Reviewer's report

Title: Diverse Convergent Evidence in the Genetic Analysis of Complex Disease: Coordinating Omic, Informatic, and Laboratory based evidence to prioritize findings for further study

Version: 1
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Reviewer: David Reif

Reviewer's report:

The authors present an eloquent case for combining multiple lines of evidence to characterize the level of support for putative associations in studies of complex disease. The rationale, illustrative anecdotes, and discussion are convincing that such “convergent lines of evidence” can be useful for prioritizing findings. The authors propose a semi-formal DiCE approach to incorporating evidence from omic (e.g. GWAS), informatic (e.g. KEGG), and laboratory (e.g. model organism experiments) sources.

- Major Compulsory Revisions

The literature cited supports the main thesis of the paper. However, the introduction of DiCE is not supported by the level statistical accompaniment typically presented in this journal. Examples of how this might be improved include:

1. Add citation(s) and some exposition of relevant statistical literature on closely-related methods for meta-analysis, inter-rater reliability, and inferential ranking.

2. Provide empirical evidence (from simulation studies or a wider set of literature examples) to justify parameters such as the “>6” threshold. While it is appreciated that this will have an element of arbitrariness, possible alternatives should receive cursory exploration, at least.

3. Discuss the dependence of DiCE on the availability/popularity of studies addressing the association in question. Relatedly, would the authors consider negative context scoring for instances where solid evidence for lack of association is provided in a convergent evidence source?

- Minor Essential Revisions

4. [page 7] “Hemoglobin S and Malaria Resistance” should be retitled, as it is nearly identical to the previous subheading.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests