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拠点：大学院工学系研究科
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“化学を基盤とするヒューマンマテリアル創成”

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ふりがな 氏名	シャリフ　ジャファル SHARIF JAFAR	生年月日
所属機関名	東京大学大学院工学系研究科化学生命工学専攻	
所在地	東京都文京区本郷	
申請時点での学年	博士１年	
研究題目	Pax5 が制御するヒストンの脱メチル化による B 細胞の分化促進機構の解析	
指導教員の所属・氏名	多比良和誠 化学生命工学専攻　（２００６年１月までの指導教官）	

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I　研究の成果　（1000 字程度）

（図表も含めて分かりやすく記入のこと）

Pax5 (BSAP) is a master regulator of B-cell lymphopoiesis. Apart from its conventional role as a transcriptional activator of B-cell specific genes, Pax5 also modulates B-cell development in an epigenetic manner. A hallmark of Pax5 mediated epigenetic regulation of B-cells is the removal of H3K9 methylation, a symbol of inactive chromatin, in the IgH locus. In Pax5 knockout mice, the H3K9 methylation is not removed due to the lack of Pax5 and the chromatin in the IgH locus remains in an inaccessible state. However, it is not clear if the H3K9 methylation is a stationary mechanism that cannot be altered once established or a more dynamic process that is continuously regulated by Pax5. To investigate this, we knocked down Pax5 expression in immature B-cells using siRNAs. Chromatin immunoprecipitation analyses revealed that H3K9 methylation in the IgH locus is returned upon downregulation of Pax5. Moreover, these Pax5-deficient cells can be rescued by expressing a mutant Pax5 gene that cannot be degraded by siRNAs. Our results indicate that the H3K9 methylation in the IgH locus of B-cells is a dynamic and reversible process that is continuously regulated by Pax5 and can be altered by downregulation or reintroduction of Pax5. Despite its importance in B-cell lymphopoiesis, the role of Pax5 has only been studied until the pre-B stage in B-cells, as the B-cell development is terminated at pre-B level in Pax5 knockout mice. Here we show that the role of Pax5 can be studied beyond the pre-B stage, in the immature B-cells, applying an siRNA-based technique.

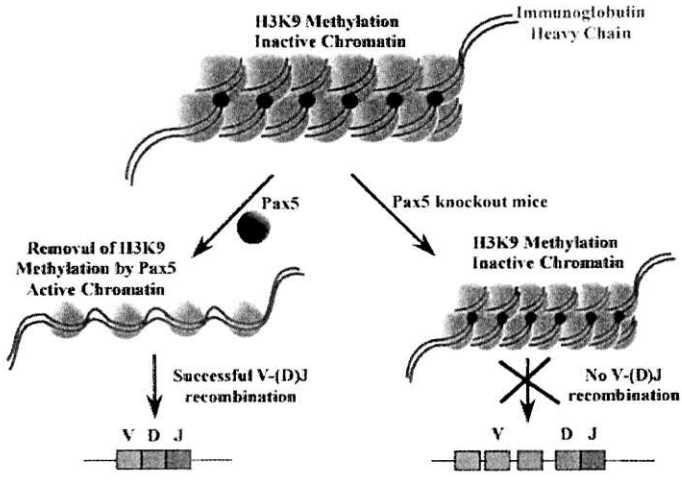

Figure 1: A schematic representation of Pax5-mediated B-cell development regulated by the loss of histone methylation in the IgH locus of B-cells.

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Ⅱ（1）　学術雑誌等に発表した論文A（掲載を決定されたものを含む.）

共著の場合、申請者の役割を記載すること.

（著者、題名、掲載誌名、年月、巻号、頁を記入）

氏　　名 SHARIF JAFAR

Ⅱ（2）学会において申請者が口頭発表もしくはポスター発表した論文
（共同研究者（全員の氏名）、題名、発表した学会名、場所、年月を記載）

1. Sharif, J.& Fukao, T., *B-cell specific loss of H3K9 methylation in the IgH locus is continuously dependent on Pax5 and can be reversed if Pax5 is downregulated,* 20th IUBMB International Congress of Biochemistry and Molecular Biology, Kyoto, 2006年6月。（発表する予定）
2. Sharif, J. & Fukao, T., *Pax5 regulates B-cell specific loss of Histone3 Lysine9 methylation in the V_H locus through all the stages of B-cell development,* 日本免疫学会総会、横浜、2005年12月。（口頭発表）
3. Sharif, J., Fukao, T. & Taira, K., *A Study of Stage Specific Gene Regulation by Pax-5 through siRNA-based Knockdown Method,* 日本免疫学会総会、北海道、2004年12月。（ポスター発表）