Reviewer's report

Title: Genome-wide linkage and exome analyses identify variants of HMCN1 for splenic epidermoid cyst

Version: 1 Date: 17 July 2014

Reviewer: David Adams

Reviewer's report:

The reviewed paper "Genome-wide linkage and exome analyses identify variants of HMCN1 for splenic epidermoid cyst" describes the use of linkage mapping plus exome sequencing to identify candidate genetic variants for causation of splenic epidermoid cyst. The paper is clear and well-written. The major conclusions are well supported by the presented evidence.

Major Compulsory Revisions: None

Minor Essential Revisions:

1. The authors used a sub-sampling approach to account for the linkage disequilibrium expected between the SNPs of a high-density SNP array. The genetic distances between the markers should be provided as supplemental data to defend the efficacy of the sub-sampling approach.

As an aside (not requiring revision), high-density SNP arrays can be used to unambiguously determine candidate regions without the need for linkage analysis (Recombination mapping using Boolean logic and high-density SNP genotyping for exome sequence filtering. Mol Genet Metab. 2012 Mar;105(3):382-9)

Discretionary Revisions:

1. Pathogenicity scores (SIFT, PolyPhen, CADD) have a relatively high false negative and false positive rate. However, they are a standard way of estimating pathogenicity. These scores (or equivalent) should be reported for completeness.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.