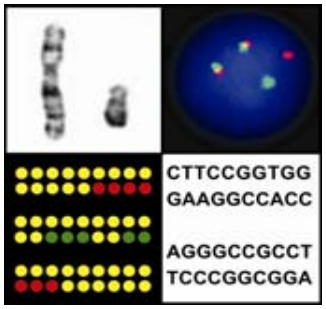

UW Cytogenetic Services

Wisconsin State Laboratory of Hygiene

Summer 2014

New testing algorithm for FISH myeloma panel

Multiple myeloma is a disorder of plasma cells causing abnormal cells to amass in the bone marrow. This can result in impaired immunity, anemia, kidney complications, as well as bone lesions. Fluorescence in situ hybridization (FISH) is a useful tool in the detection of cytogenetic abnormalities associated with plasma cell disorders such as multiple myeloma. FISH myeloma panels are used to detect the most common abnormalities seen in plasma cell myeloma as well as those abnormalities that have great prognostic significance.

The test is typically performed on interphase nuclei of CD138+ plasma cells. However, only a limited number of CD138+ cells can be separated from the plasma cells in whole bone marrow. As a result, we have implemented a two stage analysis process for the Myeloma FISH panel.

Initial FISH analysis will include the following probes:

- ATM/TP53
- 13q deletion
- 1p/1q
- IGH rearrangement

If the initial analysis is positive for IGH rearrangement, we will automatically reflex to possible translocation partner probes, which include:

- CCND1/IGH t(11;14)
- IGH/MAF t(14;16)
- FGFR3/IGH t(4;14)
- IGH/MAFb t(14;20)

If the initial analysis is negative for IGH rearrangement, further analysis of the IGH translocation probes is not necessary. No further testing will be performed, saving plasma cells and cost to the patient.

Order the myeloma FISH panel on the order form as usual. We will only bill for the components we performed.
Please call our laboratory at 608-262-0402 with any questions.

Test Menu Update:

Chromosomal microarray testing is routinely used as the first-tier genetic test for the evaluation of postnatal patients with multiple congenital anomalies, developmental/intellectual disabilities, and autism spectrum disorders. It is also now being commonly used in prenatal diagnosis. Given the increased use of chromosome microarray as a first-tier test, as well as the improved sensitivity and cost-effectiveness of the testing, we will be reducing our constitutional FISH probe offering. 22q11.2 (DiGeorge/Velo-cardio-facial syndrome) and SRY probes will still be offered along with our aneuploidy panel for pre-natal and stillbirth testing. Effective immediately, however, the following probes will no longer be offered: Angelman syndrome (15q11.2), Prader-Willi syndrome (15q11.2), Cri du chat syndrome (5p15.2), deletion 1p36 syndrome, Miller-Dieker syndrome (17p13.3), Smith-Magenis syndrome (17p11.2), Williams syndrome (7q11.23), and Wolf-Hirschhorn syndrome (4p16.3).

Please contact our laboratory at 608-262-0402 with any questions.

UW Cytogenetic Services

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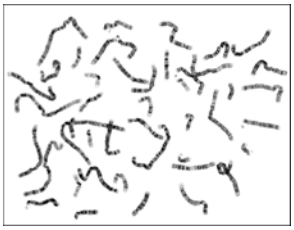

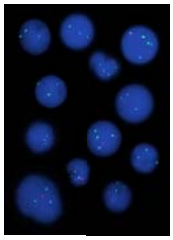

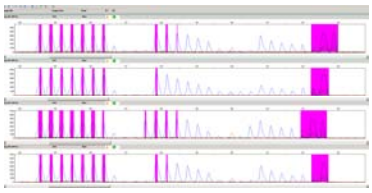

UW Cytogenetics Welcomes New Assistant Director

This April the UW Cytogenetics Laboratory hired a new assistant laboratory director. Vanessa Horner, Ph.D. DABMG has joined Director Jennifer Laffin, Ph.D. FACMG as Assistant Director of the Wisconsin State Lab of Hygiene Clinical Genetics Laboratories (Cytogenetics and Molecular Genetics).
Dr. Horner received her Ph.D. from Cornell University in 2007. She then went on to do her postdoctoral training at Emory University, where she also completed both her cytogenetic and molecular genetics fellowships.
We are excited to have Dr. Horner with us at the UW Cytogenetics Laboratory!

Spotlight: Prader-Willi Syndrome

Prader-Willi syndrome (PWS) is a genetic disorder that causes developmental delays and mild to moderate intellectual disability in both males and females.

In infancy, children with PWS have severe hypotonia, feeding difficulties, failure to thrive, and developmental delays. By early childhood, hyperphagia develops leading to excessive eating and eventual obesity by 6 years of life.
Other features include:

- Hypogonadism: genital hypoplasia and/or incomplete pubertal development
- Infertility
- Characteristic facies: narrow forehead, almond-shaped eyes, triangular mouth
- Behavioral problems: temper tantrums, obsessive-compulsive tendencies, stubbornness, manipulative behavior
- Learning disability
- Short stature
- Small hands and feet

Causes of PWS

PWS is an imprinting disorder. It is caused by a loss of function of the paternally derived genes at chromosome region 15q11.2-q13. In the majority of cases of PWS (~70%) this is caused by a deletion of the paternal allele at this region. It can also be caused by maternal uniparental disomy (UPD). Rarely, it can be due to an imprinting defect or a chromosomal rearrangement that has a breakpoint within the 15q11.2-q13 region.

Testing

More than 99% of cases of PWS can be detected by DNA methylation studies. This test is used to determine methylation patterns and thus can detect an abnormal imprinting pattern within the tested region. It will not detect which mechanism (deletion, UPD, or imprinting defect) is responsible for the abnormal methylation pattern, therefore further testing via FISH or chromosome analysis, UPD analysis, and imprinting defect analysis is necessary in order to estimate recurrence risks.

Most cases of PWS are not inherited. Thus the risk of recurrence is usually low; however, if an imprinting defect is responsible, risk of recurrence could be as high as 50%.

Methylation Specific PCR testing for Prader-Willi/Angelman syndrome can be ordered through the UW Cytogenetics lab via test code 889. Please call us at 608-262-0402 with any questions.