Reviewer's report

Title: Allele frequencies of hemojuvelin gene (HJV) I222N and G320V missense mutations in white and African American subjects from the general Alabama population

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Reviewer: Alison Merryweather-Clarke

Reviewer's report:

General
Barton et al are to be congratulated for their straightforward and coherent account of low allele frequencies of two HJV mutations in control individuals from two populations in Alabama, those with presumably European ancestry and African Americans.

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

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

Discretionary Revisions (which the author can choose to ignore)
The observation of a phenotypically normal 29-year old female double heterozygote for HFE C282Y and HJV I222N is interesting in the light of reports of double heterozygosity for mutations in HAMP and HFE causing haemochromatosis of varying severity depending on the severity of the HAMP mutation. It would be relevant to know whether this individual has had any pregnancies, is a blood donor or is a red meat eater or vegetarian if such information is accessible.
Barton et al cite their BCMD study of JH patients (ref 10) to support their point that “it does not appear that the common HFE mutations C282Y, H63D and S65C increase the severity of iron overload in persons with JH phenotypes and two HJV mutations”. It is apparent that HJV mutations cause more severe disease than those in HFE. However, only one of the six JH patients in the cited study was reported to have an HFE mutation (one was an HFE H63D heterozygote), so the authors may like to provide further observations to support their point, and for clarity should specify the relevant populations.

What next?: Accept after discretionary 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:

None