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Hydrogen gas inhibits lung cancer progression through targeting SMC3

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Abstract

Lung cancer is one of the most common lethal malignancies in the globe. The patients' prognoses are dim due to its high metastatic potential and drug resistance. Therefore, in the present study, we aim to find a more potent therapeutic approach for lung cancer. We mainly explored the function of hydrogen gas (H₂) on cell viability, apoptosis, migration and invasion in lung cancer cell lines A549 and H1975 by CCK-8, flow cytometry, wound healing and transwell assays, respectively. We used RNA-seq, qPCR and western blotting to detect the different expression genes (DEGs) between H₂ group and control group to find the gene related to chromosome condensation. Besides, we confirmed the structural maintenance of chromosomes 3 (SMC3) and H₂ on the progression of lung cancer in vitro and vivo. Results showed that H₂ inhibited cell viability, migration and invasion, and catalyzed cell apoptosis and H₂ induced A549 and H1975 cells G2/M arrest. Besides, H₂ down-regulated the expression of NIBPL, SMC3, SMC5 and SMC6, and also reduced the expression of Cyclin D1, CDK4 and CDK6. H₂ translocated the subcellular location of SMC3 during cell division and decreased its stability and increased its ubiquitination in both A549 and H1975 cells. In addition, inhibition of the proliferation, migration and invasion and promotion of the apoptosis of A549 and H1975 cells induced by H₂ were all abolished when overexpressed SMC3 in the presence of H₂. Animal experimental demonstrated that the tumor weight in H₂ group was significantly smaller than that in control group, but was bigger than cis-platinum group. The expression of Ki-67, VEGF and SMC3 were decreased when mice were treated with H₂ or cis-platinum, especially for cis-platinum. All data suggested that H₂ inhibited lung cancer progression through down-regulating SMC3, a regulator for chromosome condensation, which provided a new method for the treatment of lung cancer.

Keywords: Chromosome condensation; Hydrogen gas; Lung cancer; SMC3.

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