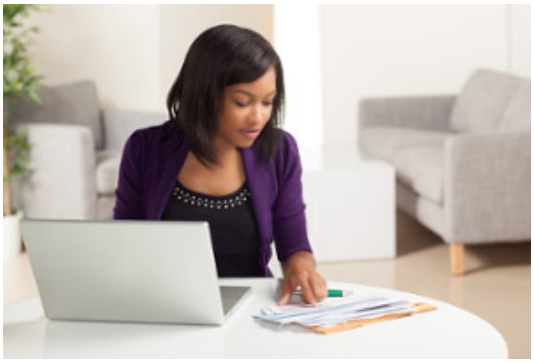
Volume 6, Number 2

Welcome to the second newsletter of 2014 from PreventionGenetics. In this issue we highlight our updated billing policy. We present our updated test menu with 46 new single gene Sanger tests, 10 new and 3 updated NextGen Panels. We also introduce Dr. Srirangan Sampath, a recent addition to our expanding team of geneticists.

In the President's corner, Dr. Jim Weber continues his discussion of obstacles to routine genomic sequencing of patients.

PreventionGenetics' Billing Policy

As we are all aware, the health care system in the US is undergoing tremendous change. Additionally, new CPT codes for genetic testing were implemented in January 2013. In light of these changes, reimbursement from public and private insurers has been a topic of discussion and concern for those requesting or performing genetic testing. In order to facilitate answers to questions regarding our billing process, we have published our billing policy on our website.



PreventionGenetics is committed to providing the highest quality genetic testing to all patients. Our philosophy is that genetic testing should enhance the quality of clinical care for the patient and be affordable to everyone. Regardless of the nature of payment or payer, we strive to provide the lowest prices in the market and therefore, our prices do not vary for different payment options. Our prices are transparent and openly published on our website. We offer three (3) convenient payment options for testing services: we can bill the ordering institution/provider directly (institutional billing), we can bill the patient directly (self-pay), or we can bill the patient's commercial insurance company (insurance billing). We will assist in obtaining insurance pre-verification and pre-authorization upon request. For additional information on billing, please see our billing policy on our website.

New Tests

NEXTGEN SEQUENCING PANELS
Hereditary Spherocytosis/Elliptocytosis 1387

Coagulation Factor Deficiency 1379
Platelet Function Disorder 1377
Bleeding Disorder 1375
Nonsyndromic Hearing Loss and Deafness 1363
Glycogen Storage Disease 1381
Centronuclear Myopathy 1373
Nemaline Myopathy 1367
Glycogen Storage Disease 1381
Malignant Hyperthermia 1383

BLOOD AND LYMPH
Glanzmann's Thrombasthenia *ITGB3* 1611
Prothrombin/Factor II Deficiency *F2* 1736
Antithrombin Deficiency *SERPINC1* 1574
TNF-Receptor Associated Periodic Syndrome *TNFRSF1A* 1463
Chronic Granulomatous disease *CYBB* 1651
Pyruvate Kinase Deficiency *PKLR* 1652
X-Linked Agammaglobulinemia *BTK* 1650
Hyper IGE syndrome *STAT3* 1613
Familial Hemophagocytic Lymphohistiocytosis, X-linked Lymphoproliferative disease *SH2D1A* 138, *XIAP* 139

CANCER
Primary Pigmented Nodular Adrenocortical Disease *PDE11A* 1292
Shwachman-Diamond Syndrome *SBDS* 1289
Infantile Myofibromatosis| Idiopathic Basal Ganglia Calcification *PDGFRB* 1609

CARDIO
Long QT syndrome *KCNE2* 1044

CILIOPATHIES
Acrocallosa, Fetal Hydrolethalus, and Joubert syndromes *KIF7* 1025

COGNITIVE
Pelger-Huet Anomaly AND Greenberg Skeletal Dysplasia *LBR* 1033

DENTAL
Amelogenesis Imperfecta *ENAM* 1601, *C4orf26* 1604

DEVELOPMENTAL
Acrocallosa, Fetal Hydrolethalus, and Joubert syndromes *KIF7* 1025

ENDOCRINE
Hypothyroidism and Hyperthyroidism *TSHR* 1521 Shwachman-Diamond Syndrome *SBDS* 1289

KIDNEY
Low Syndrome AND Dent Disease *OCRL* 1640

GASTROINTESTINAL
Chronic Pancreatitis *CPA1* 1442

METABOLIC
Succinyl-Coa:3-oxoacid CoA transferase deficiency *OXCT1* 987

NEUROLOGIC
Autosomal Dominant Nocturnal Frontal Lobe Epilepsy *CHRNA4* 1179
Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy *NOTCH3* 1210

Parkinson's Disease *PARK2* 1027
Low Syndrome AND Dent Disease *OCRL* 1640
Early Infantile Epileptic Encephalopathy and Benign Familial Neonatal Seizures *KCNQ2* 637
Autosomal Dominant Nocturnal Frontal Lobe Epilepsy *CHRNA4* 1179
Lafora Disease *EPM2A* 1425
Infantile Myofibromatosis| Idiopathic Basal Ganglia Calcification *PDGFRB* 1609

