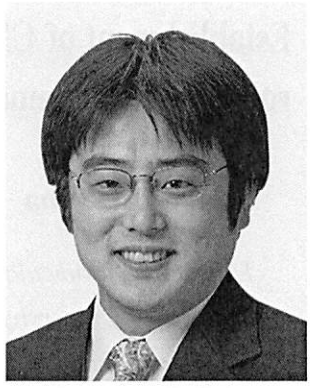
Jmjd5, a JmjC domain containing protein, modulates embryonic cell proliferation through the regulation of p53-target genes expression.



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We have performed the retroviral insertional mutagenesis in mice, resulting in identification of *Jmjd5* as one of the candidate cancer-related genes. Jmjd5 encodes a nuclear protein that contains JmjC domain, a motif for histone demethylase. Recent study indicates that Jmjd5 is a demethylase for di-methylated lysine 36 of histone H3 (H3K36me2). In this study, we have generated *Jmjd5*-deficient mice ($Jmjd5^{\tilde{\Delta}\Delta}$) to investigate the physiological role of *Jmjd5*. The $Jmjd5^{\tilde{\Delta}\Delta}$ mice howed severe growth retardation, causing the embryonic lethality around E 11.0. Quantitative PCR analysis for various cell cycle regulators showed the significant up-regulation of *p21* in $Jmjd5^{\tilde{\Delta}\Delta}$ embryos and *Jmjd5* hypomorphic MEFs ($Jmjd5^{neo/neo}$). The growth inhibition in $Jmjd5^{neo/neo}$ MEFs was rescued by the down-regulation of *p21* expression. ChIP assay indicated increased H3K36me2 and reduced recruitment of Jmjd5 on *p21* gene locus in $Jmjd5^{neo/neo}$ MEFs. We also found that the expression of several p53-target genes other than *p21* was up-regulated in $Jmjd5^{\tilde{\Delta}\Delta}$ embryos and $Jmjd5^{neo/neo}$ MEFs, although the expression level of *p53* RNA/protein was not altered. Furthermore, the growth defect of $Jmjd5^{neo/neo}$ MEFs was significantly recovered under $p53^{\tilde{\Delta}\Delta}$. genetic background. These results suggest that Jmjd5 is a novel p53 signal regulator involved in embryonic cell proliferation by fine-tuning the expression of p53-target genes including *p21*.

Reference: Ishimura et al, *Development* 139, 749-759 (2012).

EDUCATIONS AND POSITIONS

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