Author’s response to reviews

Title: Variable expression of cerebral cavernous malformations in carriers of a premature termination codon in exon 17 of the Krit1 gene.

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Version: 4 Date: 7 May 2003

Dear Sir

We have amended the manuscript according to the suggestions of the reviewer.

A) The issue of penetrance is discussed in the new version see 3rd paragraph in Discussion

A1.- We have included a new reference [13] and in the text..... Penetrance of Krit1 mutations has not been properly studied but significant locus-specific differences in penetrance have been identified. The penetrances of clinical CCMs among apparent carriers in kindreds linked to CCM1, CCM2 and CCM3 have been estimated as 88, 100 and 63% respectively [13]

A2.- Individuals usually become symptomatic between 20 and 40 years of age, although clinical signs have been described in all age groups [1, 5]

A3.- Asymptomatic carriers are probably not an unusual finding, but the demonstration of the mutation is necessary to raise this conclusion and for genetic counselling. CCMs may develop in utero decades before any clinical presentation [3] but it is possible that penetrance varies among families with particular mutations at each gene.

B) The English edition has been corrected by BIOMEDES as you recomended.
C) Additional symbols have been included in Figure 3 as suggested by the reviewer.
D) Table 1 has been modified as required by the reviewer