Highlights of This Issue

Earthquakes! Hurricanes! Genetics!

The odd (to use one acceptable euphemism) summer of 2011, with an earthquake on the east coast and a hurricane in Vermont, reminds us of the capriciousness of nature. This month in *GIM*, Andersson et al. (page 903) remind us of the potential for interruptions in routine genetic care which could result from the next emergency that visits the US. This group developed a coherent plan to ensure continuity of operations for genetic centers and laboratories, including newborn screening. We are reminded that no geographic region is protected from the effects of a variety of potential emergencies. Guidelines for ensuring continuity of operations by creating an emergency preparedness plan must be developed for each genetic center and lab, with attention to the interests of patients. This paper describes the first steps in development of a plan for individual centers to help you with the next emergency which is surely coming your way. Have a nice day.

Broadening the phenotypic spectrum of schizophrenia-associated CNVs!

This month Sahoo et al. (page 868) expand the phenotypic spectrum of CNVs associated with schizophrenia and examine the relationship of such variants to physical and intellectual disability. The investigators analyzed 38,779 individuals referred for microarray testing for the presence of CNVs encompassing 20 putative schizophrenia susceptibility loci. They identified 1,113 individuals with CNVs encompassing schizophrenia susceptibility loci and 37 individuals with CNVs overlapping those present in six individuals referred for schizophrenia. Of these, 1,035 had a CNV of one of six recurrent loci. Indications for study of these 1,150 individuals were diverse, including intellectual disability, autism spectrum and multiple congenital anomalies. This represents the largest genotype-first analysis of schizophrenia susceptibility loci to date and suggests that the phenotypic effects of CNVs associated with schizophrenia are pleiotropic, implying shared biologic pathways among multiple neurodevelopmental conditions.

News Briefs

Genetics and Justice

The power of genetics is not confined to the realm of medicine or basic research. Indeed, one of its most remarkable applications over the past decades has been as a forensic tool (and has spawned a considerable number of television shows, a distinctly less meaningful contribution). The power of DNA forensics cannot merely implicate the guilty but also exonerate the innocent. In a recent review (*Annual Review of Genomics* and *Human Genetics,* 12:97-120), the nature of DNA evidence used to exonerate and free victims of wrongful conviction was investigated. Short tandem repeat analysis prevails as the most useful technique (70%), though Y-STR analysis (16%) and mitochondrial testing (10%) are still used when STR analysis is not feasible. The types of exculpatory evidence analyzed included intimate swabs (65%), clothing (53%), hair (13%), fingernail evidence (5%), cigarettes (3%), and other evidence.

The most common factor associated with wrongful convictions was misidentification (75%), including misidentification by the victim (65%). False confessions (including admissions and pleas) were obtained in 30% of the cases, and informant testimony (including jailhouse and government informants) was used in 22% of the false convictions. The danger of not using rigorously evaluated modalities is high in forensics just as it is in medicine: several types of invalid forensic science testimony were found to have been used to wrongfully convict individuals, including serology (38%), hair comparison (22%), fingerprint comparison (2%), and bite mark comparison (3%). In 43% of the exonerations, the true perpetrator of the crime was identified through postconviction testing.

Highlights of the *AJHG*

This month in the *American Journal of Human Genetics*, a research group from Israel led by Ephrat Levy-Lahad, report on the elucidation of the genetic basis of XX female gonadal dysgenesis (XX-GD). XX-GD is a rare, genetically heterogeneous disorder characterized by lack of spontaneous pubertal development, primary amenorrhea, uterine hypoplasia, and hypergonadotropic hypogonadism as a result of streak gonads. Most cases are unexplained, but have been thought to be autosomal recessive. The team investigated a highly consanguineous Palestinian family using homozygosity mapping, and candidate gene and whole exome sequencing. They found that affected females were homozygous for a 3bp deletion in the *PSMC3IP* gene, leading to deletion of a glutamic acid residue in the highly conserved C-terminal acidic domain.

PSMC3IP (Proteasome 26S subunit, ATPase 3, Interacting Protein)/TBPIP (Tat Binding Protein Interacting Protein) is a nuclear, tissue-specific protein with multiple functions. It is critical for meiotic recombination and through its C-terminus co-activates ligand-driven transcription mediated by estrogen, androgen, glucocorticoid, progesterone and thyroid nuclear receptors.

Investigations in cell lines suggest that the mutation results in impaired estrogenic signaling which then leads to ovarian dysgenesis, perhaps by affecting the size of the follicular pool and by failing to counteract follicular atresia during puberty.

By analogy to other XX-GD genes, *PSMC3IP* is also a candidate gene for premature ovarian failure.