Different mechanisms of cyclin D1 overexpression in multiple myeloma revealed by fluorescence in situ hybridization and quantitative analysis of mRNA levels.

Abstract:
The t(11; 14)(q13; q32) is the most common translocation in multiple myeloma (MM), resulting in up-regulation of cyclin D1. We used a segregation fluorescence in situ hybridization (FISH) assay to detect t(11; 14) breakpoints in primary MM cases and real-time reverse transcriptase-polymerase chain reaction (RT-PCR) to quantify cyclin D1 and MYEOV (myeloma overexpressed) expression, another putative oncogene located on chromosome 11q13. High levels of cyclin D1 mRNA (cyclin D1/TBP [TATA box binding protein] ratio > 95) were found exclusively in the presence of a t(11; 14) translocation (11/48 cases; P < .0001). In addition, a subgroup of MM cases (15/48) with intermediate to low cyclin D1 mRNA (cyclin D1/TBP ratio between 2.3 and 20) was identified. FISH analysis ruled out a t(11; 14) translocation and 11q13 amplification in these cases; however, in 13 of 15 patients a chromosome 11 polysomy was demonstrated (P < .0001). These results indicate an effect of gene dosage as an alternative mechanism of cyclin D1 deregulation in MM. The absence of chromosome 11 abnormalities in 2 of 15 patients with intermediate cyclin D1 expression supports that there are presumably other mechanism(s) of cyclin D1...
deregulation in MM patients. Our data indicate that deregulation of MYEOV is not favored in MM and further strengthens the role of cyclin D1 overexpression in lymphoid malignancies with a t(11; 14)(q13; q32) translocation.

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