



THE HUMAN VARIOME PROJECT

Bulletin

From the Editor

This issue reports on one of the most significant events since the initiation of the Human Variome Project in 2006: the third HVP meeting at UNESCO headquarters in Paris from May 10-14th 2010. See the full report below.

This was preceded by an HVP platform session at the prestigious American

College of Medical Genetics meeting in Albuquerque, NM, USA (see inside)

Other significant events detailed inside were the first official signing of an organization to the HVP, continuing discussions with WHO and UNESCO regarding their collaboration with HVP and a major database initiative,

MUTA Database, proposed by Patrick Willems and colleagues.

Finally we are delighted to announce the birth of Maxwell Jean Martin to the Editor, Lauren Martin. Congratulations Lauren and David.

*Rania Horaitis
Acting Editor*

Meeting @ UNESCO Headquarters, Paris



Collaboration with WHO/UNESCO

The interest of WHO and UNESCO in the HVP is particularly welcome. This has been in the form of their support for the 2006 Melbourne and 2010 Paris meeting respectively. We are delighted that both organizations are pursuing further discussions regarding further, more permanent collaboration as many of the objectives of HVP parallel those of these two organizations.

Human Variome Project

Special points of interest:

> 3rd HVP Meeting: the Paris Report

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Human Variome Project meets at UNESCO Paris May 10 – 14, 2010

The Human Variome Project (www.humanvariomeproject.org) held its third meeting at the headquarters of the United Nations Educational, Scientific and Cultural Organization (UNESCO) headquarters in Paris, France from May 10 – 14. The opening statement by Mr. Walter Erdelen UNESCO Assistant Director-General for Natural Sciences



can be seen on the HVP Website at: <http://www.humanvariomeproject.org/index.php/news/speeches/103-welcoming-address-by-mr-walter-erdelen-unesco-assistant-director-general-for-natural-sciences-at-the-human-variome-project-implementation-a-integration-meeting>

It was attended by delegates from over 30 countries. Projects were reviewed and plans made for the future. The delegates called on UNESCO/WHO (World Health Organization) to become involved and discussions are continuing.

It was recognised that the aims of the Human Variome Project have strong synergies with the aims of the UNESCO Natural Sciences Sector. In this regard, delegates noted, in particular, the UNESCO strategy of promoting international multidisciplinary programs. These programs sought to reinforce intergovernmental and partner organisation cooperation to strengthen national capacities in the basic sciences and sciences education.

Parallels were also observed with the objectives of the WHO for expanding the role of genetics in medicine and health. Delegates agreed that, in the area of genetics and bioinformatics, the objectives of UNESCO and WHO can be addressed through the formation of international collaborative efforts such as the Human Variome Project to create sound and just frameworks from which to further the research and application of genomic technologies.

It was seen that joint endorsement and advocacy of the Human Variome Project by both UNESCO and WHO would advance the work of the Human Variome Project – collecting, curating, organising and sharing variation data – which in turn, will encourage global collaborations and improve health services worldwide through translation of scientific research to meet societal needs. Delegates at the meeting therefore charged the Human Variome Project Coordinating office with the task of moving forward a dialogue with UNESCO and WHO with the view to exploring possibilities for the Project to come under the joint auspices of the two Organisations.

Two important decisions were made at the meeting. First of all, the Human Variome Project Roadmap was accepted (www.humanvariomeproject.org) and a 12-member Interim Scientific Advisory Committee was elected. This is in preparation for incorporation of HVP International.

Around the meeting there were meetings with high level executives of UNESCO and WHO which continued the conversations regarding collaboration in the Human Variome Project and built on their support so far.

Satellite meetings on May 10 were held by the InSiGHT/inherited colon cancer/HVP consortium (<http://www.insight-group.org>), the Neurogenetics/HVP consortium and the Nutrigenomics Consortium (www.nugo.org). A course on bioinformatics was held by EBI/UK. Myles Axton (*Nature Genetics*) and Mark Paalman (*Human Mutation*), Chaired a Genetics Journal Editor's meeting hosted by Wiley Blackwell.

