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Randomized Controlled Trial

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Two weeks of hydrogen inhalation can significantly reverse adaptive and innate immune system senescence patients with advanced non-small cell lung cancer: a self-controlled study

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## **Abstract**

Following standard treatments, the traditional model for enhancing anti-tumor immunity involves performing immune reconstitution (e.g., adoptive immune cell therapies or immunoenhancing drugs) to prevent recurrence. For patients with advanced non-small cell lung cancer, we report here on two

objectives, the immunosenescence for advanced non-small cell lung cancer and hydrogen gas inhalation for immune reconstitution. From July 1<sup>st</sup> to September 25<sup>th</sup>, 2019, 20 non-small cell lung cancer patients were enrolled to evaluate the immunosenescence of peripheral blood lymphocyte subsets, including T cell, natural killer/natural killer T cell and gamma delta T cell. Two weeks of hydrogen inhalation was performed during the waiting period for treatment-related examination. All patients inhaled a mixture of hydrogen (66.7%) and oxygen (33.3%) with a gas flow rate of 3 L/min for 4 hours each day. None of the patients received any standard treatment during the hydrogen inhalation period. After pretreatment testing, major indexes of immunosenescence were observed. The abnormally higher indexes included exhausted cytotoxic T cells, senescent cytotoxic T cells, and killer Vδ1 cells. After 2 weeks of hydrogen therapy, the number of exhausted and senescent cytotoxic T cells decreased to within the normal range, and there was an increase in killer  $V\delta 1$  cells. The abnormally lower indexes included functional helper and cytotoxic T cells, Th1, total natural killer T cells, natural killer, and Vδ2 cells. After 2 weeks of hydrogen therapy, all six cell subsets increased to within the normal range. The current data indicate that the immunosenescence of advanced nonsmall cell lung cancer involves nearly all lymphocyte subsets, and 2 weeks of hydrogen treatment can significantly improve most of these indexes. The study was approved by the Ethics Committee of Fuda Cancer Hospital, Jinan University in China (approval No. Fuda20181207) on December 7<sup>th</sup>, 2018, and was registered on ClinicalTrials.gov (ID: NCT03818347) on January 24<sup>th</sup>, 2019.

**Keywords:** T cell; adaptive and innate immune system; gamma delta T cell; hydrogen inhalation; immunosenescence; natural killer T cell; natural killer cell; non-small cell lung cancer.

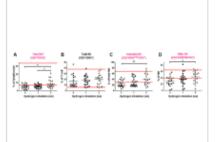
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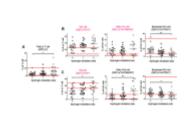
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**Figure 1** An immunoassay of the T...



**Figure 2** Immunoassay of natural killer (NK)T...



**Figure 3** Immunoassay of the gamma delta...

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