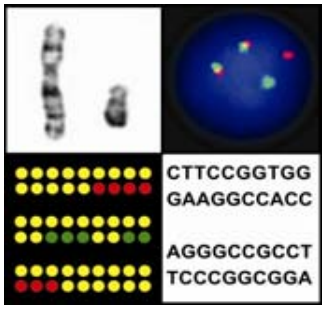


UW Cytogenetic Services

Wisconsin State Laboratory of Hygiene

Fall 2014

A Cytogenetics Lab's Experience with NIPT

Non-invasive prenatal testing (NIPT) is based on the analysis of cell free DNA fragments derived from the placenta (Liao, 2014). These tests have been rapidly adopted for the detection of fetal aneuploidy because of the lower risk of complications compared to invasive testing and the higher sensitivity and specificity rates compared to maternal serum screening. NIPT is currently recommended by the American College of Obstetricians and Gynecologists for use in populations at high-risk for fetal aneuploidy.

WSLH has received 32 cases whose reason for referral included a positive NIPT result. The average age of the patient was 36.1 years (range 28-45). Ten of the 32 (31%) cases were classified as false positives based on a normal karyotype by chromosome analysis. An abnormal result was confirmed in 22 of 32 cases (69%). Karyotype analysis can also provide information about genomic composition that is not provided by an NIPT test such as aneuploidy of chromosomes other than 13, 18, 21, X, or Y, Robertsonian translocations versus trisomy, or mosaicism. Abnormal ultrasound findings or maternal serum screening results were included in the reason for referral in 7 of 22 (32%) cytogenetically abnormal cases and in 2 of 10 (20%) cases with a normal karyotype.

The false positive rate of samples received by WSLH is in line with what has been reported by other groups (Wang, 2014). Commercially available NIPT tests have reported >99% sensitivity and specificity values. However, following a positive result, the likelihood of the fetal karyotype being abnormal can be much lower and depends on the prevalence of the condition. Appropriate counseling is essential to convey the true risk of an affected pregnancy and the importance of diagnostic testing, such as CVS or amnio, for confirmation of results.

References:

Liao GJ, Gronowski AM, Zhao Z. Non-invasive prenatal testing using cell-free fetal DNA in maternal circulation. *Clin Chim Acta* 2014; 428:44-50.

Wang J, Sahoo T, Schonberg S, Kopita KA, Ross L, Patek K, and Strom CM. Discordant noninvasive prenatal testing and cytogenetic results: a study of 109 consecutive cases. *Genet Med* advance online publication 7 August 2014.

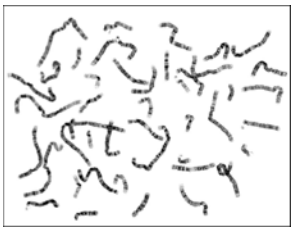
The Wisconsin Plain Community Project

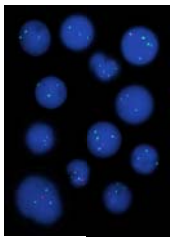
The Wisconsin Newborn Screening program screens tens of thousands of infants every year for over 40 genetic disorders, hearing loss, and congenital heart disease. However, there still remain considerable populations of infants unscreened. Through funding from the Wisconsin Partnership Program, the Plain Community project seeks to address this unmet need in Wisconsin. The Plain Communities (Amish, Mennonites and related sects) routinely participate in out-of-hospital births and have an increased frequency of unscreened newborns. In addition to facilitating a health care needs assessment, encouraging community engagement, and establishing outreach clinics, the project aims to expand newborn screening (via blood, hearing, and pulse oximeter screening) to Amish and Mennonite families. The UW Cytogenetics and Molecular Genetics Laboratory has been actively involved with the project through development of target variant testing that will provide reliable molecular diagnostic services at an affordable cost. Target variant testing is available for conditions such as phenylketonuria (PKU), severe combined immunodeficiency (SCID), glutaric aciduria (GA), primary ciliary dyskinesia, and nemaline rod myopathy (chicken breast disease). Diagnostic testing for Rett syndrome will soon be available. Please call the UW Cytogenetics and Molecular Genetics Laboratory at 608-262-0402 with questions regarding any of our test offerings.

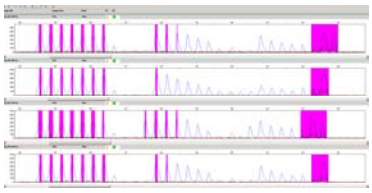
UW Cytogenetic Services

465 Henry Mall
Madison, WI 543705

Phone: 608-262-0402
Fax: 608-265-7818
www.slh.wisc.edu/cytogenetics







Kate Thompson Retires

Kate Thompson is a 30 year veteran of the UW Cytogenetics and Molecular Genetics Laboratory. She started working in the Waisman Cytogenetics Laboratory in 1984. Following the merger and relocation to the State Lab of Hygiene, Kate continued working as a technical supervisor until 2009, at which time she began her role as Education Coordinator. As Education Coordinator, Kate oversaw the training of new staff and fellows and supervised students and residents rotating through our laboratory. Kate's expertise was invaluable. The UW Cytogenetics and Molecular Genetics Laboratory wishes Kate a very happy retirement!

Disease Spotlight: Rett Syndomre

Rett syndrome is a rare progressive neurodevelopmental disorder. This condition almost exclusively affects females and is usually lethal in males. Girls with Rett syndrome can have normal development for the first year or more of life, but typically starting between the ages of 1 to 4 years there is a rapid and noticeable regression in skills, particularly purposeful hand and language skills. They also can display stereotypic hand movements such as hang wringing, clapping, washing, and mouthing. Breathing abnormalities such as apnea or autistic–like symptoms can also be seen. Following this period of regression is a plateau stage, which can last for years. Children in this stage may improve in behavior although movement problems continue to occur. The final stage of Rett syndrome is characterized by reduced mobility, scoliosis, muscle weakness, and spasticity; however, there is typically no further loss of cognition, understanding, or hand skills. Females with Rett syndrome typically survive into adulthood, but require continuous care and assistance.

<u>Causes or Rett syndrome</u>

Rett syndrome is caused by mutations in the *MECP2* gene, located on the X chromosome. It is possible to inherit a mutation from a parent who has germline mosaicism for a *MECP2* mutation, or, more rarely, is an asymptomatic female carrier; however, more than 99% of mutations are *de novo*. This means that usually there is only one affected individual in a family and risk to other family members is typically low.

<u>Testing for Rett syndrome</u>

Rett syndrome is typically diagnosed clinically, after a careful examination by a medical geneticist or other qualified health care provider. A clinical diagnosis of Rett syndrome can be molecularly confirmed in a patient by sequencing the *MECP2* gene to look for disease-causing mutations. Sequence analysis and deletion/duplication studies will find a causal mutation in 88% of children with Classic Rett syndrome.

MECP2 testing will soon be available through the UW Cytogenetics and Molecular Genetics lab. Please call us at 608-262-0402 with any questions.