

# **Hypoxia-inducible factor-1 correlates with MET and metastasis in node-negative breast cancer**

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摘要

## **Abstract**

The mechanism of tumor hypoxia promoting metastasis remains uncertain. Hypoxia-inducible factor-1alpha (HIF-1alpha) is a key mediator of the cellular response to hypoxia and binds the met promoter, resulting in increased expression of MET. In breast cancer, MET overexpression is associated with death caused by metastatic disease. Aim of this study is to investigate the role of HIF-1alpha in MET expression and metastasis in lymph node negative breast cancer. We recruited a homogeneous cohort of 104 patients with T(1-2)N(0)M(0) breast carcinoma, who had undergone primary surgery. Fifty-three patients had distant metastases and 51 patients had no evidence of disease for more than 10 years. We analyzed the expressions of HIF-1alpha and MET in these patients using immunohistochemistry. HIF-1alpha and MET were positively correlated (Spearman's rank correlation coefficient, 0.35;  $P < 0.01$ ), were independent predictors of distant metastasis ( $P = 0.002$  and  $P = 0.03$ , respectively), and correlated with poor 10-year disease-free survival rate ( $P < 0.001$  for both). Furthermore, co-overexpression of HIF-1alpha and MET was a significant independent predictor of distant metastasis (odd radio, 10.78;  $P < 0.001$ ), and patients with co-overexpression had a significantly worse 10-year disease-free survival rate. The results provide evidence that tumor hypoxia promotes metastasis through the induction of MET overexpression by HIF-1alpha and emphasize the promising status of HIF-1alpha as a therapeutic target against metastasis in node-negative breast cancer.