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Neuroprotective role of CCL2 and its intracellular signaling pathway in the primary cultured rat cortical cells

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CCL2, a member of the CC-chemokine sub-family, plays an important role in recruiting leukocytes to inflammatory sites. Studies have suggested that CCL2 and its major receptor CCR2 are associated with a variety of neurological disorders. However, emerging evidence indicates that CCL2 exerts neuromodulatory actions and plays a neuroprotective role in certain injuries and insults, although the underlying mechanism remains elusive. The present study investigated the neuroprotective effects of CCL2 against excitotoxic insult and elucidated the intracellular signaling cascades triggered by this chemokine using primary cultured rat cortical neuronal cells as a model. CCL2 alone had no effect on viability and caspase 3 activity of the cultured cells under the prevailed experimental conditions. Rather, it significantly attenuated excitotoxic neuronal damage as well as reactive oxygen species production induced by N-methyl-D-aspartate (NMDA) or L-glutamate, and inhibited the NMDA-induced activation of caspase 3. CCL2 induced phosphorylation of MEK1/2, extracellular regulated kinase (ERK)1/2, p90RSK, and Akt in concentration- and time-dependent manners. CCL2-induced activations of ERK1/2 and p90RSK were inhibited by U0126, a MEK1/2 inhibitor, suggesting that CCL2-triggered activation of p90RSK is mediated through the MEK/ERK signaling pathway. CCL2-induced phosphorylations of Akt, ERK1/2, and p90RSK were inhibited by the broad spectrum PI3K inhibitors wortmannin and LY294002, as well as the PI3Kγ inhibitor AS605240, suggesting that these three kinases are downstream modulators of PI3Kγ in the CCL2 signaling pathway. Taken together, these findings contribute to the understanding of the neuroprotective role of CCL2 and its signaling pathways in the brain where PI3Kγ plays a vital role.

Biography

Jungsook Cho has completed her PhD from State University of New York at Buffalo, USA and been engaged as a Professor at Dongguk University, Republic of Korea, since 1996. She is the Director of Drug Target Control Research Center.

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