

저칼륨상태에서 Nrf2 발현조절에 의한 이온수송체 증가

전남대학교 의과대학 해부학교실, 전남대학교 유전자제어 기초의과학센터

조혜정 · 정채용 · 안규윤

Low Potassium Upregulates Ion Transporters Through the Regulation of Nrf2 Expression

Hye Jung Cho, Chae Yong Jung, Kyu Youn Ahn

Department of Anatomy Chonnam National University Medical School
Medical Research Center for Gene Regulation, Chonnam National University

The transcription factor nuclear factor-erythroid-2-related factor 2 (Nrf2) plays a key role in the cellular defense against oxidative stress. Low K⁺ increased the reactive oxygen species and it stimulate Nrf2 activation. Previous our study demonstrated that low potassium promoted expression of H/K-ATPase and kNBC1 by Nrf2 transcription factor in cultured models. Nrf2 increases the promoter activity of kNBC1 and colonic H/K-ATPase and co-transfection of Nrf2 with Sp family genes drives additional enhancements of the ion-transporter's promoter activities. In addition, phosphorylation of ERK, JNK, p38 and PI3K was involved in the activation of Nrf2 expression. This study aims to elucidate the mechanism which low potassium regulates Nrf2 expression through various in vitro and in vivo models.

Using various kinase inhibitors, promotion of Nrf2 expression in low potassium condition was inhibited by LY294002 and SP600125 while PD98059 and SB203580 did not affect Nrf2, suggesting that phosphorylation of Akt and JNK is specifically involved in Nrf2 expression in low potassium condition. Kidney tissues from low potassium diet rats showed increased phosphor-ERK1/2 and phosphor-Akt in diet time dependent manner but no effect to JNK and p38 phosphorylation. Specifically, Phospho-Nrf2 was also increased in nuclear compartment by low potassium diet. In order to demonstrate direct evidence that low potassium regulates ionic transporters by Nrf2, Nrf2 knockout mice were employed. Mouse embryonic fibroblasts (MEF) were harvested for the study. As expected, low potassium promotes expression of Nrf2 and level of phosphor-ERK1/2 and phosphor-Akt in MEF-Nrf2 (+/+). Low potassium promoted expression of kNBC1 and H/K-ATPase in MEF-Nrf2 (+/+), but unchanged or even decreased in MEF-Nrf2 (+/-) and MEF-Nrf2 (-/-).

Taken together, these results show that Nrf2 was activated by ERK1/2 and AKT in low potassium condition and further regulates expression of kNBC1 and colonic H/K-ATPase.

Key Words: 저칼륨상태, Nrf2, 이온수송체

Low potassium, Nrf2, Ion transporters