TEMPUS | ONCOLOGY

Tempus xG Sample Report Guide

Germline testing identifies potential hereditary cancer risk factors that may affect patients and their family members.

By combining both somatic and germline results, Tempus provides a more comprehensive view of your patient's molecular profile.

xG SAMPLE REPORT: PAGE 1

xG+ (extended hereditary cancers) or xG (common hereditary cancers)

xG report dates may vary from somatic tests (xT and xF). They follow separate testing timelines and can be ordered at different time points.

88 (xG+) or 52 (xG) genes associated with hereditary cancer risk

Positive Result:
Pathogenic variant in BRCA2 and variant of uncertain significance in PMS2 identified by germline sequencing.

NCCN Guidelines for management are available for pathogenic/likely pathogenic variants. Testing may also be considered for at-risk relatives for these findings.

Due to unclear clinical significance of variants of uncertain significance, management guidelines are not available.

Smith, Jane

TEMPUS POWERED BY GeneDx xG

DOB 3/31/2000

Accession 5521985

Submitter Patient ID(s) 123456789

Sample
Source: Blood in EDTA
Date Collected: 3/31/2022
Date Received: 3/31/2022

Testing
Date Started: 3/31/2022
Date Reported: 4/19/2022

Provider
DOE, M.D., JOHN
Additional Provider: Lauricella, Chris

Test(s) Requested
xG (common hereditary cancers) - 52 genes

Genes Evaluated
APC, ATM, AXIN2, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, FANCC, FANCM, FH, FLCN, GALNT12, HOXB13, MET, MITF, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS2, POLD1, POLE, POT1, PTEN, RAD51C, RAD51D, RECQL, RNF43, RPS20, SCG5, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL

Result: Positive

Gene	Variant	Zygosity	Classification
BRCA2	c.4456_4459delGTTA p.(V1486Nfs*5)	Heterozygous	Pathogenic Variant
PMS2	c.5 A>G p.(E2G)	Heterozygous	Variant of Uncertain Significance

No additional reportable variants were identified in any of the genes on this panel by sequencing or deletion/duplication analysis.

Interpretation
This individual is heterozygous for a pathogenic variant in BRCA2, consistent with Hereditary Breast and Ovarian Cancer syndrome and associated with the following lifetime cancer risks: female breast 38-84%, second primary breast 62%, ovarian 16.5-27%, pancreatic 2-7%, prostate 20%, male breast 8.9%.

Recommendation(s)
- Genetic counseling is recommended.
- The "NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic" include management recommendations for Hereditary Breast and Ovarian Cancer syndrome. In addition, the "NCCN Guidelines for Prostate Cancer Early Detection" include recommendations for prostate cancer screening in men with BRCA2 pathogenic/likely pathogenic variants.
- For individuals of reproductive age, assessment of the reproductive risk associated with being a carrier of a pathogenic/likely pathogenic BRCA2 variant is recommended.
- First degree relatives have up to a 50% chance of also having the pathogenic/likely pathogenic variant(s) identified in this individual. Targeted testing for these variant(s) is available for at-risk relatives.
- The clinical implications of the variant(s) of uncertain significance remain unclear. For that reason, predictive testing for variants of uncertain significance is not recommended for at-risk family members. However, targeted testing of certain family members may help to clarify the effect of such variants. Detailed review of the patient's clinical and family history information by our clinical genetics team is necessary for enrollment in our variant testing program.

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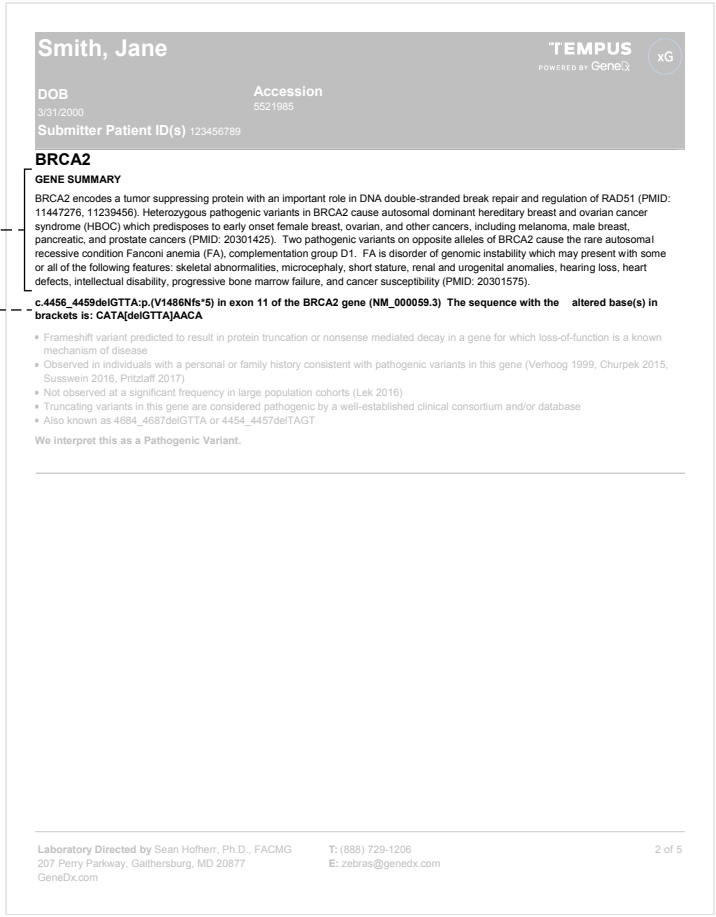
SAMPLE REPORT: PAGE 2

Gene specific summaries are included with gene function and information about associated syndromes and cancers.

Information utilized to classify variant(s) is included for all pathogenic/likely pathogenic variants and variants of uncertain significance.



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BRCA2

GENE SUMMARY

BRCA2 encodes a tumor suppressing protein with an important role in DNA double-stranded break repair and regulation of RAD51 (PMID: 11447276, 11239456). Heterozygous pathogenic variants in BRCA2 cause autosomal dominant hereditary breast and ovarian cancer syndrome (HBOC) which predisposes to early onset female breast, ovarian, and other cancers, including melanoma, male breast, pancreatic, and prostate cancers (PMID: 20301425). Two pathogenic variants on opposite alleles of BRCA2 cause the rare autosomal recessive condition Fanconi anemia (FA), complementation group D1. FA is disorder of genomic instability which may present with some or all of the following features: skeletal abnormalities, microcephaly, short stature, renal and urogenital anomalies, hearing loss, heart defects, intellectual disability, progressive bone marrow failure, and cancer susceptibility (PMID: 20301575).

c.4456_4459delGTTA:p.(V1486Nfs*5) in exon 11 of the BRCA2 gene (NM_000059.3) The sequence with the altered base(s) in brackets is: CATA[delGTTA]AACA

- Frameshift variant predicted to result in protein truncation or nonsense mediated decay in a gene for which loss-of-function is a known mechanism of disease
- Observed in individuals with a personal or family history consistent with pathogenic variants in this gene (Verhoog 1999, Churpek 2015, Susswein 2016, Pritzlaff 2017)
- Not observed at a significant frequency in large population cohorts (Lek 2016)
- Truncating variants in this gene are considered pathogenic by a well-established clinical consortium and/or database
- Also known as 4684_4687delGTTA or 4454_4457delTAGT

We interpret this as a Pathogenic Variant.

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