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Characterization of p16(INK4A) expression in multiple myeloma and plasma cell leukemia.

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Loss of p16(INK4A) (p16) expression is frequently associated with the development of epithelial and lymphoid malignancies. However, the frequency and significance of p16 abnormalities in multiple myeloma (MM) and the more aggressive phase of plasma cell leukemia (PCL) have not been well defined. Accordingly, the goal of this study was to define the expression and function of p16 in fresh samples of MM and PCL. We found that p16 protein was highly expressed in primary MM cells, although it was undetectable in fresh samples of PCL. Additionally, p16 protein was also absent in four of four MM-derived cell lines. To determine the mechanism for p16 underexpression in PCL and MM-derived cell lines, we performed PCR analysis to evaluate both gene deletion and the presence of methylation. Interestingly, the p16 gene was present and methylated in all patient PCL cells and MM cell lines, whereas it was unmethylated in patient MM cells and normal B cells. Furthermore, treatment with the demethylating agent 5-deoxyazacytidine or p16 retrofection restored p16 protein expression and induced G1 growth arrest in patient PCL cells and MM cell lines. These results suggest that inactivation of the p16 gene by methylation may be associated with decreased growth control and the development of PCL in a subset of patients with MM.