

## Gastric Cancer

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### **Overexpression of Transcription Factor FoxM1b Promotes Human Gastric Cancer Angiogenesis and Metastasis and Predicts Poor Patient Survival**

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**Background:** FoxM1b, a mammalian Forkhead Box (Fox) transcription factor, has been implicated in tumorigenesis. However, the expression and role of FoxM1b in gastric cancer remains unknown.

**Methods:** FoxM1b expression was investigated in 86 cases of primary gastric cancer, 57 normal gastric tissues and 53 lymph node metastases. The effects of altered FoxM1b expression on gastric cancer growth and metastasis were further investigated using an orthotopic mouse model of gastric cancer.

**Results:** FoxM1b protein was expressed predominantly in the nuclei of cells in the mucous neck region and in the cytoplasm of cells in the glandular epithelium, whereas FoxM1b expression was not detected in the cells located toward the gastric pit. In contrast, strong FoxM1b staining was seen in the tumor-cell nuclei of various types of gastric cancer. We also evaluated the effect of FoxM1b expression on the survival of patients who have undergone surgical resection. FoxM1b expression, disease stage, completeness of resection, age, and sex were entered into a Cox proportional hazard model. FoxM1b ( $P=.003$ ) and stage ( $P<.001$ ) were independently prognostic of survival in multivariate analysis. Furthermore, overexpression of FoxM1b by gene transfer

significantly promoted the growth and metastasis of GT5 gastric cancer cells in an orthotopic mouse model, whereas knockdown of FoxM1b expression by small interference RNA did the opposite. Regulation of gastric tumorigenesis by FoxM1b was directly correlated with vascular endothelial growth factor (VEGF) expression and angiogenesis.

**Conclusions:** Given the importance of FoxM1b in regulating the expression of genes key to cancer biology, its dysregulated expression and activation may play important roles in gastric cancer development and progression.