of motor neurons in the brain stem and the spinal cords. One of the causes for the familial ALS has been attributed to the mutations in copper-zinc superoxide dismutase (SOD1). Although the toxic function of the mutant enzyme has not been fully understood, the final cell death pathway has been suggested as caspase-dependent. In the present study, we present evidence that the activation of AIF may play a role to induce motor neuron death during ALS pathogenesis. In the spinal cord of G93A SOD1 transgenic mice, expression of AIF was detected in the motor neurons and astrocytes. The level of AIF expression increased as the disease progressed. In the symptomatic G93A SOD1 transgenic mice, AIF released from the mitochondria and translocated into the nucleus in the motor neurons as evidenced by confocal microscopy and biochemical analysis. These results suggest that AIF may play a role to induce motor neuron death in a mouse model of ALS.

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An ERK-dependent novel checkpoint delays the entry into mitosis in response to actin dysfunction in mammalian cells

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The proper separation and migration of duplicated centrosomes at the onset of mitosis is critical for spindle positioning to determine the axis of cleavage plane for cell division. In this study, we examined the function of cortical actin cytockeleton in positioning the duplicated centrosomes at the entry of mitosis with several synchronized cells. Using immunofluoroscence and time-lapse microscopy, it was observed that depolymerization of cortical actin cytoskeletons with cytochalasin D or the inhibition of non-muscle myosin at the cortex with butanedione monoxime in G2 blocked the migration and positioning of duplicated centrosomes, and thus the proper spindle formation. The progression into mitosis was also delayed in these actin-disorganized cells: the degradation of mitotic cyclins A and B1, and CDK1 activation by dephosphorylation were deferred. In addition, ERK1/2, but not p38 was continuously activated in the cells that showed the delay in mitotic entry, and this delay disappeared with the treatment of a specific ERK inhibitor U0126 or the transfection of dominant negative ERK2. These observations demonstrate that ERK might regulate the mitotic entry in response to the dysfunction of cortical actin cytoskeleton as reported in S. pombe, and suggest a presence of actin checkpoint at the G2/M transition that monitors disorganization of actin cytoskeleton in mammalian cells.

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Anti-apoptotic Effect of Ethanol Extract of Bojungbangam-tang on Cisplatin-Induced Apoptosis in Rat Mesangial Cells

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Cisplatin is a anti-neoplastic agent which is commonly used for the treatment of solid tumor. Cisplatin activates multiple signal transduction pathways involved in the stress-induced apoptosis in a variety of cell types. Cytotoxicity of cisplatin was detected in rat mesangial cell (RMC) and the value of IC50 is about 20 μM. The treatment of cisplatin to RMC showed the apoptotic bodies and DNA fragmentation. The activation of caspase-3, -8, and -9 and proteolytic cleavage of PARP was observed in the RMC treated time-dependently with cisplatin. The activation of ERK, p38 and JNK was also observed in the apoptosis induced by cisplatin in RMC. The ethanol extract of Bojungbangam-tang (EBJT), a new herbal prescription composed of nine crude drugs, inhibited cisplatin-induced apoptosis in RMC. EBJT reduced DNA fragmentation and caspase-3 activity in cisplatin-treated RMC. The cisplatin–induced ERK and JNK activation in RMC was blocked by EBJT, but EBJT had no effect on p38 activation. Taken together, these results can suggest that EBJT prevents cisplatin-induced apoptotic cell death in RMC through inhibition of ERK and JNK activation.

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Anti-oxidative and anti-proliferative effect of (-)-epigallocatechin gallate (EGCG)

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EGCG [(-)-epigallocatechin gallate], a major component of green tea has been considered as a major antioxidant constituent. It has been considered as potential chemo-preventive and chemotherapeutic agents. EGCG showed significant radical scavenging activity in all ranges of concentration (0.8-100 μg/ml) used. Protective effect of EGCG against hydrogen peroxide induced cell death was observed. Relatively high lipid peroxidation inhibitory activity were detected (IC50 was about 20 μg/ml). EGCG also dose-dependently enhanced the activities of antioidative enzymes, superoxide dismutase, catalase and glutathione peroxidase in V79-4 cells. Human osteogenic sarcoma (HOS) cells were used to investigate anti-proliferative effect of EGCG. EGCG was anti-proliferative on HOS cells with IC50 value of 35.3 6.0 g/ml. The anti-protliferative propertiy of EGCG appears to be attributed to its induction of apoptotic cell death as determined by morphological changes, chromosomal DNA degradation and increased proportion of sub-G1 apoptotic cell population. EGCG treatment resulted in gradual activation of caspase-3 which is known as an execute molecule in the induction of apoptotic cell death.