Volume 2, Number 4

IN THIS ISSUE

QUICK LINKS

Our Website

Requisition Form

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October 2010 Newsletter

Welcome to our Newsletter. In this issue, we present new DNA sequencing tests for Alström, Oral-Facial-Digital, Griscelli, Lynch and PTEN Hamartoma Tumor Syndromes, MUTYH-Associated & Familial Adenomatous Polyposis, Familial Hemophagocytic Lymphohistiocytosis, Lissencephaly, and Achromatospsia. In addition, we make a few announcements regarding our continued growth as a company. And in the President's Corner, Jim Weber discusses the use of the terms "Polymorphism" and "Mutation" in Clinical Genetics.

Announcements

PreventionGenetics is now licensed as a Clinical Laboratory by the State of California. This should make it easier for our California colleagues to make use of our services.

We are also pleased to announce that PreventionGenetics was named one of the 2010 Wisconsin Companies to Watch, an awards program presented by the Wisconsin Entrepreneurs' Network (WEN) with support from the Wisconsin Department of Commerce and the Division of Entrepreneurship and Economic Development (DEED).

In addition, we have begun construction of a new building to complement our existing facilities in Marshfield, WI. This new building will house up to 50 additional employees which we expect to hire over the next few years.

New Tests at PreventionGenetics

Please follow the gene link for additional information

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Lissencephaly (PAFAH1B1/LIS1, ARX, TUBA1A, RELN, YWHAE, and DCX)
Alström Syndrome (ALMS1)
Oral-Facial-Digital Syndrome
Type1 (OFD1)
For more information on these disorders, please contact Marwan Tayeh, PhD, by email or at 715-387-0484 ext. 108.

Familial Hemophagocytic Lymphohistiocytosis
Type2 (PRF1)
Type3 (UNC13D)
Type4 (STX11)
Type5 (STXBP2)
Griscelli Syndrome (RAB27A)
For more information on these disorders, please contact Michael Chicka, PhD, by email or at 715-387-0484 ext. 141.

Achromatopsia (CNGA3, CNGB3, GNAT2, PDE6C, and as

a sequencing panel)
For more information on these disorders, please contact Khemissa Bejaoui, PhD, by email or at 715-387-0484 ext. 119.

Lynch syndrome (MSH3, MLH6, and PMS1)
MUTYH-Associated Polyposis (MUTYH)
Familial Adenomatous Polyposis (APC)
PTEN Hamartoma Tumor Syndrome (PTEN)
For more information on these disorders, please contact Keith Nykamp, PhD, by email or at 715-387-0484 ext. 140.

Come visit us in Washington DC & Nova Scotia!

PreventionGenetics is privileged to be exhibiting next month at the American Society for Human Genetics (ASHG) 60th annual meeting in Washington DC (Booth #1207). We will also be at the Canadian College of Medical Geneticists (CCMG) meeting in Halifax, Nova Scotia (Booth #6). Please stop by our booths to learn more about our services and to say hello!

Interested in a test we don't currently offer?

PreventionGenetics continues to expand on one of the largest gene sequencing test menus in the industry. If you are interested in a particular test that we don't currently offer, please contact us. There is an excellent chance we can develop a test to suit your needs.

PRESIDENT'S CORNER
Jim Weber, PhD

Use of the terms "Polymorphism" and "Mutation" in Clinical Genetics.

Clinical geneticists have developed definitions for the terms "polymorphism" and "mutation" that are different from those used by the general genetics community. Use of these terms can therefore be ambiguous.

The term DNA polymorphism originally meant a relatively common sequence variant within a population. The most widely used definition identifies a polymorphism as a variant for which the most common allele has a population frequency of no more than 99% (see for example Jobling, Hurles and Tyler-Smith in Human Evolutionary Genetics, Garland Publishing, p. 48, 2004). Clinical geneticists, however, primarily use the term polymorphism to indicate a benign sequence variant. The two definitions are in conflict because some pathogenic variants, such as the cystic fibrosis ΔF508 in Northern Europeans and the β-globin sickle cell anemia p.Glu6Val in Africans, have allele frequencies > 1%. In addition, GWAS and other research studies have revealed that many common polymorphisms act as genetic modifiers altering a patient's risk for disease. Based on these findings it is clear that polymorphism does

not always mean benign.

Similarly, the term "mutation" has varied definitions. Clinical geneticists typically define mutation to mean a disease causing sequence variant. Many other geneticists, however, define mutation as any change in DNA sequence, regardless whether pathogenic or benign. As we all know, mutation is a normal human biological process occurring in at least a large fraction of cells and during development of all gametes. To the lay person, however, mutation usually indicates something abnormal or freakish.

Although it will not be possible to get all geneticists to agree on definitions for polymorphism and mutation (I can't even get all geneticists at PreventionGenetics to agree), one simple solution is to avoid the use of these terms in test reports altogether. Indeed, this approach was recommended by Bell et al. ("Practice guidelines for the Interpretation and Reporting of Unclassified Variants (UVs) in Clinical Molecular Genetics." Clinical Molecular Genetics Society, 2007). All differences from the reference sequences can simply be referred to as sequence variants which can then be interpreted as pathogenic or benign (or something in between). I think patients will also appreciate this approach, as no one enjoys being called a mutant.