



THE HUMAN VARIOME PROJECT

NEUROGENETICS CONSORTIUM WITHIN THE HUMAN VARIOME PROJECT

INITIATING MEETING: OCTOBER 19, HONOLULU (HAWAII)

SUMMARY OF THE MEETING AND MAIN CONCLUSIONS

This was a full-day meeting aimed at discussing the goals, challenges and action plans towards a coordinated effort in Neurogenetics within the Human Variome Project (HVP). The HVP is a multinational, multidisciplinary initiative to collect all the genetic variation affecting human health and disease in a way that is comprehensive, well organized, curated and publicly available for an efficient and safe use of this information by the research and healthcare communities. Researchers in a variety of Neurogenetic disorders, researchers and database curators were speakers at the meeting (<http://www.humanvariomeproject.org/fora/hawaii/>), which was attended by around 70 participants representing research groups, clinical groups, public institutions, private companies and biomedical journals. Some main points about neurogenetic mutation databases raised during the meeting were:

- The need for a global system to access genetic variation in a comprehensive and curated form is especially true for Neurogenetics because of the following: (i) Very large number of diseases/genes, (ii) High degree of genetic heterogeneity, (iii) Clinical variability and phenotypic overlap, (iv) Complex biological processes influence the genotype to phenotype relationship in neurological disorders, (v) Lack of standardized procedures to capture phenotype data and transfer them to databases, among other reasons.
- The current database situation in Neurogenetics is insufficient/inefficient because: (i) The structure and nomenclature is diverse in the existing databases, (ii) Many genes/disorders are not covered, (iii) Some genes/disorders are duplicated in independent databases, with overlapping or contradictory information, (iii) Insufficient multidisciplinary knowledge in the curating teams, among other reasons.
- There is a need for standards on: (i) Phenotype assessment, coding and transfer, (ii) Assessment of pathogenicity, (iii) Database collection of specific classes of mutations and disorders (mitochondrial, repeat expansions, association studies), (iv) Database structure, (v) Ethical and legal aspects, among others.
- There is a need of strategies: (i) To ensure collection of genetic data, (ii) To ensure collection of clinical data.

Among the specific problems identified in the way towards high quality neurogenetic databases were: working with the neurological phenotype (complexity, overlap and change with time), dealing with genetic data on complex diseases, capturing modifying genetic factors, quality control of direct submissions to databases, integration of information from different datasets, inadequate interpretation of mitochondrial variation, need to get the clinical community more involved, ethical challenges, funding and long-term sustainability.

There was general agreement that:

1. Most of these questions are not unique to Neurogenetic disorders; similar problems affect the construction of genetic databases for other areas of human health and the global HVP initiative. However, a number of facts and characteristics of the disorders of the nervous system, as well as the need of expert participation from the clinical and basic neurosciences provide the rationale to address these issues referred to the neurological disorders within a Neurogenetics Consortium which, in turn, will be guided by the general recommendations of the HVP. And vice-versa: the achievements and recommendations from the Neurogenetics Consortium will contribute to the global HVP initiative.

2. Although the field of neurogenetics is very extensive and there will be work for many groups (multidisciplinary, geneticists and clinicians) on many databases/disorders, common issues of neurogenetics databases should be worked out in a coordinated manner, allowing the necessary level of integration of the information in databases developed by different groups.

3. Coordination and different levels of integration is indispensable in order to address some of the above mentioned challenges and others, for proper delineating the priority objectives to be accomplished and organize the work efficiently. Some suggested directions:

- Develop a phenotype coding system
- "Quality stamp" for phenotype data
- Integrate already existing databases
- Agree upon consensus database structure/tools that are upgradable
- Work together with big research groups producing high-throughput data
- Syndrome-centered, multidisciplinary working groups (e.g. Parkinson's disease, motor neuron disease, dementias, etc) seem the best organization for constructing and maintaining the databases, following the model of the Insight project for colorectal cancer genetics.

Resolutions:

- A Steering committee was organized with eight initial participants.
- Six working committees were also proposed, on: (i) Phenotype nomenclature & Recording; (ii) Pathogenicity & Interpretation; (iii) Software, Informatics and Implementation; (iv) Mitochondrial Disorders; (v) Complex Neurological Disorders; (vi) Funding; (vii) Any syndrome-specific initiative (Parkinson's disease and motor neuron disease initiatives starting to be planned, others should follow).

Most of the attendees signed up to participate in one or several of the working committees. These committees are open to discussion on their structure and work. Anyone interested in the field is welcome to actively participate, be a member of any of the committees and share their thoughts.

A follow-up meeting will be held in Paris at the UNESCO Headquarters on May 10, in the context of the Third Human Variome Project Meeting 10-14 May 2010 (<http://www.humanvariomeproject.org/meetings/paris/>). This second Neurogenetics consortium meeting will present the achievements since the Honolulu meeting, and will be aimed at giving continuity to the proposed actions.

Since electronic discussions were being held in the days after the meeting, a Neurogenetics Forum Listserve was created at the University of Michigan server. Individuals wishing to join the Neurogenetic Forum listserv should send an email to neurogenetic-forum-request@umich.edu with the word SUBSCRIBE as the subject of the message. This should

facilitate having an “ongoing” discussion on the neurogenetic databases, problems, specific tasks and advancements. We invite all the neurogenetics community worldwide to join this effort, which we believe will be for a widespread benefit of the patients with neurological disorders.

21 December 2009

Neurogenetics Consortium Steering Committee: María-Jesús Sobrido, Lars Bertram, John Fink, Andrea Haworth, Sherifa Hamed, Marc Cruts, Birgitt Shuele, Matthew Farrer.

Richard GH Cotton, Convenor, Human Variome Project.