Inspiratory hyperoxia suppresses lung cancer metastasis through a MYC/SLC1A5-dependent metabolic pathway

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Abstract

The lack of knowledge about the effect of inspiratory hyperoxia on the lung-specific tumour microenvironment and progression of lung cancer has attracted considerable attention. This study proposes that inspiratory hyperoxia has special significance for the malignant phenotype of lung cancer cells. The effects of different oxygenation parameters on the proliferation, apoptosis, invasion and migration of lung cancer cells were systematically evaluated *in vitro* and *in vivo*. Our results reveal that inspiratory hyperoxia treatment (60% oxygen, 6 $h \cdot day^{-1}$) not only has no tumour progression-promoting effects, but also suppresses lung cancer metastasis and promotes long-term survival. In addition, we combined transcriptome, proteome and metabolome analysis and found that hyperoxia treatment induced significant intracellular metabolic changes in lung cancer cells. Overall, we established that MYC/SLC1A5-induced metabolic reprogramming and glutamine addiction is a new mechanism that drives lung cancer metastasis, which can be significantly suppressed by inspiratory hyperoxia treatment. These findings are relevant to the debate on the perils, promises and antitumour effect of inspiratory hyperoxia, especially for patients with lung cancer.

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