UNESCO are formally thanked for the use of their wonderful headquarters as were the “beyond the call of duty” efforts of Heather Howard, Rania Horaitis, Lauren Martin and Tim Smith, together with Julia Hasler and Casimiro Vizzini to run this highly successful meeting.

Maija Corish is thanked for volunteering to facilitate the meeting report.

Neurogenetics Satellite Meeting, Paris, May 10th 2010

The **Neurogenetics Consortium** held their second HVP Workshop for the implementation and improvement of mutation databases for genetic disorders of the nervous system. The specific challenges of this task were discussed, including clinical complexity and overlap, genetic heterogeneity, phenotype nomenclature, variant interpretation, informatics procedures and

ethical aspects. Specific case examples on inherited neuropathies, channelopathies, motor neuron diseases, Parkinson's disease and mitochondrial cytopathies were presented. This multidisciplinary meeting was attended by clinical neurologists, clinical geneticists, basic researchers, private companies and informaticians. The meeting resolved to form interna-

tional expert working groups with the aim to establish coordinated LSDBs on neurogenetic disorders such as spastic paraparesis, Charcot-Marie-Tooth and mitochondrial diseases. Researchers and healthcare professionals with an interest in the field are encouraged to join these efforts by contacting the author.

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InSiGHT Satellite Meeting, Paris, May 10th 2010

The International Society for Gastrointestinal Hereditary Tumours (InSiGHT) held a combined meeting with the HVP on May 10th at the UNESCO meeting. The meeting focussed on the operations of the InSiGHT/LOVD Mismatch Repair Gene database, incorporation of InSiGHT to protect the Society from medico-legal challenge as a result of publishing pathogenicity assignments on the InSiGHT/LOVD database; <http://www.insight-group.org/mutations/> (an issue of consider-

able concern in the field), the scale of curation and need for a full-time curator (now funded through the Hicks Foundation in Melbourne - our immeasurable thanks to the Foundation!), processes of the international Interpretation Committee, presentations of the Bayesian Likelihood Ratio approach to pathogenicity assignment of variants of uncertain significance, in vitro functional assays - for which there is intense interest within our

European colleagues, phenotype descriptors to allow quantitative expression of a family history, and cost benefit analyses of centralized data collections such as the Human Variome Project.

UNESCO provided a venue that truly recognizes the value of the work done by InSiGHT as it moves to share its experiences world-wide and with the HVP.

Finlay Macrae
Secretary, InSiGHT

NuGO Satellite Meeting, Paris, May 10th 2010

Nutrigenomics has been called a "post-genome" field of research. The ongoing discovery of new SNPs, insertions/deletions, and copy number variants shows that the genomic era is far from ending, particularly since the next generation sequencing technologies will soon allow for complete analyses of all coding sequences (i.e., the exome) of all individuals in a research study or even for complete sequencing of individual genes, including the regulatory regions. Genetic variation not only alters how individuals respond to drugs or the outcome of genetic diseases, but also alters how nutrients are absorbed, distributed, metabolized, and excreted.

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"UNESCO provided a venue that truly recognizes the value of the work done by InSiGHT as it moves to share its experiences world-wide together with the HVP"

EBI Satellite Meeting, Paris, May 10th 2010

The European Bioinformatics Institute held a small hands-on training Workshop as a Satellite of the Human Variome Project meeting. The Workshop was attended by 16 people. The purpose of the Workshop was to enable participants to use the Ensembl genome browser to solve their real-life problems.

Consortium of Funders for Human Variome Project Launched

The gathering which initiated the Human Variome Project in 2006 nominated the Genomic Disorders Research Centre to coordinate the activities of the Human Variome Project and this was again confirmed at the recent 3rd Meeting at UNESCO. This means that the coordination activities need to be funded. For secure funding private and philanthropic sector funding is needed to supplement any government funding.

