Reviewer's report

Title: Familial autoimmunity

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Reviewer: Didac Mauricio

Reviewer’s report:

The review article by Cárdenas-Roldán et al deals with an interesting issue, i.e. familial autoimmunity, that has important clinical and research implications. The subject is relevant to many potential readers.

The authors aimed to review the available literature on familial autoimmunity defined as the presence of different autoimmune diseases in a given nuclear family. They state that the review will discuss what they consider classic autoimmune diseases with a focus on five of them.

- Major Compulsory Revisions

1. The authors performed a literature search with a systematic approach. There are essential data concerning the search that should be provided for any researcher potentially interested in reproducing the literature search. Please, provide the following information in the text:
   - Clarify whether only Medline and Embase were searched.
   - Also, please specify to which year the search dates back in each database.
   - State whether there was any language restriction (where articles in any language included?).
   - Did the authors search the reference lists of the 46 articles included to indentify any additional relevant studies?
   - Concerning the 1,746 references identified, did the authors assess the abstracts (this is the usual way) or the full articles? Was each reference assessed only by one author or in duplicate?
   - In systematic reviews, the use of truncating search terms is usual (for example, famil* instead of familial). This strategy is aimed at not missing potentially relevant studies. Did the authors use this strategy for the words (non-MeSH terms) familial, clustering and aggregation?

2. The literature search strategy included only the specific search terms for five autoimmune diseases. However, the authors state that they “did not constrain the search for the 5 ADs” and decided to include articles “if familial autoimmunity was assessed in other ADs”. The identification of articles on these other ADs probably retrieved a number of potential studies well below the number that could be obtained using a specific search for each given disease (as was done with the main five diseases). This means that the risk of bias is high and, also, that the conclusions reached may not be solid. Therefore, this should be acknowledged
as an important limitation of the information provided for these other diseases. Actually, I would recommend to focus on the five major diseases proposed and to rearrange the content of the review. The authors may alternatively choose to include all other ADs under ‘Other ADs’ and they should then acknowledge the limitation of the information retrieved on these diseases.

- Minor Essential Revisions

1. In the second section of the article (The mosaic of autoimmunity), the second paragraph describes mainly the potential use of autoantibodies in disease prediction and prevention. Actually, this does not belong to the subject of the review. Thus, I would recommend to delete this section.

2. Please, to be consistent throughout the different diseases, state at the beginning of all disease subheadings how many studies where identified.

3. The information provided in figure 2 is already included in table 1. Therefore, the figure might be deleted.

4. The term ‘Grave’s disease’ should be changed to ‘Graves disease’ throughout the text.

- Discretionary Revisions

1. For the non-expert reader, it would be nice to have a more specific definition of the term ‘autoimmune tautology’ (second paragraph, page 4).

2. At the beginning of page 7, the authors state that they adopt the terms poliautommunity and familial autoimmunity and refer the reader to figure 1. In my opinion, the figure does not add relevant information. Instead, it would be preferable to have additional text that expands on the two terms adopted.

3. Under T1D (line 4), the authors probably meant ‘replicated’ instead of ‘duplicated’.

4. For the clinician, it would be relevant to have a section of the manuscript that summarizes the available evidence for screening of first-degree relatives of probands with any of the diseases. A section describing any available recommendations for or against screening in relatives would be very interesting.

5. To the opinion of this reviewer, the use of an excessive number of abbreviations is not desirable (in the main text and also in figures and tables). The number of abbreviations should be restricted to those terms that are used more frequently in the text. Further, the abbreviation SSc is not defined under the list of abbreviations.

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