PB-9

Extracellular Signal-Regulated Kinase (ERK1/2) Regulate Glucose Deprivation-Induced Cell Death in Immunostimulated Astrocytes

Byoung Kwon Yoo*, Ji Woong Choi, Seo-Young Yoon, Mi-Jin Jeon, Gyu-Hwan Park, Hyun-Joo Chun and Kwang Ho Ko.
Department of Pharmacology, College of Pharmacy, Seoul National University, Seoul 151-742, Korea

In our previous study, glucose deprivation was reported to induce the potentiated death and ATP loss in immunostimulated astroglia. And this vulnerability to glucose deprivation was due to overproduction of nitric oxide (NO) and hydrogen peroxide (H_2O_2). In the present study, the role of extracellular signal-regulated kinase 1/2 (ERK1/2) in the glucose deprivation-induced death of immunostimulated astroglia was examined. We showed that immunostimulation with LPS+IFN-γ activated the ERK1/2 signal pathway and produced a large amount of NO and H_2O_2. Generation of NO and H_2O_2 in immunostimulated astroglia was mediated via ERK1/2 signal pathways, since addition of the ERK kinase (MEK1) inhibitor PD98059 reduced NO and H_2O_2 production. ERK1/2 activation-mediated NO and H_2O_2 production is due to an activation of iNOS and NADPH oxidase, respectively. Finally, we found that glucose deprivation caused ATP depletion and the augmented death in immunostimulated astroglia, which was also prevented by PD98059 treatment. These results demonstrate that the ERK1/2 signal pathways play an important role in glucose deprivation induced the death in immunostimulated astroglia by regulating the generation of NO and H_2O_2.