A Consortium of Funders was launched at a function in support of the Human Variome Project at Government House, Victoria, Australia hosted by the Governor of Victoria Professor David de Kretser AC with the speakers Professor Sir Gustav Nossal AC, Professor Ingrid Winship, David Abraham and Professor Richard Cotton. Copies of their speeches are available on request.

Founding members of the Consortium have providing funding per year for three years and fall into the following categories:
Diamond members (over \$100,000)
Platinum members (over \$50,000) - Peter

& Lindy White Foundation
Gold members (over \$20,000) – Geoff. Handbury AO
Silver members (over \$10,000)
Copper members (up to \$5,000 -up) – Prof. Richard Cotton AM, J.S. Collingwood, H. Hansen, C.G. Clarke, E. Canty, L. Gourlay

Supporters (one-off Donation) :

Dame Elizabeth Murdoch AC, June Danks, A. Chernov AO, G. Ripper, Australian Cancer Network.

We aim to raise 1 Million dollars per year by this mechanism thus we need e.g. 100 x \$10,000 donations. (All in Australian \$)

We sincerely thank the above who will help make a difference to those unfortunate families with inherited disease world wide.

If you are interested in making a tax-deductible donation; please contact Prof. Richard Cotton for further information: *See page 8 for contact details.*

HVP Education Working Group Update

There was a broad interest in education from participants in the May 2008 HVP Planning and May 2010 HVP Implementation meetings. The Education Working Group conducted a survey of HVP participants. From the responses, we identified the following themes, which will be discussed at the HVP Educational Strategy Forum in Washington DC in November 2010:

of data.

2. SHARING –e.g., knowledge, curricula
3. EDUCATION – e.g., of patients, scientists, policy makers, other stakeholders, by developing teaching materials and workshops.

See: <http://www.humanvariomeproject.org/fora/washington2010/>

1. COLLABORATION – i.e. among different groups, in accessing education resources for standardization and unification

Making their Dollar Count

Human Variome Project Consortium of Funders established

Save the Date!

Human Variome Project Educational Strategy Forum

**1st November 2010
Washington DC**

ASHG Satellite meeting

The Signing of the Collaborative Agreement between King Abdul Aziz University, Jeddah, Saudi Arabia and the Human Variome Project

On Tuesday 25 May 2010, a delegation from the King Abdul Aziz University, Jeddah, Saudi Arabia (KAU) visited the University of Melbourne. This included the President of KAU, Professor Osama S Tayeb and the Saudi Arabian Minister for Higher Education, His Excellency Dr Khalid bin Mohammed Al Ankary. One of the activities was to sign an agreement between HVP and

the Princess Al-Jawhara Center of Excellence in Research of Hereditary Disorders, KAU. This was signed by the Deputy Director of the Florey Neuroscience Institute on behalf of HVP/GDRC and the University of Melbourne. The agreement calls for cooperation in all areas of mutual interest and research programs.



Egyptian Research Core Facility towards studying Genomic Alterations amongst Egyptians

At the Human Variome Project Neurogenetics Forum held in Honolulu Oct. 2009 Sherifa Hamed, Director of the Neurogenetic program at the Dept. of Neurology and Psychiatry, Assiut, Egypt announced her willingness along with other enthusiastic Egyptian colleagues to build a Research Core Facility directed towards studying genomic alteration as among Egyptians. Since then, some positive steps have been taken:

1. Jan. 2010 succeeded to obtain funding to start the project. Further periodic funds with further progress.
2. Established a local electronic database which has health information from various families having members with inherited neurological disorders.
3. Established a DNA bank, which has samples of various inherited neurological disorders for future mutation analysis.

