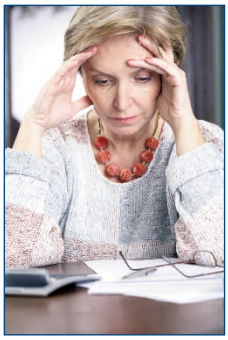
Highlights of This Issue

Differing views of consent

Anyone who has participated in a biomedical research study, either as a participant or as an investigator, knows how formidable the consent process can be. Consent documents in general have grown in both length and complexity. An intriguing study in this month's issue by Laura Beskow et al (page 567) addresses divergent views of biorepository consent forms by differing stake holders. Among 52 research participants, 12 researchers and 20 IRB representatives the authors found strikingly different interpretations of the importance of various components of the consent. IRB representatives identified 72% of sentences as important; researchers 53%, and participants 40%.

This study nicely demonstrates the differing mandates of these three groups and how they might translate into widely divergent opinions about what information belongs in a consent form. Such differences could well frustrate efforts to move to more simplified forms. The interests of all parties will have to be reconciled as we move forward with even more complex genomic studies in the future.



What conditions are right for NBS?

In this month's issue Kemper et al (page 539) tackle the thorny issue of whether infantile Krabbe disease is a suitable candidate for newborn screening. In some ways this condition serves as an interesting test case since while it is severe, rare and can be diagnosed by newborn screening, available interventions are clearly inadequate. It is thus not clear whether the benefits of screening outweigh the costs in individual, societal and economic terms.

The authors examine the experience in New York State where newborn screening for Krabbe disease has been ongoing, and review the literature over the past decade. The disease is indeed rare with 550,000 newborns screened in New York, 25 testing positive and 4 considered to be high risk for early-onset Krabbe disease. Two newborns underwent stem cell transplantation of whom one died from complications.

While early treatment with stem cell transplant appears to alter early childhood mortality and to some extent mitigates morbidity associated with this disease, we still have considerable gaps in our understanding of the disease and whether a net benefit to families and society accrues from NBS.

News Briefs

Undercover Investigation of DTC Genomic Offerings

Direct to consumer genetic testing continues to be in the news. Most recently it was the subject of a Government Accountability Office (GAO) undercover investigation designed to ascertain the reliability and consistency of such offerings DTC by prominent companies.

In their investigation the GAO sent the same DNA sample to several DTC companies. What they found was a stark reminder and elegant demonstration that such offerings are far from being ready for widespread implementation.

Most notably the GAO found striking differences between risk estimates on the same samples when analyzed by different companies. For example, one sample of a male 48 years of age revealed that his risk of prostate cancer was either average, below average, or above-average depending on which company performed the analysis.

Congressional hearings on July 22, 2010 were held to highlight the GAO investigation. The different estimates of risk provided by these companies were met with a certain degree of incredulity by the members of Congress. The hearings also featured testimony by the companies themselves as well as one independent expert (*GIM's* editor-in-chief).

The GAO investigation is a poignant reminder that DTC genetic testing is far from being ready for clinical implementation and that claims of its medical utility are premature. We must all work to ensure that the claims made for such tasks actually comport with reality. People certainly deserve access to the information in their own genomes. However, they also deserve a full and honest accounting of what that information means.

Highlights of the *AJHG*
Chipping away at the genetics of RP

A paper by Li et al. in this month's *AJHG* chips away at the etiology of a condition famous for its genetic and phenotypic heterogeneity—Retinitis Pigmentosa (RP). This group of conditions is characterized by night blindness, progressive constriction of the visual fields and loss of vision. To date, more than 45 genes causing RP have been identified and numerous modes of inheritance have been documented, making molecular diagnosis particularly challenging.

In this paper the authors describe a consanguineous Pakistani family with autosomal recessive RP, whose condition had been previously linked to the short arm of chromosome 2 at p22.3-p24.1. They now report identification of the causative gene, demonstrating homozygous missense mutations (c.1015T>C, p.C339R) in *ZNF513*, a gene which encodes a presumptive transcription factor. *ZNF513* is expressed in the retina, especially in the outer nuclear layer, inner nuclear layer, and photoreceptors. The gene's expression and phenotypic effects have been studied in zebra fish, nicely complementing the human work. ChIP analysis indicates that wild type (but not mutant) gene product binds to the *Pax6, Sp4, Arr3, Irbp,* and photoreceptor opsin promoters. Taken together, this work implicates mutations in *ZNF513* as yet another cause of human RP and demonstrates that it is a key regulator of photoreceptor-specific genes in retinal development and photoreceptor maintenance.