Fragile X Trinucleotide Repeat Sizing

Test Description:
Detection of expansions in FMR1 that affect the severity of Fragile X syndrome. Test is done on peripheral blood specimens for confirmation of clinical diagnosis, carrier status or presymptomatic testing.

Indication:
Fragile X syndrome is the most common form of inherited mental retardation and the second most frequent cause of mental retardation after Down Syndrome. The disorder is inherited in an X-linked dominant manner, with 30% of males carrying the fragile X chromosome being phenotypically normal. For females with a full mutation, 50% will have cognitive impairment and 50% will be of normal intellect. It is typically caused by expansion of a CGG repeat region in the 5' UTR of the FMR1 gene and is rarely caused by deletions or point mutations within this gene. The length of the CGG repeat in the normal population is polymorphic and ranges between 5 and 44 repeats, with a repeat number of 29 or 30 being the most common. Premutation carrier females and transmitting males show no phenotypic effect and range between 56 and 200 repeats. Accurate determination of CGG repeat numbers is essential for appropriate risk assessment and counseling of premutation carriers. Patients possessing premutation alleles (56-200 CGG repeats) were once thought to be asymptomatic. Recent work has shown that individuals with premutations can manifest Fragile-X associated tremor/ataxia syndrome (FXTAS), premature ovarian failure, or mild cognitive/behavioral defects. The number of repeats correlates to the severity of disease. In a full mutation, there are over 200 repeats and the CpG island is methylated. AGG interruptions of the CGG repeat domain are thought to lead to a lowered risk of CGG expansion in the next generation.


OMIM: 300624

Methodology:
A PCR assay is performed by utilizing a set of primers that encompass the Fragile X CGG repeat region. The resulting PCR products are run on a capillary sequencer, product size is determined using a size standard, and CGG repeat number is calculated. In addition to the sizing primers an additional primer
consisting of 5 CGG repeats is used to produce a stutter plot that allows confirmation of total repeat size and indicates the presence or absence of AGG interruptions within the CGG repeat domain.

**Loci Tested:** *FMR1* 5’UTR

**Performed:** Weekly

**Reported:** Within 3-10 business days of receipt

**Specimen Required:**
Peripheral blood collected in EDTA (purple top) is preferred, 3-10mL.

**Shipment Must Include:**
- [ ] Specimen
- [X] Requisition form
- [ ] Patient pathology report