Response to Stenson *et al.* in *Human Genomics* Vol. 4, No. 2, pp. 69–72: 'The Human Gene Mutation Database: Providing a comprehensive central mutation database for molecular diagnostics and personalised genomics'

From Professor Richard G. H. Cotton

Date received (in revised form): 2nd December, 2009

The Human Variome Project (www.humanvariomeproject.org) (HVP) is a large and complex undertaking and one that is not easily understood at first glance. We therefore appreciate the comments of Stenson *et al.*[1] and duly acknowledge the features and benefits of the Human Genome Mutation Database (HGMD) that they have highlighted. Their comments, however, are indicative of several common misconceptions regarding the HVP, how it operates and what it plans to do.

The HVP was conceived and created in 2006 by the global genetic variation community to address the deficiencies of genetic variation databases, especially those in locus-specific databases (LSDBs), as noted by Stenson *et al.*

It should be noted that the HVP is not a closed group of individuals seeking to impose a mandate on the databasing community; rather, we consider anyone who is working towards achieving the overall vision of universal access to information on all genetic variation affecting human health to be contributing to the HVP. We encourage contributions from everyone in numerous ways, including:

- attendance at the HVP bi-annual meetings;
- attendance at HVP fora, held several times a year in conjunction with major genetics conferences; or
- by becoming a member of one or more HVP working groups, which focus on key action areas identified by members of the Project.

The HVP is working closely with all members of the genetic variation community, including established central databases, to facilitate the creation of systems that will ensure the transmission of genetic variation data from the source through to ultimate deposition in a central location.

(1) Country-specific nodes.

The HVP has identified the collection of data directly from the laboratories and clinics that generate that data to be a priority, rather than waiting for those same data to filter through the published scientific literature. Ethical requirements differ dramatically between countries, however, and prevailing cultural differences and technical idiosyncrasies mean that a centrally mandated, 'one-size-fits-all' approach is not feasible. Therefore, the HVP is facilitating the creation of collection nodes by genetics societies within individual countries. Data collected by these nodes would then flow to LSDBs.

(2) Disease/gene-specific LSDBs

It is the firm belief of the HVP that curation of genetic data by experts in specific genes is the best way to ensure the accuracy

and quality of those data. This is currently happening in a network of LSDBs, but we agree with Stenson *et al.* that it could be improved. The HVP is therefore developing systems and standards to help LSDB curators to improve their databases and curatorial practices.

(3) Central repositories

The deposition of all genetic variation data in central databases, such as the National Center for Biotechnology Information (NCBI), European Bioinformatics Institute (EBI), Online Mendelian Inheritance in Man (OMIM), Human Gene Mutation Data (HGMD) and the University of California, Santa Cruz (UCSC) Genome Browser, is the ultimate goal of the HVP. Ensuring that data first undergo a period of expert curation in an LSDB will improve the quality and accuracy of these important resources.

This integrated system of collection will give clinicians, researchers and therapists worldwide access to all examples of all variations in every country. We believe that the HVP can be 'dovetailed' into any existing facility wishing to collect, store or use the data. Already, LSDBs have been loaded on to NCBI and UCSC Genome Browser. It is the aim of the HVP to provide these data free of charge to any repository wishing to host them. Plans are currently being developed to address the issues surrounding the costs of curation.

In conclusion, we agree with Stenson *et al.* that there is no way that the HVP could, or indeed should, wish to administer the databases and activities of others. Rather, we hope that our policy of consultation, inclusion and facilitation will foster a community that is able to achieve the vision of the HVP. In this light, we hope that Stenson and his colleagues will be able to attend the third HVP meeting in Paris on 10–14th May 2010, to assist the community in developing further.

Professor Richard G.H. Cotton
Genomic Disorders Research Centre
Convenor, Human Variome Project
Founding Co-Editor, Human Mutation
Past President, Human Genome Variation Society
Level 2, 161 Barry Street, Carlton South
Vic 3053, Australia
Tel: +61 3 8344 1893; Fax: +61 3 9347 6842;
E-mail: cotton@unimelb.edu.au

Reference

1. Stenson, P.D., Ball, E.V., Howells, K., Phillips, A.D. *et al.* (2009), 'The Human Gene Mutation Database: Providing a comprehensive central mutation database for molecular diagnostics and personalized genomics', (Guest Editorial), *Hum. Genomics* Vol. 4(2), pp. 69–72.