CENTER FOR PRECISION DIAGNOSTICS

BRCA1 & *BRCA2* Full Deletions/Duplications - Only (MLPA)

BRCA1	*BRCA2*								

Indication

This panel analyzes BReast CAncer genes 1 and 2 (*BRCA1* and *BRCA2*), that code for proteins that help repair DNA damage. Inherited mutations in *BRCA1* or *BRCA2* are associated with autosomal dominant hereditary breast and ovarian cancer (HBOC) syndrome (OMIM ID: 604370) which is characterized by increased lifetime risk for developing breast, ovarian and other types of cancer. Mutations in *BRCA1* and *BRCA2* are responsible for approximately 20 to 25% of hereditary breast cancers and about 5 to 10% of all breast cancers. In addition, mutations in *BRCA1* and *BRCA2* cause around 15% of ovarian cancers. Specific cancer risks are different between *BRCA1* and *BRCA2*. *BRCA1* pathogenic mutations are associated with increased lifetime risk for breast cancer (40-87%), ovarian cancer (16-54%), male breast cancer (1-2%), prostate cancer (up to 20%), and pancreatic cancer (1-3%). *BRCA2* pathogenic mutations are associated with increased lifetime risk for breast cancer (up to 84%), ovarian cancer (up to 27%), male breast cancer (6%), prostate cancer (up to 20%), pancreatic cancer (2-7%), and melanoma. Updated NCCN guidelines for familial cancer risk assessment and clinical managements of individuals with HBOC syndrome are available at www.NCCN.org.

Testing requirements

This MLPA assay should only be used in combination with next generation sequencing (NGS) analysis for comprehensive testing of *BRCA1* and *BRCA2* mutations. This assay only detects gross deletions and duplications caused by large genomic rearrangements in *BRCA1* and *BRCA2*, which are responsible for approximately 10% of known cancer-predisposition mutations in these genes. However, this MLPA assay will not detect other pathogenic variants such as point mutations or small insertions/deletions (indels), which comprise approximately 80-90% of cancer-predisposition mutations in *BRCA1* and *BRCA2*. Hence, this test should only be used in combination with NGS analysis of *BRCA1* and *BRCA2* coding sequence for detection of all classes of known inherited mutations in *BRCA1* and *BRCA2*. When ordering this MLPA test, please provide previous *BRCA1* and *BRCA2* sequencing report to our laboratory to allow a combined interpretation of test results and cancer risk assessment.

Testing method

This is a Multiplex Ligation-dependent Probe Amplification (MLPA) assay that includes three MLPA probe mixes (MRC-Holland, www.mlpa.com): SALSA MLPA P002, P239 (*BRCA1*) and P090 (*BRCA2*/*CHECK2*). This assay only detects common and rare gross deletions and duplications caused by large genomic rearrangements in *BRCA1* and *BRCA2*. As a result, this assay is predicted to miss approximately 80-90% of known cancer-predisposition mutations in *BRCA1* and *BRCA2*, most of which are caused by point mutations or insertions/deletions. The use of this assay as a stand-alone test without previous NGS sequencing is not recommended as this can lead to misinterpretation of test results.

Turnaround time
5-10 business days

Sample requirements
3 ml peripheral blood in EDTA (lavender) top tube
Specimen stability: Ambient - 72 hours; Refrigerated - 1 week

CPT codes
81164, G0452

References

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