A Pilot study was done by starting mutation collection from Egyptian families with muscular dystrophies. Two molecular studies are part of the Pilot initiatives:

- (a) Mutation analysis and carrier detection of families with Duchenne/Becker muscular dystrophy.
- (b) In collaboration with colleagues from the Harvard Center of Genomics that are sharing a program of "Linkage analysis of families with limb girdle muscular dystrophy".

We feel our efforts are important steps pertaining to technology acquisition and organizing groups of scientists and clinicians to make contributions to the Human Variome Project with other countries. We have already begun talks with important local government for funding to establish the Egyptian contribution to the Human Variome Project.

*Condensed report of
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BRIF: Bioresource Impact Factor Working Group

Dear Sir/Madam,

Our team 'Genomics and public health' from the Inserm (French National institute for health and medical research) and University of Toulouse, France, is taking part in the GEN2PHEN and BBMRI EU pro-

jects. (www.gen2phen.com; www.bbmri.eu). As part of these projects, we are committed to creating tools for the development of strong incentives for bioresource sample and data sharing, and for a better recognition, evaluation and optimization of use of these resources worldwide.

With this in mind, our team is setting up an international working group aiming to create a Bioresource Impact Factor/ Framework, or BRIF. The main objective of this BRIF is to assess and optimize the value and use of bioresources internationally. We believe your contribution is essential for the progress of this project.

Bioresources, or all organized collections of human biological material and associated information stored for one or more research purposes usually involve a number of different actors and institutions from the scientific and biomedical communities, in academic, associative or

industrial contexts.

While biobanking is on the increase worldwide, and generates wider scientific and economic activity, there is no standardized way to assess the use of these resources, as one of the ways to promote their sharing. Additionally, it is becoming essential to properly recognize the amount of work it represents for researchers to set up a bioresource, and give them higher credit for their effort to make them accessible. Creating strong incentives for optimal and transparent data access policies can be achieved by: 1. creating a link between the constructor's team; and the impact of the scientific discoveries enabled by the general use of the bioresource. 2. standardizing the bioresources citation process in publications.

To address this, a central concept that has been introduced by Anne Cambon-Thomsen in 2003, and further developed in 2004, is that of a bioresource Impact factor (BRIF). The idea is to construct a quantitative parameter to describe bioresources, modelled on the publication 'Impact Factor'. Such a BRIF would make it possible to document: 1. the quantitative use of a Bio-Resource, 2. the quality and the importance of

research results involving it, and 3. the scientific and management efforts of those who set up and made available a valid bioresource and their institution.

This system could be used much more rationally than informal 'reputation' in the evaluation of bioresources activities over time. Also, if such a factor was taken into account in assessing researchers/ contributors' professional results, it would increase the quality and sharing of bioresources.

We have identified several steps towards the creation of this BRIF:

1. Opening an online forum to discuss the concept and keep the working group going
2. Creating a bioresource unique identifier, or digital ID
3. Standardizing bioresource acknowledgement in papers
4. Clearly identifying bioresources data access and sharing policies
5. Identifying the factors to take into account when calculating the Impact Factor
6. Prototype testing

We therefore call for your participation in our online working space on the GEN2PHEN knowledge center website, where you can find more details on the BRIF, as well as spe-

“The main objective of this BRIF is to assess and optimize the value and use of bioresources internationally”

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cific discussions on each step described above:

<http://www.gen2phen.org/groups/brief-bio-resource-impact-factor>

If you are interested in being part of our working group, and in contributing further to the realisation of one or more steps of the project, do contact us directly by email, at your earliest convenience and preferably before September 8th 2010.

cambon@cict.fr, with cc to: gabrielle.bertier@gmail.com, mabile@cict.fr

Do not hesitate to circulate this information to people who could have an interest in this.