NEUROMUSCULAR
Brown-Vialoetto-Can Laere syndrome and Fazio-Londe Disease *SLC52A2* 920
Dystrophinopathy - Duchene muscular dystrophy and Becker muscular dystrophy 1200 (del/dup), 1773
RYR1-Related Congenital Myopathies 1771

SKELETAL
Shwachman-Diamond Syndrome *SBDS* 1289
Pelger-Huet Anomaly AND Greenberg Skeletal Dysplasia *LBR* 1033

VISION
NDP-Related Vitreoretinopathies *NDP* 1067
Cone-Rod Dystrophy *RAX2* 1607
Familial Exudative Vitreoretinopathy *TSPAN12* 1069 Low Syndrome AND Dent Disease *OCRL* 1640
Familial Exudative Vitreoretinopathy *FZD4* 1068

REVISIONS:
WDR19 was added to the Nephronophthisis 1058 and Ciliopathy 1056 NGS panels
Chronic Pancreatitis Sanger Panel Added *CPA1* 1445
Ciliopathy NGS Panel added *ANKS6, B9D2, CCDC103, CCDC11, CCDC114, CEP164, HEATR2, KIF7, LRRC6, TCTN1, TCTN3, TMEM231, TTC21B, WDPCP, ZNF423* 1056

Dr. Srirangan Sampath

Srirangan Sampath, Ph.D., joined PreventionGenetics in October 2013 as an American Board of Medical Genetics certified clinical cytogeneticist. He currently heads the microarray laboratory at PreventionGenetics. His main area of focus will be Chromosomal Microarray Analysis (CMA) testing. CMA testing is an in silico method of analyzing chromosomes for a large number of genetic disorders. "Although traditional chromosome analysis is still relevant today, CMA is so much more sensitive and provides significantly better diagnostic yield," said Dr. Sampath. He completed an ABMG fellowship in Clinical Cytogenetics at Baylor College of Medicine, Department of Molecular and Human Genetics.

"Although many now design targeted arrays, Baylor was a pioneer in the field, opting to design an exon-targeted CMA while the rest reached for off-the-shelf arrays for both postnatal and prenatal samples. This put them ahead in the field with a rich knowledge base of clinically

relevant copy number changes that I hope one day would be opened up to larger clinical community." Dr. Sampath finds it ironic he is now working for a genetic testing laboratory, as he never expected to end up working in an industry setting. "I heard that PreventionGenetics is a more relaxed company, with more flexibility. My goal was to play a leadership role in developing these new CMA tests. While this is something unique to PreventionGenetics, I'm using the lessons I've learned at Baylor to incorporate CMA analysis here."

President's Corner

In the previous issue of our Newsletter, I began a discussion of obstacles to routine genomic sequencing of patients. Here again is the list of what I think are the major obstacles. Last time, I advocated genetics education as the best approach to overcome the last item on the list. In this issue, I discuss the first item, sequencing technology.

- Sequencing technology is insufficient.
- Patient sequences are not being stored in electronic health records.
- Patient sequences are not being shared across providers and family members.
- Sequence interpretation is in its infancy.
- Health care providers and patients are not ready.

Although exome sequencing is powerful, genome sequencing is ultimately preferable for healthcare because it covers the entire genome and because it is superior for detection of large insertions, deletions and other large scale rearrangements. While there have been dramatic improvements in sequencing technology over the last 30 years, to be practical for genomic sequencing, I think that sequencing costs need to drop at least another order of magnitude. Probably disruptive technology, rather than incremental improvements of existing approaches, will be required.

What other features of new sequencing technology besides much lower cost would we like to see? First, we would like to avoid any lab methods that produce bias due to GC content (or other sequence parameters). Today that means primarily PCR, including cluster generation on the Illumina instruments. Second, we would like long reads, at least thousands of nucleotides and preferably > 10,000 nucleotides. Long reads will greatly aid sequence assembly, detection of copy number variants, and analysis of genes with close copies at other sites within the genome. Third, we would like the capability to detect nucleotide variants, especially methylated nucleotides. Fourth, easy preparation of DNA for loading on the sequencers is a must. Today's lengthy, complicated methods for preparation of sequencing libraries have to go. Finally, it would be great to be able to sequence short tandem repeats accurately. This would aid in diagnosis of repeat expansion disorders and would permit useful application of the powerful multiallelic microsatellite polymorphisms.

Fortunately, hundreds of millions of dollars, both public and private, are now being spent each year on new sequencing technology. It's tough to predict the future, but I think there is good reason for optimism. Hopefully, by the time patients and physicians are ready for clinical genomic sequencing, the necessary sequencing technology will be available.

Quick Links:

Our website
Req forms

Visit us at:

NSGC AEC, booth #208
ASHG 2014, booth #1034

Kit requests
Join our mailing list

PREVENTION GENETICS

DISEASE PREVENTION THROUGH GENETIC TESTING

3800 South Business Park Ave. Marshfield, WI 54449 Ph: 715-387-0484 Fax: 715-207-6602