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

Authors:
- Jose Luis Soto (miguel.lopez.nevot.sspa@juntadeandalucia.es)
- Carmen M. Cabrera (mcabrm@fundacionhvn.org)
- Sabio Serrano (miguel.lopez.nevot.sspa@juntadeandalucia.es)
- Miguel Angel Lopez-Nevot (miguel.lopez.nevot.sspa@juntadeandalucia.es)

Version: 2 Date: 22 February 2005

Author's response to reviews: see over
Reviewer: Arndt Hartmann

Major Compulsory Revisions:

-The DNA sequence variations are considered as polymorphisms when they are constitutive, and therefore are present both in normal tissues and tumors. Accordingly, the DNA variations found in tumors M42 (11701C>T, intron 1) and M43 (11818delC, intron 2) (page 7, paragraph 3, Table 3) have been included in the text as “mutations” and not as “polymorphisms”, because are absent in the autologous PBLs. Mutations (including polymorphisms) can be harmful, beneficial, or have no effect. The presence of mutations not necessary imply their role in melanoma tumorigenesis, may occur as result of tumoral growth.

-The three new single point mutations described in text were compared with the most actualised and largest TP53 Mutation Database IARC (International Agency for Research on Cancer) (http://www-p53.iarc.fr/Somatic.html), and were not found in melanoma and other tumor types. The web direction of the IARC TP53 Mutation Database has been included in the section corresponding of Results (page 7, paragraph 1).

-Our manuscript is focused to describe the mutations of genes that control the progression of G1/S cell cycle (TP53, CDKN1A, CDKN2A, and CDKN2B), but not in to study other structural alterations as homozygous deletions or promoter methylation. These other alterations are the aim of a future study.