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Sapropterin treatment preserves brain function in young PKU patients

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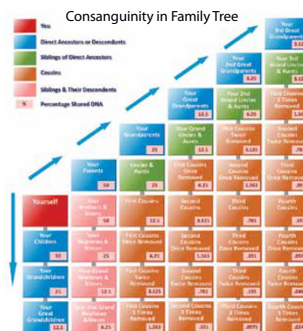
Infants born without a functional enzyme essential to metabolizing the amino acid phenylalanine (Phe) must endure a highly restrictive diet to avoid the severe intellectual impairments that accompany untreated phenylketonuria (PKU). These dietary restrictions are difficult to comply with and if not adhered to properly and closely monitored may hinder a child's growth. Synthetic Phe-free medical foods and supplements provide essential amino acids but have a strong unpleasant taste. Treatment to reduce blood Phe levels allows some to liberalize their diet to some extent. Slightly more than half of individuals with PKU respond to treatment with sapropterin, a synthetic form of an essential enzyme cofactor that can boost Phe metabolism. The drug can reduce blood Phe levels, allowing PKU patients to eat a less protein-restricted diet. In this issue, Longo et al. report the results of a 2-year interim analysis of cognitive performance in 55 young children who started sapropterin treatment as infants or toddlers. The children who responded to the drug had no significant changes in intelligence testing after 2 years of treatment. In all the children, researchers measured changes in height, weight, and head circumference, and the average growth in all three parameters after 2 years was slightly above the 50th percentile compared with reference values. None of the children had a measurable development delay. The team reported no serious adverse events associated with the treatment. The ongoing 7-year study will continue to evaluate the long-term effects of sapropterin in these very young children. —Karyn Hede, News Editor



A framework for disclosing unexpected relatedness revealed by genetic testing

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An estimated 1 in 10 people, globally, is produced by the union of second cousins or closer relatives, and these relationships will be increasingly revealed by genomic testing. Particularly because closely related individuals are more likely to have children with genetic issues, the number of individuals with closely related parents who are referred for genetic testing is likely higher.



The ACMG publishes guidelines for documenting suspected consanguinity as a secondary finding of genomic testing. However, there are no formal guidelines that consider potential legal reporting obligations when disclosing unexpected consanguinity to families. Delgado et al. provide just such a framework, based on their experience with a recent case. After a thorough clinical evaluation did not achieve a specific diagnosis, clinicians ordered a microarray test for an 8-week old infant with structural and metabolic defects. The results revealed long stretches of homozygosity on multiple chromosome pairs. The child's mother, a 24-year-old Spanish speaker, insisted that she and the child's father were not related. A clinical geneticist, genetic counselor, social worker, medical Spanish interpreter, and patient advocate met as a team with the mother to deliver the results. The research team developed a decision tree to assist in meeting legal reporting obligations while maintaining patient communication and trust. Because consanguinity laws vary by state, the authors suggest that health-care providers consult locally applicable statutes. In the case presented here, both parents were adults, there was no disclosure of abuse, and the team decided that pressuring the family to make additional disclosures would not assist in making a diagnosis. —Karyn Hede, News Editor

NEWS BRIEFS

New genetic syndrome sheds light on human development

The recent discovery of a first-of-its-kind genetic syndrome provides new insight into the most fundamental processes of human development. CHOPS syndrome, so-named for the constellation of symptoms seen in the three children known to be affected, is the first example of a human developmental disorder caused by mutations in a protein complex that controls gene expression in early embryonic development.



Children's Hospital of Philadelphia

A team of researchers from the Individualized Medical Genetics Center at the Children's Hospital of Philadelphia and the University of Tokyo described the new syndrome in a study published in March 2015 in *Nature Genetics*. The parents of the affected children, all of whom had developmental defects similar to those seen in Cornelia de Lange syndrome, sought the assistance of study leader Ian Krantz, an expert on that disorder. Krantz's research team sequenced the coding regions of the genome and identified the candidate gene *AFF4*, which was mutated in all the affected children but