Sincerely,

Gabrielle Bertier
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Anne Cambon-Thomsen
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Papers of Interest

- | | |
|--|--|
| <p>David N. Cooper¹, Jian-Min Chen, Edward V. Ball, Katy Howells, Matthew Mort, Andrew D. Phillips, Nadia Chuzhanova, Michael Krawczak, Hildegard Kehrer-Sawatzki, Sten-son. Genes, mutations, and human inherited disease at the dawn of the age of personalized genomics. <i>Hum. Mutat.</i> Vol 31, Issue 6, pages 631–655, June</p> | <p>2010</p> <p>Cotton RGH and Macrae FA. Reducing the burden of inherited disease: the Human Variome Project. <i>MJA</i> 2010; 192 (11): 628-629</p> <p>Helt, G.A., et al., Genoviz Software Development Kit: Java tool kit for building genomics visualization applications. <i>BMC Bioinformatics</i>, 2009. 10: p. 266.</p> <p>Li, R., et al., Building the sequence map of the human pan-genome. <i>Nat Biotechnol</i>, 2010. 28(1): p. 57-63.</p> |
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The MutaDATABASE Initiative

Dr Patrick Willems and colleagues have proposed a major new mutation database initiative called MutaDATABASE. Beside the aim of placing a complete set of LSDB on a single uniform platform, its major features are: Capture of mutation data from US corporate diagnostic labs, which process enormous numbers of mutations, and a method to make the collection from some laboratories automatic and trivial through a system referred to as 'MutaREPORTER'. Collaboration and possible affiliation with the HVP community is now under discussion.

www.mutadatabase.org

NuGO Satellite Meeting (continued from page 3)

Unbalanced diets in genetically susceptible individuals also leads to chronic diseases.

Ideally, nutrigenomics experiments are to be designed, conducted and analyzed with specific knowledge of genes involved in nutrient metabolism and physiological processes.

The goals, plans, activities, and global character of the Human Variome Project provide additional genetic information for nutrigenomic researchers.

The principals of the HVP and nutrigenomics community, in particular the Nutrigenomics Organization (NuGO – <http://www.nugo.org>) realized the benefits of creating synergies between genetic and nutrigenomic researchers. As a consequence, members of the HVP and nutrigenomics community have attended conferences and workshops, including the 2nd HVP planning meeting (Costa Brava, Spain) and at the 3rd HVP meeting at UNESCO (Paris, France). NuGO organized a micronutrient genomics workshop at the UNESCO meeting. Future meetings include co-hosting workshops at the International Conference on Nutrigenomics (ICON) in Guarujá, Brazil (September 2010). The HVP and NuGO are exploring the best means to formally recognize their ongoing interactions. The HVP has a similar ongoing relationship with the International Society for Gastrointestinal Hereditary Tumors (<http://www.insight-group.org>).

Condensed Report of
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THE HUMAN VARIOME PROJECT

Vision

The Human Variome Project will establish systems to collect and make available information on all genetic variations associated with human disease.

Mission

The Human Variome Project is dedicated to improving health outcomes by facilitating the unification of data on human genetic variation and its impact on human health. It supports the use of human variation information in clinical & research environments across the world.

Values

- Free public access to information
- Inclusive of all countries, peoples and disciplines
- Provision of appropriate credit and acknowledgement
- Respect ethical, legal and social issues

Human Variome Project

Contact:

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Meetings of interest

4th International Biocuration Conference

11th—14th October

Tokyo, Japan

<http://hinj.jp/biocuration2010/>

Human Variome Project:

Educational Strategy Forum

1st November 2010

Washington DC

ASHG Satellite meeting

<http://www.humanvariomeproject.org/fora/washington2010/>

Human Genome Variation Society: "Exploring the functional consequences of genomic variation"

2nd November 2010

Washington DC

ASHG Satellite meeting

<http://www.hgvs.org/DC/>

Mutation Detection 2011: 11th International Symposium on Mutations in the Genome

6th - 10th June 2011

Santorini, Greece

www.mutationdetection.org

www.mutationdetection.org/santorini/