Reviewer’s report

Title: HFE H63D mutation frequency shows an increase in Turkish women with breast cancer.

Version: 3 Date: 21 December 2005

Reviewer: Ernest Beutler

Reviewer’s report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Most revisions are satisfactory.

However, two problems remain:

1. Re: Referee 1 Major Revision #2, The HEIRS study, which the authors cite as not finding any effect in H63D homozygotes and heterozygotes, in fact reported increasing transferrin saturation levels from wildtype to H63D/wt to C282Y/wt to H63D homozygotes to compound homozygotes, a trend consistent with the other two studies demonstrating an effect of the H63D mutation. The reason some studies do not show an effect is that the effect is small and requires very large sample sizes for adequate power.

2. Re: Referee 1 Major Revision #7: The Bonferroni correction made by the authors (dividing the alpha by 4) has the same effect as multiplying the calculated p value by 4: the comparison of interest in this paper is no longer significant making this adjustment, whether it’s p = 0.02 vs. a = 0.0125 or p = 0.08 vs. a = 0.05. This effect would be most appropriately addressed in the Discussion with a caution that not only is the study small, but when even a small number of multiple comparisons are made, the power of the study is further diminished.

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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)

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Discretionary Revisions (which the author can choose to ignore)

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