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Urate mitigates oxidative stress and motor neuron toxicity of astrocytes derived from ALS-linked SOD1 ^{G93A} mutant mice

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Abstract

Dominant mutations in an antioxidant enzyme superoxide dismutase-1 (SOD1) cause amyotrophic lateral sclerosis (ALS), an adult-onset neurodegenerative disease characterized by loss of motor neurons. Oxidative stress has also been linked to many of the neurodegenerative diseases and is likely a central mechanism of motor neuron death in ALS. Astrocytes derived from mutant SOD1^{G93A} mouse models or patients play a significant role in the degeneration of spinal motor neurons in ALS through a non-cell-autonomous process. Here we characterize the neuroprotective effects and mechanisms of urate (a.k.a. uric acid), a major endogenous antioxidant and a biomarker of favorable ALS progression rates, in a cellular model of ALS. Our results demonstrate a significant protective effect of urate against motor neuron injury evoked by mutant astrocytes derived from SOD1^{G93A} mice or hydrogen peroxide induced oxidative stress. Overall, these results implicate astrocyte dependent protective effect of urate in a cellular model of ALS. These findings together with our biomarker data may advance novel targets for treating motor neuron disease.

Keywords: Amyotrophic lateral sclerosis; Oxidative stress; SOD1(G93A) mice; Uric acid.

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