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Molecular hydrogen upregulates heat shock response and collagen biosynthesis, and downregulates cell cycles: meta-analyses of gene expression profiles

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Abstract

Molecular hydrogen exerts its effect on multiple pathologies, including oxidative stress, inflammation, and apoptosis. However, its molecular mechanisms have not been fully elucidated. In order to explore the effects of molecular hydrogen, we meta-analysed gene expression profiles modulated by molecular hydrogen. We performed microarray analysis of the mouse liver with or without drinking hydrogen water. We also integrated two previously reported microarray datasets of the rat liver into meta-analyses. We used two categories of meta-analysis methods: the cross-platform method and the conventional meta-analysis method (Fisher's method). For each method, hydrogen-modulated pathways were analysed by (i) the hypergeometric test (HGT) in the class of over-representation analysis (ORA), (ii) the gene set enrichment analysis (GSEA) in the class of functional class scoring (FCS), and (iii) the signalling pathway impact analysis (SPIA), pathway regulation score (PRS), and others in the class of pathway topology-based approach (PTA). Pathways in the collagen biosynthesis and the heat-shock response were up-regulated according to (a) HGT with the cross-platform method, (b) GSEA with the cross-platform method, and (c) PRS with the cross-platform method. Pathways in cell cycles were down-regulated according to (a) HGT with the cross-platform method, (b) GSEA with the cross-platform method, and (d) GSEA with the conventional meta-analysis method. Because the heat-shock response leads to up-regulation of collagen biosynthesis and a transient arrest of cell cycles, induction of the heat-shock response is likely to be a primary event induced by molecular hydrogen in the liver of wild-type rodents.

Keywords: Molecular hydrogen; cross-platform analysis; heat-shock protein; meta-analysis; pathway analysis.

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