Premature Ovarian Failure: \textit{FMR1} CGG Repeat Analysis

\textbf{Test Code:} MOFMR  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81243 x1

\textbf{Condition Description}

\textit{FMR1}-related disorders include fragile X syndrome, fragile X-associated tremor/ataxia syndrome (FXTAS), and \textit{FMR1}-related premature ovarian failure (POF). \textit{FMR1}-related premature ovarian failure (POF) is the onset of ovarian dysfunction or menopause before the age of 40 years. Women who are carriers of \textit{FMR1} premutation range expansions are at increased risk for POF (estimated as high as 21\%), though penetrance of POF is not complete. Recent reports indicate that women who carry a premutation size expansion may have a slight increased risk for developing fragile X-associated tremor/ataxia syndrome (FXTAS), a disorder that causes tremors, balance problems, difficulty walking, and memory difficulty.

The \textit{FMR1} gene is located on the X chromosome. \textit{FMR1}-related disorders are associated with the presence of a triplet (CGG) repeat expansion in the promoter of \textit{FMR1} leading to methylation and subsequent inactivation of the \textit{FMR1} gene. The normal range of CGG repeats is approximately 5-44. Repeats in this range are considered stable when passed from parent to child. Repeats in the 45-54 range are considered intermediate (or grey-zone), for which the risk of expansion to a full mutation of 200 repeats or more when passed to children is low but not well defined at this time. Individuals with approximately 55-200 CGG repeats are premutation carriers. Females with expansions in this range are at risk for POF. The number of repeats in this range is unstable and may expand when passed to children. Individuals with fragile X have over 200 CGG repeats. Males with over 200 repeats are almost always affected, while females may be more mildly affected. Women who are carriers of a full size expansion are not at increased risk of POF. Mosaicism has also been reported in some individuals with \textit{FMR1} mutations, indicating the presence of two different repeat sizes or variation in the extent of methylation.

Click here for the GeneReviews summary on this condition.

\textbf{Genes}

\textbf{FMR1}

\textbf{Indications}

This test is indicated for:

- Adult females with premature ovarian failure.

\textbf{Methodology}

The DNA surrounding the CGG repeat in the \textit{FMR1} gene is amplified by PCR and the size of the repeat is determined by capillary electrophoresis.

\textbf{Detection}

All cases of premutation expansion mutations for \textit{FMR1} will be detected by this assay.

\textbf{Reference Range}


\textbf{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\textbf{Type: Whole Blood (EDTA)}

\textbf{Specimen Requirements:}

EDTA (Purple Top)  
Infants and Young Children (2 years of age to 10 years old): 3-5 ml  
Older Children & Adults: 5-10 ml  
Autopsy: 2-3 ml unclotted cord or cardiac blood

\textbf{Specimen Collection and Shipping:}

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

\textbf{Type: DNA, Isolated}

\textbf{Specimen Requirements:}

Microtainer 20µg  
Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

\textbf{Specimen Collection and Shipping:}
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- A comprehensive panel of genes associated with premature ovarian failure is available via test code MFMR1.
- FXTAS (FJ) is indicated for older men with late-onset, progressive ataxia and intention tremor or for fathers of women who are premutation range carriers of an FMR1 expansion.
- Testing for fragile X syndrome (MFRAX) is indicated for males and females with symptoms of Fragile X.
- The female infertility panel (XM051) is available for women experiencing infertility due to ovarian dysfunction or menopause.