THE HUMAN VARIOME PROJECT

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MINUTES

Gene/Disease Specific Database Advisory Council
Tuesday 12 January, 2016
1200-1300hrs UTC/GMT

MEMBERS

Present
Peter E M Tashner (Chair)
Arleen Auerbach
Rosemary Ekong
Mauno Vihinen
Mary Fujiwara
Tamas Hegedus
Yves Sabbagh

ICO Staff
Timothy D. Smith
Catherine Carnovale

Apologies
Raymond Dalgleish
Sarah E A Leigh
Nenad Blau
Olubunmi K D Abel
Ammar Al-Chalabi
Stefan Aretz
Timothy Barret
David Baux
Jean-Pierre Bayley
Daniel Bichet
Nancy Braverman
Paola Carrera
Johan T den Dunnen
Pascal Escher
Marc Ferre
Bruce Gottlieb
Daniel Hampshire
Raoul Hennekam
Alex Hewitt
Ammar Husami
Derek Lim
Finlay Macrae
Eamonn Maher
Etienne Mornet
Magali Olivier
Sue M Povey
Judith Anne Savige
Sarah Sim
Carli Tops
Ronald Trent
Richard van Wijk
Katarzyna Wertheim-Tysarowska
Tom Winder
Bing Yu
Martina Witsch-Baumgartner
Johannes Zschock

AGENDA

1. **Welcome**

2. **Apologies**

   Apologies were noted as above

3. **Confirmation of minutes of previous meeting**

   A minor correction was made to Item 7 from the minutes of the previous meeting.
   Where it was previously noted that Rosemary Ekong contacted Global Alliance, this has now been changed to the following;

   "She further noted that Dr Mats Hansson of the Centre for Research Ethics & Bioethics in Uppsala (Sweden) was contacted however he felt that he would not be able to participate due to time constraints".

   Further to this discussion, it was decided that the Council would re-approach in a face-to-face setting (suggested for HGVS on 20th May 2016) to allow time for further developments to occur.

4. Report from Chair – Peter Taschner

Peter Taschner reported that he is planning an activity with the University of Applied Sciences for DNA Day (25th April). The current idea involves looking through the list of published papers currently on the Human Variome Project website, with particular attention to papers which mention variant submission to databases or nomenclature to determine if this is indeed correct. It would be advantageous to also include papers from highly ranking journals (Nature Genetics) which are not listed on the website for comparison. Peter will contact the Council in the future for suggestions of which papers should be included. The parameters and method for checking the papers is currently being developed.

5. HVP/DA/003/01/EN: Variant Terminology and Exon Numbering Draft Guideline for Approval – Timothy Smith

Timothy Smith reiterated that this document has been circulated to the Council at various stages of development previously, however it has now undergone community consultation and revision. Timothy Smith asked the Council if they felt that the guideline could now be put forward to the Scientific Advisory Committee and recommend that they publish it as a Human Variome Project guideline.

Arleen Auerbach indicated that the document may lack a strong recommendation, which was acknowledged by Timothy Smith who countered that this was deliberate as it is a recommendation rather than a requirement. Timothy noted that with regards to exon numbering, previous discussions established the standpoint that the Human Variome Project should allow for exons to be numbered, but shouldn't require them to be so.

Arleen suggested that the title may be misrepresentative of what is included in the guideline, with people expecting more discussion on variant terminology and nomenclature rather than a guideline for the use of the term variant (to describe sequence changes).

Peter Taschner suggested that adding a reference to the last sentence of the Scope section, linking to further information on how specific changes should be named and that the recommendations throughout the guideline be bolded for clarity. Mauno Vihinen agreed to make this change.

Mary Fujiwara noted that further clarification is required when describing the frequency of a polymorphism. While the report provides a frequency of 0.01%, this should be clarified to be 0.01% within a defined population due to differences in prevalence of certain polymorphisms between populations. Mauno Vihinen agreed with this point, however he noted that the current recommendation was not to use the term polymorphism. It was agreed that the term would remain, however Mauno would make a clarification about the population such that it is used correctly.

Overall, there was widespread support for the material within the guideline from Council members present in the meeting and as such it was agreed that the guideline be approved.

6. Solution Blueprint Edition 1 – Timothy Smith

Timothy Smith thanked Council members who have submitted comments and suggestions for the content of the Solutions Blueprint and informed the Council that it is nearing the point where it can be made public. Any further suggestions should be made before the 1st February 2016 (by email to Timothy or through the link on each page of the Solutions Blueprint). If no further comments are made prior to this date, it will be made public pending approval from the Country Node Council on 2nd February 2016.

7. Gene/Disease Specific Database Activities

Peter Taschner drew the Council's attention to the document circulated by Tamas Hegedus. Peter queried Tamas's intent to establish a new database, rather than contributing variant data to an existing database, however Tamas explained that both the Muscular Dystrophy Society and their bioinformaticians did not want to pursue this route.

Rosemary Ekong informed the council that her group recently received a 2 year grant to continue their work on Tuberous Sclerosis 2 databases.

Timothy Smith relayed the following report from Marc Ferre:

> We have set up the MITOchondrial DYNamics variation portal (http://mitodyn.org), dedicated to disorders of mitochondrial dynamics, including the GDAP1 gene [Cassereau et al., 2011] and the OPA1 gene [Ferre et al., 2015]. This DSDB will therefore incorporate other genes involved in neurological diseases affecting mitochondrial dynamics and bioenergetics.
>
> In 2016, we plan to expand this DSDB to optic neuropathy (in which we specialize in) with, among others, ACO2, DRP1, TMEM125A genes, and new genes that we will soon publish (and OPA1, which is also linked).
>
> Currently, our main sticking point is that Mitodyn.org based on LOVD 2.0 and we have to deal with non-overlapping transcript variants. So, we need LOVD 3.0, but no upgrade tool is available.
>
> I contacted Ivo Fokkema who offered his help to do the update « manually" because his team has good experience. I will answer positively, as it will be crucial assistance.

Peter Taschner suggested to other council members who may be in a similar situation that they too contact the LOVD development team for assistance. He further reported that collaborations would be taking place between Johan den Dunnen and Ivo Fokkema while they are both in Melbourne during February 2016. Following this it is likely that an Australian would carry out work in the Netherlands on LOVD to facilitate further developments.

8. Recommendations to the Scientific Advisory Committee

Peter Taschner recommended that the HVP/DA/003/01/EN: Variant Terminology and Exon Numbering Guideline should be put forward to the Scientific Advisory Committee, pending the changes detailed in Item 5.

9. Other matters

Arleen Auerbach requested further information relating to the special issue of Human Mutation which will be a tribute to Richard Cotton. Mauno Vihinen informed the Council that the issue is due out in May, prior to HVP6. The focus of the issue is on papers which are related to Dick's research interests - databases, standards etc. as well as containing submissions from the authors featured in the first issue of Human Mutation.

10. Next meetings

8 March - Virtual
10 May - Virtual
3 June – Face-to-face at HVP6
12 July - Virtual
13 September - Virtual
8 November - Virtual