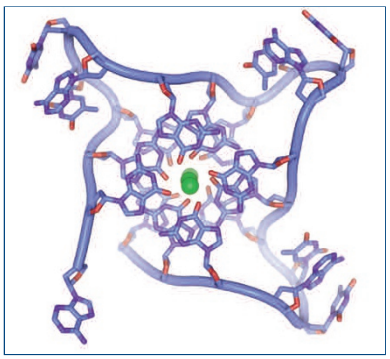
Highlights of This Issue

Surgical History in MPSII

As readers of *GIM* are well aware, MPS type II is a progressive multi-system disease which results in a spectrum of severity from severe to attenuated. The diagnosis of MPSII may be considerably delayed, presumably because of the rarity of this disorder and the range of its phenotypic attributes. In a study in this month's issue, Mendelsohn et al (page 816) used the Hunter Outcome Survey multinational database to document that a majority of MPSII patients underwent at least one surgical intervention before their diagnosis. Types of surgery that were associated with a diagnosis of MPSII included tympanostomies, repairs of inguinal hernias and operations for carpal tunnel syndrome. These data reveal that patients with MPSII typically undergo surgical interventions at a young age, often prior to diagnosis. Thus, in children who require surgery for hernias or carpal tunnel syndrome (especially) practitioners should be alert to the possibility of MPSII and refer those patients for genetic evaluation and testing.



Telomeres from Beginning to End

We are pleased this month to feature an invited review exploring the genetics and clinical manifestations of telomere biology disorders. Our understanding of telomeres has been one of the signal accomplishments of the last decade. We are now beginning to understand them in the context of clinical medicine as discussed in this review by Sharon Savage (page 756). The most characteristic disorder directly related to a disruption of telomere biology is that of dyskeratosis congenita. Affected individuals demonstrate nail dystrophy, abnormal skin pigmentation and oral lukoplakia. More significantly, they are also at a high risk of bone marrow failure, cancer and pulmonary fibrosis. In at least 50-60% of such individuals a mutation in one of 6 different genes, each involved in some aspect of telomere biology, can be identified. Given that progressively shorter telomeres are inherited from generation to generation in this condition, disease is observed.

News Briefs

Genetics, Environment and Politics

Considerable data has accrued that specific personality attributes have a genetic component. Recently, a group of investigators from prominent institutions waded into the potentially explosive realm of genetics and politics. In *The Journal of Politics* (2010;72:1189-1198) the authors postulated that individuals with a gene variant implicated in novelty seeking, who were also exposed to a wide variety of social norms, might be disproportionately politically liberal. They investigated 2000 subjects from the National Longitudinal Study of Adolescent Health and found, congruent with their hypothesis, that individuals with the *DRD4* variant of the dopamine receptor were more likely to be liberal than conservative, but only if they had an active social life in adolescence.

That personality attributes, and thus political positions, might be in part genetic is a rather uncontroversial claim (at least to this geneticist). Although this study must be subjected to verification, it may contribute to our understanding of social behavior.

Highlights of the *AJHG*

This month's *AJHG* features an article which is significant for how it demonstrates our increasing ability to parse complex phenotypes by molecular analysis. Williams-Beuren syndrome (WBS) is a variable condition characterized by supravalvular aortic stenosis, multiple peripheral pulmonary arterial stenoses, elfin face, infantile hypercalcemia, and cognitive and behavioral abnormalities. Most such patients have a ~ 1.6-Mb hemizygous deletion in 7q11.23. However, occasional patients demonstrate WBS plus infantile spasms and more severe developmental delay. Larger deletions have been reported in some such patient but the specific genes involved in this variable phenotype are unknown. Ramocki et al. studied 26 individuals with variable expression and/or incomplete penetrance of epilepsy, learning difficulties and intellectual disabilities due to a microdeletion distally adjacent to the WBS region at 7q11.23.

They identified sites for nonallelic homologous recombination in two patients and three individuals with smaller, nonrecurrent deletions that include *HIP1* but not *YWHAG* suggest that deletion of *HIP1* is sufficient to cause neurological disease.

The authors' data characterize a neurodevelopmental epilepsy syndrome that is likely caused by deletions including *HIP1*. The authors propose that *HIP1* haploinsufficiency in humans may be amenable to rational drug design for improved seizure control and cognitive and behavioral function.