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Molecular hydrogen regulates gene expression by modifying the free radical chain reaction-dependent generation of oxidized phospholipid mediators

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Free PMC article

Abstract

We previously showed that H2 acts as a novel antioxidant to protect cells against oxidative stress. Subsequently, numerous studies have indicated the potential applications of H2 in therapeutic and preventive medicine. Moreover, H2 regulates various signal transduction pathways and the expression of many genes. However, the primary targets of H2 in the signal transduction pathways are unknown. Here, we attempted to determine how H2 regulates gene expression. In a pure chemical system, H2 gas (approximately 1%, v/v) suppressed the autoxidation of linoleic acid that proceeds by a free radical chain reaction, and pure 1-palmitoyl-2-arachidonyl-sn-glycero-3-phosphocholine (PAPC), one of the major phospholipids, was autoxidized in the presence or absence of H2. H2 modified the chemical production of the autoxidized phospholipid species in the cell-free system. Exposure of cultured cells to the H2-dependently autoxidized phospholipid species reduced Ca(2+) signal transduction and mediated the expression of various genes as revealed by comprehensive microarray analysis. In the cultured cells, H2 suppressed free radical chain reaction-dependent peroxidation and recovered the increased cellular Ca(2+), resulting in the regulation of Ca(2+)-dependent gene expression. Thus, H2 might regulate gene expression via the Ca(2+) signal transduction pathway by modifying the free radical-dependent generation of oxidized phospholipid mediators.

Figures

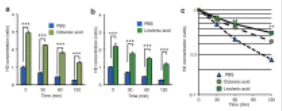

Figure 1. Solubility of H_2 in...

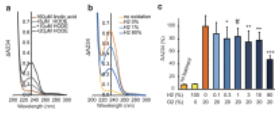

Figure 2. Suppression of autoxidation of linoleic...

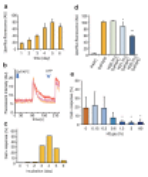

Figure 3. PAPC autoxidized with H_2...

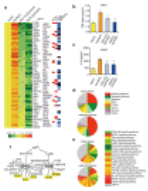

Figure 4. Changes in gene expression regulated...

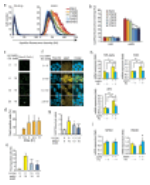

Figure 5. H_2 suppressed free radical...

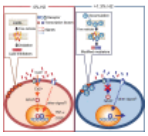

Figure 6. A model of the proposed...

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