Highlights of This Issue

Sorting the wheat from the chaff in clinical genomic analyses

In the current issue, Poot and Hochstenbach (page 478) address a matter of increasing importance and urgency in the genomics community. As we proceed with whole genomic analysis, either in the guise of microarray assays or ultimately whole genome sequencing, one of our more profound challenges will be to sort out clinically meaningful variants from insignificant genomic changes. In this study the authors review the characteristics of copy number changes (CNCs) from microarray CGH analyses which contribute to their interpretation as either clinically relevant or incidental. With an eye toward to operationalizing such analyses for clinical use, the authors helpfully discuss several published workflow schemes designed to identify CNCs that may contribute to abnormal phenotypes. Finally, they propose a three-step procedure which aims to rapidly evaluate CNCs on a case–by-case basis regarding their possible contribution to the phenotype of patients with malformations and mental retardation. Studies such as this will be critical as we begin to try and harness the daunting complexity of whole genome analysis in the service of patient care.

Protecting privacy while maximizing social good

Large amounts of data are generated in research involving genomic analysis and these data have the potential to uniquely identify an individual subject. Thus sharing study data among researchers creates a fundamental tension between two important goals: promoting scientific progress on one hand, and protecting the privacy of subjects on the other. Trinidad et al explore this tension in a manuscript in this month's issue of *GIM* (page 486). The authors sought to explore the perceptions, beliefs and attitudes of research participants regarding GWAS and repository-based research. Participants in the study expressed a wide-range of opinions about the acceptability and desirability of broad data sharing in genotypic and phenotypic information. There was a general consensus that making de-identified study data available to the research community was a social good and should be pursued. While there existed privacy and confidentiality concerns these would not necessarily preclude participation but there were significant reservations regarding sharing data with for-profit organizations.

As we move forward with genomic research it will be critical that we find ways to balance these two competing goals. We should not forget that subjects in research studies not only have an interest in maintaining privacy, but by their very participation in research have expressed an interest in promoting social good and seeing that the fruits of their participation in research are maximized.

News Briefs

Shedding light on the genetics of aging…or not?

Genome wide association studies (GWAS) have begun to shed light on the fundamental genetic underpinnings of virtually every disease imaginable. Now in a controversial study recently published in *Science* (Online July 1, 2010), GWAS has been focused on the ultimate "disease" of humanity: aging. Sebastiani et al identified approx 150 SNPs which appear predictive of living to exceptional ages. Interestingly, it appears that the implicated SNPs are related to protective variants which delay disease as opposed to simply the lack of risk factors for common diseases associated with aging. There is a fly in the ointment, however. It appears that two different types of microarray chips were used to test the experimental and control group, a potentially significant problem in the study design. If this research holds up it begs far more provocative questions than the simple molecular basis of longevity. Rather, a true understanding of longevity and the means to extend life significantly would have profound social repercussions. On the other hand, if the research ultimately proves to be irreproducible, it will further emphasize important standards which genomic research must adhere to.

Highlights of the *AJHG*

More on sorting the wheat from the chaff

This month's featured article in *AJHG*, like the work by Poot and Hochstenbach in this month's *GIM* (page 478), tackles the tricky issue of assigning potential causality to copy number variants discovered in the evaluation of patients with cognitive disability.

Whibley et al. investigated copy number variants and indels in 251 families with evidence of X-linked intellectual disability (XLID) by array comparative genomic hybridization on a high-density oligonucleotide X chromosome array platform. 10% of families had pathogenic copy number variants with mutations ranging from 2kb-11Mb in size. Critical to the assignment of causality was prior knowledge of XLID-associated genes and the ability to test for co-segregation. Their analyses led to four novel genes that were implicated in cognitive dysfunction. Interestingly (and perhaps frustratingly for those who will be wading through such analyses for years to come) the authors also identified the presence of deletions and duplications in X chromosome genes without apparent disease consequences. Finally, this study informs discussions of alternative mutational mechanisms, such as the potential importance of non-coding variants that might explain the shortfall of mutation yield in the well-characterized International Genetics of Learning Disability (IGOLD) cohort, where currently disease remains unexplained in two thirds of families.