Author's response to reviews

Title: Type 2 Diabetes Genetic Association Database manually curated for the study design and odds ratio.

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Author's response to reviews: see over
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Editor
Melissa Norton, MD

Dear Editor,

Thank you for the kind and positive response to our manuscript “Type 2 Diabetes Genetic Association Database manually curated for the study design and odds ratio”. We revised the manuscript according to the reviewers’ suggestions and explained the changes in the response.

We hope this revised manuscript and responses satisfy you and reviewers so that the manuscript can be accepted to the BMC Medical Informatics and Decision Making.

Sincerely,
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Response to Reviewer #1

Major Compulsory Revisions

• The completeness of the published literature is a key for such databases. The literature in this database was retrieved from Phenopedia of HuGE Navigator which is designed for displaying genetic association summary information by disease. Sometimes Phenopedia is more specific but not sensitive enough to catch all possible literature due to some design limitations. For more sensitive literature search in HuGE Navigator, HuGE Literature Finder should be used. If you search “type 2 diabetes” in Literature Finder and limited it from 2001 to 2009, you will get 3013 articles. Besides, although the collection of genetic association literature in HuGE Navigator is in general very comprehensive, it may miss some articles. Is there any other literature search strategy being used for catching some possible missing articles?

: HuGE Navigator is a well established genetic associations and human genome epidemiology tool, updating data every month. This is why we used HuGE Navigator as a reference for the selection of literature for T2DGADB.

• Comparisons with other databases are important to demonstrate the completeness of the database. Although the manuscript made comparisons with other databases, it should be more specific on literature coverage, such as how many overlaps with other db, how many missing, how many unique records in the T2DGAD, etc.

: We compared the records of PubMed ID, genes and SNPs in T2DGADB with those of OPG (NHGRI data in table1, reference 2[5]) and Andrew’s data (table1, reference 3[12]), which are made of the publications of only GWAS data. As shown below, T2DGADB has records of 688 unique publications, 421 unique genes, and 1874 unique variations. However, T2D-Db (table1 reference 1[6]) provided the limited information of PubMed ID, genes and SNPs, and was not compared. These comparisons were added in Table 1 of revised manuscript.

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<td>Variations(SNPs)</td>
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• I have a concern about the continuous usefulness of the database if the database only collects the data from 2001 to 2009 without future updating. I am sure it will be obsolete very soon. Is there any updating plan?
  : Yes, we are planning to update T2DGADB.

Minor Essential Revisions

• Meta-analyses articles usually provide very important summary information about re-synthesis of the data. It should be included in the database. I am sure they should be fitted into the current data format.
  : We used 701 publications for T2DGADB, and among them 30 meta-analysis articles were already included.

• I recommend that the data from GWAS published be flagged since it provides more reliable information about association compared to the traditional candidate gene approach, especially in current GWAS era. The same thing is for Meta-analyses publications if included.
  : We added flags for “GWAS” and “META” data in the database and described in the text of manuscript.
Response to Reviewer #2

Major Comments:

• The database would have been more interactive if the chromosomal position of the SNPs were mentioned or diagrammatically represented
  : We agree with the reviewer’s comment, but the information about the chromosomal position of SNPs change as the version of dbSNP build changes. Therefore we hyperlinked SNPs to NCBI reference SNP (refSNP) cluster report.

• In the 'Association Result' section of the gene view page, the bar graph representation for the SNPs needs to be labeled as 'A' and 'B' clearly
  : We changed it as reviewer’s comment.

• Authors should add chromosome wise search system for all the genes and candidate regions
  : We added a chromosome wise search option in the front page of web site.

• I think they should also add download section for all the rsIDs, corresponding PMIDs belonging to each gene and all the genes for a selected chromosome.
  : We added a download option for all genes and SNPs in the front page so that user can download the list of genes and PubMed ID.

• Since there are many candidate genes, which are overlapping to many Diabetes II complications, I think Authors should also take care of some important complications, their genes and corresponding rsIDs
  : We found about 1771 diabetes related publications. Among them about 600 publications are related to diabetes complication and listed the complication articles separately. We will extend our application to diabetes complications in the future.
**Minor Comments:**

- Since the database has disease-associated information, gene related information like gene ontology, pathway information, possible links to OMIM can be included
  : We agree with the reviewer’s comment. Gene related information such as gene ontology, pathway and OMIM are diverse and enormous, therefore we hyperlinked genes with NCBI Entrez gene.

- Please include a data flow diagram in method section of the manuscript. It should be presented like standard database paper
  : We expanded “Web implementation and Database design” section in method and modified the data flow diagram.