Reviewer's report

Title: Relevance of cyclin D1b expression and CCND1 polymorphism in the pathogenesis of multiple myeloma and mantle cell lymphoma

Version: Date: 1 June 2006

Reviewer: Jean-Philippe Merlio

Reviewer's report:

General
The study is relevant especially in addressing the fact that either the A or G allele at nucleotide 870 may encode for cyclin D1 b isoform.
There is also a clear evidence that both cyclin D1 isoforms are coexpressed in MCL whatever the genotype but there was a predominant expression of the a form.
The authors should comment on the fact that discordant data have been generated in the past according to the patient's genotype. Their group (reference 13) and the group of Howe et al (reference 18) have previously indicated a differential expression of cyclin D1 a and b according to the genotype at position 870 (and not according to the mechanism of CCND1 activation).
Is there a technical explanation (RQ-PCR also employed in reference 17 vs standard RT-PCR) or another explanation such as tumour cells content, purification method or tissular origin to account for such discrepancies.

It should also be taken in mind that the expression of cyclin D1b isoform is an abnormal overexpression and not a normal constitutive expression. Moreover the expression in normal B lymphocytes as well as the protein half time and properties may be different between normal and tumoural cells.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

In the abstract
page 2 line 16 "The two properties of cyclin D1b for its transforming activity are missing in MCL" Unless, the transforming activity of such protein has been ruled out, it is supposed that either cyclin D1 a or b have a transforming activity in MCL. A specific transforming activity of the b form over the a form is simply unlikely. This should be discussed in view of the predominant overexpression of the a form.

page 4 How did the authors check the absence of genomic DNA for RQ-PCR, did they perform a no RT control for all samples
The position of the primers for cyclin D1a quantification could be indicated in the text of figure legend.

page 5: How can the experiment indicate that cyclin D1b is not a stabilized form of cyclin D1 a ? There is no specific experimental proof of such assessment.

figure 2B: the authors should comment the fact that the monoclonal DCS-6 antibody that would recognize both isoforms provides a weaker signal that the anti-cyclinD1a antibody. This could indicate that the latter is not specific only for cyclin D1 a.

Discretionary Revisions (which the author can choose to ignore)

All MCL cases expressed less cyclin D1b mRNA than cyclin D1 a, as shown in table 1. Therefore, cyclin D1b oncogenic properties could be altered by a dominant oncogenic effect of the cyclin D1a isoform. This may be the opposite in MCL cases with a predominant overexpression of cyclin D1 b.

Conclusion: no relationship instead of relationships

What next?: Accept after minor essential revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

'I declare that I have no competing interests'