Overexpression of the JmjC histone demethylase KDM5B in human carcinogenesis: involvement in the proliferation of cancer cells through the E2F/RB pathway

ABSTRACT

Background: Although an increasing number of histone demethylases have been identified and biochemically characterized, their biological functions largely remain uncharacterized, particularly in the context of human diseases such as cancer. We investigated the role of KDM5B, a JmjC histone demethylase, in human carcinogenesis. Quantitative RT-PCR and microarray analyses were used to examine the expression profiles of histone demethylases in clinical tissue samples. We also examined the functional effects of KDM5B on the growth of cancer cell lines treated with small interfering RNAs (siRNAs). Downstream genes and signal cascades induced by KDM5B expression were identified from Affymetrix Gene Chip experiments, and validated by real-time PCR and reporter assays. Cell cycle-dependent characteristics of KDM5B were identified by immunofluorescence and FACS.

Results: Quantitative RT-PCR analysis confirmed that expression levels of KDM5B are significantly higher in human bladder cancer tissues than in their corresponding non-neoplastic bladder tissues ($P < 0.0001$). The expression profile analysis of clinical tissues also revealed up-regulation of KDM5B in various kinds of malignancies. Transfection of KDM5B-specific siRNA into various bladder and lung cancer cell lines significantly suppressed the proliferation of cancer cells and increased the number of cells in sub-G_1phase. Microarray expression analysis indicated that E2F1 and E2F2 are downstream genes in the KDM5B pathway.

Conclusions: Inhibition of KDM5B may affect apoptosis and reduce growth of cancer cells. Further studies will explore the pan-cancer therapeutic potential of KDM5B inhibition.

Keyword: JmjC histone demethylase; Cancer growth; Cancer cells; Cancer cell culture