Reviewer’s report

Title: Mutation analysis of genes that control the G1/S cell cycle in melanoma: TP53, CDKN1A, CDKN2A, and CDKN2B

Version: 1 Date: 11 February 2005

Reviewer: Arndt Hartmann

Reviewer’s report:

General
This paper describes a mutation analysis of the genes p53, CDKN1A, CDKN2A and CDKN2B in 39 malignant melanoma. The results show that these genes are not frequently involved in melanoma development. This is the first study to investigate all of these genes in melanomas and therefore should be published. However, the authors will have to change some statements in the manuscript.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
My main concern is in the term "mutation" for some intronic base alterations in p53. Although these changes were not found in the germline of the patients, there is no evidence that these changes have anything to do with melanoma development. The authors should look in 100 chromosomes if these changes are rare polymorphisms. Are they reported in the p53 database in other tumor types? In summary, there are two melanomas with mutations in any of the genes, one with a p53 nonsense mutation in Exon 10 and one with mutations in p16. So mutations seem to play no major role in these genes. However, other mechanisms of inactivation could be important (e.g. homozygous deletion or promoter methylation). The authors should look for these changes, at least in p15 and p16 (e.g. by MSP or FISH).

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

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No