nature genetics

Marshaling the Variome

From the Human Genome Organization (HUGO) onward, there has been a desire to get together to talk about using our shared genomic heritage to improve human health and development. We now have all the organizations we need and should collaborate on multiple practical demonstrations of the usefulness of genomic knowledge—be it human, animal or plant—for human health.

One of the greatest frustrations in the wake of the decoding of multiple human genomes has been turning research on the mutational burden of disease into actionable information to improve health. All too often, we hear that this objective is outside the remit of health research agencies, that "it is not research, we cannot fund it."

For human genomics, many of the obstacles have now been overcome by groups of dedicated individuals who have worked on standardizing the reporting of human mutations with correct genomic reference sequences and coordinates, providing journals in which to report mutation detection and mutations and phenotypes found, and simplifying the numerous databasing options. Many of these are signal achievements of the Human Genome Variation Society (HGVS; http://www.hgvs.org/) founded by the late Dick Cotton (page 850) and his colleagues. Larger societal problems, including international variability in standards for ethical approval, differing local frequencies of disease-causing gene variants, and differences in national research infrastructure and provision for clinical genetics, have been tackled by Cotton's last and biggest project, the Human Variome Project (HVP; http://www.humanvariomeproject.org/). Now, with recognition by and collaboration with the World Health Organization and UNESCO, HVP is in an excellent position to coordinate ever more pragmatic implementations of genomic knowledge for clinical use, research and genetics education.

The principles these organizations established in the last decade have been to provide a broad welcome to keep everyone on board, to recognize that different contributory organizations, groups and agencies fit into specific roles (*Nat. Genet.* **44**, 233, 2012), to reduce duplication of effort by agreeing on standards and workflows, and to provide focused, deliverable projects to demonstrate usefulness. Now that we have excellent international channels for these post-research activities (including but not limited to HGVS, HVP and the Global Alliance for Genomics and Health (http://genomicsandhealth.org/), we look forward to community projects such as the BRCA Challenge (http://genomicsandhealth.org/work-products-demonstration-projects/brca-challenge-0). This project is using genome databases and software as well as genetic epidemiology approaches to extend the evaluation of pathogenicity of heritable constitutive variants beyond what can be achieved by collaborative expert assessment alone, as was used here in the evaluation of mismatch-repair genes in colorectal cancer (*Nat. Genet.* **46**, 93, 2014).

Another important development is the Global Globin 2020 Challenge (GG2020), an initiative of HVP that will tackle a very common set of causes of disease and disability in developing and diaspora populations. From evidence in this journal, reevaluation of the pathogenicity and protective effects of hemoglobin variants can make both good research articles and clinically useful decision tools (*Nat. Genet.* **43**, 295–301, 2011 and *Nat. Genet.* **46**, 1197–1204, 2014).

It is most important to look forward to the future uses of genomic knowledge rather than to obsess about where our data collection started, since in growing disciplines almost all of the data are ahead of us rather than in legacy collections. From the perspective of this journal, human genome exceptionalism is an obstacle to implementing genomic knowledge in health and in learning the broader lessons of the place of genetics in human society. On the whole, variants are no longer collected piecemeal from clinical laboratories but are harvested from the whole genomes of people in populations. The genome variants of crop plants and livestock directly influence human health more readily than the mutated genes found in rare families and the common variants found by human genomic epidemiology. Now that we have inclusive international organizations dedicated to turning genomics into educational and health tools, we can readily partner them—demonstration project by demonstration project—with crop and livestock breeders who also speak the common languages of genomics and societal development. These projects may generate tools and educational packages for their target groups and partners, and they will surely create the next generation of interdisciplinary scholarship for our journals. They will certainly have at least as much societal impact as the human genome, adding to its already considerable legacy. ■