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wellcome trust

Characterizing and Displaying Genetic Variants for Clinical Action Workshop
December 1-2, 2011
Workshop Recommendations

1. The National Human Genome Research Institute and the Wellcome Trust should serve as a "convener" in conjunction with other NIH Institutes and Centers, professional organizations, and other groups to build consensus, prioritize and publicize recommendations regarding clinical validity and utility/actionability.

2. Create and support a coordinated resource to extend Ensembl, ClinVar, and other databases for use in clinical care by providing relevant phenotype information, other clinical annotation, and recommendations regarding clinical utility/actionability. Bridge the gap between researchers and primary care clinicians, who will need user-friendly clinical support tools and/or an EHR integration layer to readily utilize these data in clinical care.

3. Promote, enhance, and facilitate the clinical annotation of both germline and somatic variants and genes in relation to specific traits (including specificity, sensitivity, prevalence, positive and negative predictive values, and penetrance). Capture of penetrance data from exome chip studies may be a unique opportunity to capture information on the "most common of the rare" variants.

4. Ensure that 1) ClinVar and similar resources capture genetic variants of unknown significance (VUS) and isolated reports of variant – condition associations identified through clinical sequencing projects, and 2) scripts/computer programs are developed to enable clinical sequencing labs to efficiently transmit data to such resources.

5. Hold a workshop or convene a working group to identify reasonable technical standards for exchange of genetic variant and clinical data to maximize ongoing interactions among existing databases.

6. Support and expand research to determine clinical validity and utility/actionability of sequence and structural genetic variants.

7. Design studies to ensure that variants labeled as "clinically valid, but not directly actionable" are appropriately stratified and have identified pathways for becoming actionable.

8. Support functional and other follow-up studies on novel variants found in specific genes with known utility (e.g. determine consequence of every BRCA1 missense mutation) to generate data to support better interpretation of variants of uncertain significance.

9. Ensure that discovery of gene-disease and gene-drug associations is funded to occur in diverse populations representative of US and UK populations.

10. Explore mechanisms to facilitate communication between labs studying specific genes with potentially clinically relevant variants and researchers and clinicians with family, phenotype and other clinical information willing to partner to understanding functionality of the genes and variants.

11. Coordinate with US and UK agencies, such as Agency for Healthcare Research and Quality (AHRQ), the Office of the National Coordinator for Health Information Technology (ONC), Department of Veterans Affairs (DVA), National Health Service (NHS), commercial electronic health record (EHR) vendors, and other relevant organizations to address data interoperability and viable approaches for integration of genomic information and actionable variants into a variety of EHR systems.

12. Encourage the dissemination of decision support logic and interpretive tools, including making a publicly available library, to enable diverse EHR systems to use the same logic and tools when developing clinical decision support tools.

13. Consider supporting competitions that promote development of algorithms for interpreting genomic variants and compare algorithm performance, such as the Critical Assessment of Genome Interpretation (CAGI) experiment.

14. Collaborate with data warehouses (e.g. Medco) on large scale studies to better evaluate outcomes of specific applications use of genomic variants in clinical care. Specifically develop a process to identify research questions that could be answered using data warehouses.

15. Develop approaches for long-term follow-up of patients with rare variants to better understand relationship of variants with disease and other phenotypes, leveraging existing resources with healthcare systems (e.g. Payer information, NHS records).

16. Maximize interactions among epidemiologists, bioinformaticians, and genomic scientists to facilitate obtaining needed information on clinical validity and utility. For example, develop training programs that bring these three disciplines together to tackle specific aspects of the pipeline needed to identify actionable variants and move them into the clinic.

17. Develop and test innovative genetic education tools for providers specifically focused around the appropriate use of genomic variants.

18. Catalyze discussion with the Office for Human Research Protections (OHRP) / National Research Ethics Service (NRES) regarding institutional review board guidance on boundaries and synergy between clinical care and research. One specific area for concern is the proposed changes to the common rule that would determine that any genetic results or tissues would be considered identifiable.

19. Conduct policy analyses to better understand the perspectives of relevant organizations (e.g., FDA, CMS, NICE, UKGTN) regarding using genetic variant information to inform clinical care.