The role of protein arginine-methyltransferase 1 in gliomagenesis

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INTRODUCTION

Protein arginine methyltransferase 1 (PRMT1), a type-I arginine methyltransferase, has been implicated in diverse cellular events. We have focused on the role of PRMT1 in gliomagenesis. In this study, we showed that PRMT1 expression was up-regulated in glioma tissues and cell lines compared with normal brain tissues. The knock-down of PRMT1 resulted in an arrest in the G1-S phase of the cell cycle, proliferation inhibition and apoptosis induction in four glioma cell lines (T98G, U87MG, U251, and A172). Moreover, an in vivo study confirmed that the tumor growth in nude mouse xenografts was significantly decreased in the RNAi-PRMT1 group. Additionally, we found that the level of the asymmetric dimethylated histone H4R3, a substrate of PRMT1, was higher in glioma cells than in normal brain tissues and decreased after PRMT1 knock-down. Our data suggest a potential role for PRMT1 as a novel biomarker of and therapeutic target in gliomas. [BMB Reports 2012; 45(8): 470-475]

RESULTS

PRMT1 is up-regulated in human glioma tissues and cell lines

To detect the expression pattern of PRMT1 in gliomas, western
blotting was performed in 2 normal brain tissues and 17 primary glioma samples. In addition, the total RNA and protein were extracted from two normal brain tissues and four glioma cell lines, and real-time PCR and western blotting were performed to analyze the expression profile of PRMT1. As shown in Fig. 1A, the expression of PRMT1 was increased in more than 76% of glioma samples compared with the two normal brain tissues. In the glioma cell lines, PRMT1 expression was also upregulated (Fig. 1B, 1C). Furthermore, one grade II glioma patient sample was analyzed with HE staining and immunohistochemistry with a specific PRMT1 antibody (Fig. 1D). The tumor area showed a strong positive signal for PRMT1. By contrast, the normal tissue area showed weak staining. These data indicated that PRMT1 expression was elevated in glioma tissues and cells compared with normal brain tissues.

The knockdown of PRMT1 with Stealth™ RNAi inhibited the proliferation and promoted apoptosis in glioma cells

To examine the role of PRMT1 in glioma cells, we synthesized Stealth™ RNAi duplexes of PRMT1. On the third day after transfection with the RNAi, PRMT1 expression was examined in T98G, U87MG, U251 and A172 cell lines with western blotting. The results showed that the protein level of PRMT1 in the RNAi-PRMT1 group was reduced by at least 70% compared with the RNAi-NC group (Fig. 2A). To investigate whether the knockdown of PRMT1 affected the cell cycle in glioma cells, flow cytometry analysis was performed. The results showed a different cell cycle profile in the RNAi-PRMT1 group compared with the RNAi-NC group. As shown in Fig. 2B, knocking down PRMT1 with RNAi significantly decreased the cell population in S phase in the four glioma cell lines (U87MG: 18.5 ± 1.03% vs. 24.15 ± 1.28%; T98G: 22.03 ± 4.37% vs. 27.93 ± 3.06%; A172: 15.55 ± 0.78% vs. 21.9 ± 0.99%; and U251: 19.32 ± 0.62% vs. 23.12 ± 0.82%). Additionally, the percentage of cells in G1 phase was higher in glioma cells transfected with RNAi PRMT1 RNAi than in the control (U87MG: 69.7 ± 1.62% vs. 64.35 ± 2.10%; T98G: 69.87 ± 1.09% vs. 62.6 ± 0.79%; A172: 78.45 ± 0.62% vs. 71.17 ± 1.89%; and U251: 76.08 ± 1.03% vs. 71.87 ± 1.19%). These results showed that the cell cycle of glioma cells was arrested...