# HOXB9

Even after multimodal therapy, the prognosis is dismal for patients with brain metastases from non-Small-cell lung cancer (NSCLC). Although the blood-brain barrier (BBB) limits tumor cell penetration into the brain parenchyma, some nevertheless colonize brain tissue through mechanisms that are not fully clear. Zheng et al. showed that homeobox B9 (HOXB9), which is commonly overexpressed in NSCLC, promotes epithelial-mesenchymal transition (EMT) and tumor migration and invasion. Animal experiments showed that HOXB9 expression correlates positively with the brain metastatic potential of human NSCLC cells, while brain metastatic cells derived through in vivo selection showed greater HOXB9 expression than their cells of origin. Comparable results were obtained after immunohistochemical analysis of clinical primary NSCLC and matched brain metastases samples obtained after surgery. Using an in vitro BBB model, knockdown and overexpression experiments showed that HOXB9-dependent expression of MMP9 in NSCLC cells leads to reduced expression of junctional proteins in cultured human vascular endothelial cells and enhanced transmigration of tumor cells. These data indicate that HOXB9 enables NSCLC cells to break away from the primary tumor by inducing EMT, and promotes brain metastases by driving MMP9 production and degradation of intercellular adhesion proteins in endothelial cells comprising the BBB [1)].

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Zheng H, Li C, Li Z, Zhu K, Bao H, Xiong J, Liang P. HOXB9 enhances the ability of lung cancer cells to penetrate the blood-brain barrier. Aging (Albany NY). 2020 Dec 19;12. doi: 10.18632/aging.202324. Epub ahead of print. PMID: 33411683.