PARTNERS HEALTHCARE | PERSONALIZED MEDICINE
MASSACHUSETTS GENERAL HOSPITAL | BRIGHAM AND WOMEN'S HOSPITAL

Laboratory for Molecular Medicine
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www.partners.org/personalizedmedicine/lmm

Unit Number(s):

Lab Accession: **PM-16-A07001**
Patient Name: **68282505, 10038176**
Birth Date: **1/1/1800**
Age Sex: **215 Year old Female**

MOLECULAR DIAGNOSTICS REPORT

Specimen Type:	DNA, Isolated - Blood, Peripheral (edit)	**Received Date:**	9/1/2016
Related Accession(s):		**Referring Facility:**	HARVARD
Referring Physician:	EMERGE-CLINIC-TEST	**Referring Fac. MRN:**	
Copies To:	GENEINSIGHT	**Lab Control Number:**	10038176_68282505-2_SM-B3NZL
	EMERGE-HUB-TEST GENEINSIGHT	**Family Number:**	FAB123

TEST DESCRIPTION - Sequence Confirmation Test

TEST PERFORMED - SeqConV2

INDICATION FOR TEST - Not selected for trait

RESULTS

DNA VARIANTS:
Heterozygous c.338C>A (p.Ser113X), Exon 4, PMS2, Pathogenic

INTERPRETATION:
Positive. DNA sequencing of the coding regions and splice sites of 97 genes (see methodology section below) identified the variants listed above. Copy number analysis using NGS could not be completed because data did not meet quality standards for CNV detection. For a list of exons that are incompletely covered please see "Additional notes and disclaimers" section below.

SUMMARY:
This individual carries a Pathogenic variant in the PMS2 gene. The available information on this variant is described below. Disease-causing variants in the PMS2 gene are strongly associated with Lynch syndrome and this individual may be at risk for developing colorectal cancer / polyps.

ADDITIONAL NOTES AND DISCLAIMERS:
Disease penetrance and severity can vary due to modifier genes and/or environmental factors. The significance of a variant should therefore be interpreted in the context of the individual's clinical manifestations

DETAILED VARIANT INTERPRETATIONS:
p.Ser113X, c.338C>A (PMS2; NM_000535.5; Chr7g.6043336G>T; GRCh37):
The p.Ser113X variant in PMS2 has not been previously reported in individuals with Lynch syndrome and was absent from large population studies. This nonsense variant

MOLECULAR DIAGNOSTICS REPORT

leads to a premature termination codon at position 113, which is predicted to lead to a truncated or absent protein. Heterozygous loss of function of the PMS2 gene is an established disease mechanism in Lynch syndrome (http://www.ncbi.nlm.nih.gov/books/NBK1211/). In summary, this variant meets our criteria to be classified as pathogenic for Lynch syndrome (http://www.partners.org/personalizedmedicine/LMM) based upon predicted impact to the protein and absence in controls.

RECOMMENDATION:
Genetic counseling is recommended for this individual and their relatives. Familial variant testing is available for other relatives if desired. For assistance in locating genetic counseling services or disease specialists, please call the laboratory at 617-768-8500 or email at LMM@partners.org.

Please note that variant classifications may change over time if more information becomes available. Please contact us at 617-768-8500 or LMM@partners.org.

TEST INFORMATION

BACKGROUND:
HOLD FOR BACKGROUND TEXT

METHODOLOGY:
HOLD FOR METHODOLOGY TEXT

REFERENCES:
Hendriks YM, Jagmohan-Changur S, van der Klift HM, Morreau H, van Puijenbroek M, Tops C, van Os T, Wagner A, Ausems MG, Gomez E, Breuning MH, Bröcker-Vriends AH, Vasen HF, Wijnen JT. 2006. Heterozygous mutations in PMS2 cause hereditary nonpolyposis colorectal carcinoma (Lynch syndrome). Gastroenterology. 130(2):312-22.

REPORT PREPARATION by Alyssa Woulfe, on Friday September 09, 2016 at 04:22:23PM
REPORT by Alyssa Woulfe, on Friday September 09, 2016 at 04:22:36PM
Final Diagnosis by **Alyssa Woulfe,** Electronically signed on Monday September 12, 2016 at 10:56:03AM