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Interaction of hydrogen sulfide and nitric oxide in brain

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Both hydrogen sulfide (H_2S) and nitric oxide (NO) are important gaseous mediators. We and others previously reported that these two gases react with each other to generate a new mediator, nitroxyl (HNO) and regulate cardiovascular functions. We also reported that the interaction between the two gases also existed in microglia. The biological functions of HNO in microglial cells were further studied with Angeli's salt (AS), an HNO donor. We found that AS attenuated lipopolysaccharide (LPS)-evoked production of reactive oxygen species (ROS) and pro-inflammatory cytokines (e.g., IL-1 β and TNF- α) through down-regulating the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2). HNO significantly reduced the phosphorylation of P38 mitogen-activated protein kinase (MAPK) and the activation of nuclear factor- κ B (NF- κ B) through suppression of phosphorylation p65 and I κ B α . The above effects were abolished by L-cysteine, an HNO scavenger, but were not mimicked by nitrite, another product of AS during generating HNO. A Cys-179-to-Ala mutation in inhibitory κ B kinase β (IKK β) mimicked the effect of HNO on LPS-induced NF- κ B activation. Interestingly, AS abolished the inflammation in cells overexpressing WT-IKK β , but had no significant effect in cells overexpressing C179A-IKK β . These data suggest that HNO may act on C179 to prevent IKK β -dependent inflammation. Taken together, our data demonstrated for the first time that H_2S interacts with NO to generate HNO in microglial cells. HNO produces anti-inflammatory effects through suppressing the IKK β dependent NF- κ B activation and P38 MAPK pathways.

Biography

Jinsong Bian is an Associate Professor in Department of Pharmacology, Yong Loo Ling School of Medicine, National University of Singapore, Singapore. His main research interests include biology of endogenous mediators (e.g., hydrogen sulfide) and novel functions of Na⁺/K⁺ ATPase. He has published over 90 papers in international journals including *Cir Res*, *ARS*, *JASN*, and has delivered over 70 lectures on invitation at international and regional scientific societies, institutes and conference organizations.

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