Highlights of This Issue

Happy Birthday, ACMG!

Welcome to this special issue of *Genetics in Medicine*, which celebrates the founding of the ACMG 20 years ago this month. To commemorate this anniversary we feature a look back (notes on the founding of the college by David Rimoin; page 179), a glimpse of our exciting present (several articles which employ next generation sequencing in patient care) and a variety of commentaries in which contrasting futures for medical genetics are envisioned. Highlighting the accelerating scale of genomic activity, we also feature a tour-de-force of worldwide collaboration by Piero Rinaldo and colleagues. In this study, the authors describe a collaboration involving 130 sites in 45 countries that examined appropriate target ranges for newborn screening results by comparing over 25 million normal newborn results with over 10,000 positive cases. Stay tuned to *GIM* over the next 20 years as we see how the increasingly fast paced world of genomics is applied to the care of our patients.

Richard King Award Winner 2010

Each year we are fortunate, through a gift from the ACMG foundation, to be able to recognize the best annual contribution to *Genetics in Medicine* by a genetics trainee. This award helps reward tomorrow's leaders for their efforts and helps attract talent to our field. This year we are delighted to bestow the King award (named for *GIM*'s first Editor-in-Chief) upon Rebekah Zimmerman for an article published in May entitled "A novel custom resequencing array for dilated cardiomyopathy". In this article, Dr. Zimmerman describes the use of a custom array for the rapid analysis of 19 genes known to be implicated in the etiology of dilated cardiomyopathy. She and her coauthors demonstrated an analytical sensitivity for known and novel substitution variants of 100% and 98%, respectively. Compared to traditional Sanger based sequencing, test cost and turnaround time were reduced by approximately 50% and the test yielded a projected clinical sensitivity of 26-29%. This development demonstrates another way in which screening multiple genes will be the norm for the diagnosis of genetically heterogeneous disorders.

News Briefs

DTC and Changing Behavior

A recent report in the *New England Journal of Medicine* regarding DTC genetic testing has attracted considerable press coverage. Bloss et al. (published online January 12, 2011) measured the impact of direct to consumer genetic testing on approximately 2000 individuals. While important, the results are far from surprising. Anyone who has spent time trying to get people to eat right and exercise will not be stunned to learn that merely providing an estimate of one's genetic risk for disorders like diabetes and heart disease is ineffective in promoting meaningful changes in behavior. The authors also studied whether the provision of these results caused significant anxiety. Again, it is hardly surprising that patients were not overly distressed by receipt of their results. What was less publicized about this study is the fundamental irrelevance of such results to practical matters of health and the inconsistency of interpretations by the various purveyors of such testing. Indeed, perhaps the best reason that individuals who undergo such testing should not be anxious about the results is that they are essentially meaningless. Finally, it is of interest that participants received their analyses at a discounted rate. This is in keeping with most available information which suggests that the public has not robustly embraced DTC genetic testing. Perhaps people are smarter than we sometimes think they are.

Highlights of the *AJHG*

When Rare Becomes Common

The power of next generation sequencing as a diagnostic and gene-discovery tool continues to be demonstrated in a broad range of diseases. In a report by Norton et al. in the *AJHG* this month, this technology was turned to a major public health problem, dilated cardiomyopathy (DCM). This condition is the most frequent precipitating cause of heart transplantation. DCM is a profoundly genetically heterogeneous condition with over 30 genes implicated in its genesis. Most of those genes remain unidentified but that situation will likely change quickly as the approach described in this paper picks up steam.

The authors analyzed a multigenerational family with autosomal dominant DCM by whole exome sequencing (WES) in the proband and three family members as well as copy number analysis in several members of the same family. Sorting through the 428 single point variants (representing missense, nonsense or splice site changes) and approximately 500 copy number variants was facilitated greatly by the family analysis. The investigators identified a 8,733bp deletion, encompassing exon 4 of the heat shock protein co-chaperone *BAG3*, in seven affected family members and in none of 355 controls. When *BAG3* was analyzed in 311 unrelated DCM probands, 4 harbored clearly deleterious mutations in this gene.

Thanks to the power of next generation sequencing, it is now becoming tractable to identify rare variants which result in high risk of disease for conditions that have significant public health impact.