KDM5B histone demethylase controls EMT of cancer cells by regulating the expression of microRNA-200 family

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Histone methylation is implicated in various biological and pathological processes including cancer development. Using retroviral insertional mutagenesis in mice, we have identified novel candidate cancer genes including the genes encoding histone methyltransferases and demethylases. Further we have found that some of these enzymes are involved not only in tumor initiation, but also in the process of tumor progression. Recently we discovered that the ectopic expression of KDM5B, a histone H3 lysine 4 (H3K4) demethylase, promoted epithelial-mesenchymal transition (EMT) of cancer cells. KDM5B increased the expression of transcription factors ZEB1 and ZEB2, followed by downregulation of E-cadherin and upregulation of mesenchymal marker genes. The expression of microRNA-200 (miR-200) family, which specifically targets ZEB1 and ZEB2, was reduced in the cells with KDM5B overexpression. We found that KDM5B repressed the expression of the miR-200 family by changing histone H3 methylation status of their regulatory regions. The introduction of miR-200 precursor in the cells inhibited EMT induction by KDM5B, suggesting that miR-200 family is a critical downstream mediator of KDM5B-promoted EMT. Furthermore, knockdown of KDM5B was shown to affect the expression of EMT-related genes, indicating the involvement of endogenous KDM5B. Our study demonstrated the novel role of KDM5B histone lysine demethylase in EMT, which may contribute to malignant progression of cancer.

Reference: Enkhbaatar Z, Terashima M et al., *Cell Cycle 12:13, 2100-2112; July 1, 2013.*

EDUCATIONS

2002-2006	Undergraduate study program, National University of Mongolia, Ulaanbaatar
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