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Molecular hydrogen protects chondrocytes from oxidative stress and indirectly alters gene expressions through reducing peroxynitrite derived from nitric oxide

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Abstract

Background: Molecular hydrogen (H2) functions as an extensive protector against oxidative stress, inflammation and allergic reaction in various biological models and clinical tests; however, its essential mechanisms remain unknown. H2 directly reacts with the strong reactive nitrogen species peroxynitrite (ONOO-) as well as hydroxyl radicals (•OH), but not with nitric oxide radical (NO•). We hypothesized that one of the H2 functions is caused by reducing cellular ONOO-, which is generated by the rapid reaction of NO• with superoxides (•O2-). To verify this hypothesis, we examined whether H2 could restore cytotoxicity and transcriptional alterations induced by ONOO- derived from NO• in chondrocytes.

Methods: We treated cultured chondrocytes from porcine hindlimb cartilage or from rat meniscus fibrecartilage with a donor of NO•, S-nitroso-N-acetylpenicillamine (SNAP) in the presence or absence of H2. Chondrocyte viability was determined using a LIVE/DEAD Viability/Cytotoxicity Kit. Gene expressions of the matrix proteins of cartilage and the matrix metalloproteinases were analyzed by reverse transcriptase-coupled real-time PCR method.

Results: SNAP treatment increased the levels of nitrated proteins. H2 decreased the levels of the nitrated proteins, and suppressed chondrocyte death. It is known that the matrix proteins of cartilage (including aggrecan and type II collagen) and matrix metalloproteinases (such as MMP3 and MMP13) are down- and up-regulated by ONOO-, respectively. H2 restoratively increased the gene expressions of aggrecan and type II collagen in the presence of H2. Conversely, the gene expressions of MMP3 and MMP13 were restoratively down-regulated with H2. Thus, H2 acted to restore transcriptional alterations induced by ONOO-.

Conclusions: These results imply that one of the functions of H2 exhibits cytoprotective effects and transcriptional alterations through reducing ONOO-. Moreover, novel pharmacological strategies aimed at selective removal of ONOO- may represent a powerful method for preventive and therapeutic use of H2 for joint diseases.

Figures

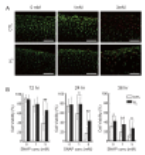

Figure 1 Hydrogen protects chondrocytes of hyaline...

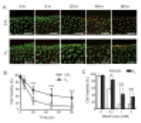

Figure 2 Hydrogen protects chondrocytes of fibrocartilages...

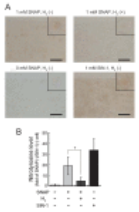

Figure 3 Hydrogen decreases nitrotyrosine in

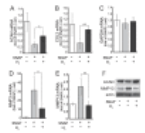

Figure 4 Hydrogen alters mRNA and protein...

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