

# Mutation (variation) databases and registries: a rationale for coordination of efforts

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The importance of gene- or locus-specific databases (LSDBs) has recently been extolled in this journal (The case for locus-specific databases. *Nature Reviews Genetics* **12**, 378–379 (2011))<sup>1</sup>. Here we argue that coordination of international efforts for developing comprehensive mutation databases and patient phenotype registries is essential for optimal genetic health care.

Well-funded international efforts for setting up mutation databases or registries are crucial for several reasons. Many variants that are found during clinical testing worldwide are not submitted to databases, where they could form an important resource for patient care. Many laboratories and clinicians do not have the capacity or incentive to submit data to databases. This is especially the case in developing countries owing mainly to technical insufficiency, lack of public awareness, lack of international communications, the absence of the concept of DNA biobanking, national authority restrictions and lack of translation from original languages to English.

The [Human Variome Project](#) (HVP) was initiated to facilitate the collection of all variants in all genes from all countries and to include annotation of these variants for pathogenicity and relevance to clinical medicine<sup>2</sup>. It was established at a meeting in 2006 that was attended by representatives of the World Health Organization (WHO), the United Nations Educational, Scientific and Cultural Organization (UNESCO), the Organisation for Economic Co-operation and Development (OECD), the European Commission, March of Dimes, the US National Center for Biotechnology Information, the European Bioinformatics Institute (EBI) and 30 countries<sup>3</sup>. The third HVP meeting at UNESCO Headquarters in 2010 allowed the election of an International Scientific Advisory Committee and affirmation of a Roadmap<sup>4</sup>. Most recently, China has committed \$300 million to the project<sup>5</sup>,

and UNESCO has awarded the HVP the status of 'NGO in operational relations with UNESCO'. Many working groups are establishing standards for collecting, presenting and sharing variation information.

Registries for inherited diseases have been developed in some countries, especially where therapies are available (for example, see REF. 6). Recently, there has been a call for global registries of rare diseases (more than 80% of which are genetic)<sup>7,8</sup>. Most recently, the US National Institutes of Health and the European Commission have developed the International Rare Diseases Research Consortium (IRDiRC)<sup>9</sup>.

These two initiatives, the HVP and IRDiRC, have been developing essentially independently and in parallel. The HVP was driven by clinicians and laboratories wishing to have access to complete disease-associated variation information to support diagnostic advice and to facilitate the publication of novel mutations of interest. Recently, the focus has moved to collecting all mutations in all genes from all countries<sup>10</sup> as a means of assisting the interpretation of functional effects of genetic variations. The IRDiRC has been driven by patient groups who are anxious to achieve therapy for their families' diseases and to recruit cohorts for clinical trials in registries.

Practically, the promised funds from China in support of the HVP will allow 5,000 databases to be properly set up. If the decision is to set up these databases as both mutation and patient registries, this will assist both initiatives and avoid duplication.

Each group has their own networks, methodology, experts, data content and specifications. It would seem wasteful if two parallel systems were developed when many data are in common and when global reach is needed by both. In the case of the HVP, key components that are in place are a federated model, forums for sharing experiences, development of best informatics practices that are relevant to the task, and leadership.

Clearly in the case of the IRDiRC, the key components are model registries, Orphanet experience and Genetic Alliance experience.

Future generations will pay the price for a failure to establish a joint international approach to the recording of and provision of access to human molecular variation, as such access is the most important step in approaching the diagnosis, and thus prevention, of inherited disorders.

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## Competing interests statement

The authors declare no competing financial interests.

## FURTHER INFORMATION

The Human Genome Variation Society: [www.hgvs.org](http://www.hgvs.org)  
The Human Variome Project: [www.humanvariomeproject.org](http://www.humanvariomeproject.org)

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