Patient Name:
Date of Birth:
Gender:
Accession ID:
Cross Reference:

Specimen Type:

Receive Date:
Collection Date:
Report Date:

Client Name:

Mailing Address:

Phone Number:

Client Name:

Test Performed: Whole Exome Sequencing and Deletion/Duplication Analysis, Trio

Analyses of genes related to all

No pathogenic sequence variant(s) in gene related to all detected .

Relevant Findings and Interpretation

Sequence variants related to all:

Nr.	Classification	Gene	Exon/ Intron	SNP ID	DNA change	Protein change	Chromosomal location	Zygosity	Inheri-tance	Disease Groups	Associated Disease(s)
1	benign	MASP2	1	rs1782455	c.1479C>T	p.Ser493=	Chr1:11087524	heterozygous	not given	N/A	Dominant;MASP2 deficiency;Frontotemporal dementia;Amyotrophic Lateral Sclerosis, Dominant
2	likely_benign	MASP2	1	rs2273346	c.1130T>C	p.Val377Ala	Chr1:11090897	heterozygous	not given	N/A	MASP2 deficiency;MASP2 deficiency
3	benign	MASP2	1	rs12142107	c.891G>A	p.Ala297=	Chr1:11097867	heterozygous	not given	N/A	MASP2 deficiency
4	benign	MASP2	1	rs7536030	c.729C>T	p.Tyr243=	Chr1:11103408	heterozygous	not given	N/A	MASP2 deficiency
5	benign	MTHFR	1	rs4846051	c.1305C>T	p.Phe435=	Chr1:11854457	heterozygous	AR	Prenatal screening panel	folate-sensitive;Homocystinuria due to MTHFR deficiency
6	drug response	MTHFR	1	rs1801133	c.665C>T	p.Ala222Val	Chr1:11856378	heterozygous	AR	Prenatal screening	Venous thrombosis;Neoplasm of stomach;Gastrointestinal stroma tumor;MTHFR deficiency, thermolabile type;Neural tube defects, folate-sensitive;carboplatin response - Efficacy;cyclophosphamide response - Toxicity/ADR;methotrexate response - Dosage, Efficacy,

										panel	Toxicity/ADR;Neural tube defects, folate-sensitive;Homocystinuria due to methylene tetrahydrofolate reductase deficiency;MTHFR deficiency, thermolabile type;MTHFR deficiency, thermolabile type;Homocystinuria due to MTHFR deficiency

Gene Name: **MASP2**. SNPs in Gene: **rs1782455;rs2273346;rs12142107;rs7536030**. Associated diseases: MASP2 deficiency
Description: This gene encodes a member of the peptidase S1 family of serine proteases. The encoded preproprotein is proteolytically processed to generate A and B chains that heterodimerize to form the mature protease. This protease cleaves complement components C2 and C4 in order to generate C3 convertase in the lectin pathway of the complement system. The encoded protease also plays a role in the coagulation cascade through cleavage of prothrombin to form thrombin. Myocardial infarction and acute stroke patients exhibit reduced serum concentrations of the encoded protein. Alternative splicing results in multiple transcript variants, at least one of which encodes an isoform that is proteolytically processed. [provided by RefSeq, Feb 2016].
(Mut.Nbr. 2):**MASP2 c.1130T>C (p.Val377Ala) - MASP2 deficiency** This variant was observed in the ICSL laboratory as part of a predisposition screen in an ostensibly healthy population. It had not been previously curated by ICSL or reported in the Human Gene Mutation Database (HGMD: prior to June 1st, 2018), and was therefore a candidate for classification through an automated scoring system. Utilizing variant allele frequency, disease prevalence and penetrance estimates, and inheritance mode, an automated score was calculated to assess if this variant is too frequent to cause the disease. Based on the score and internal cut-off values, a variant classified as benign is not then subjected to further curation. The score for this variant resulted in a classification of benign for this disease.
(Mut.Nbr. 3):**MASP2 c.891G>A (p.Ala297=) - MASP2 deficiency** This variant was observed in the ICSL laboratory as part of a predisposition screen in an ostensibly healthy population. It had not been previously curated by ICSL or reported in the Human Gene Mutation Database (HGMD: prior to June 1st, 2018), and was therefore a candidate for classification through an automated scoring system. Utilizing variant allele frequency, disease prevalence and penetrance estimates, and inheritance mode, an automated score was calculated to assess if this variant is too frequent to cause the disease. Based on the score and internal cut-off values, a variant classified as benign is not then subjected to further curation. The score for this variant resulted in a classification of benign for this disease.
(Mut.Nbr. 4):**MASP2 c.729C>T (p.Tyr243=) - MASP2 deficiency** This variant was observed in the ICSL laboratory as part of a predisposition screen in an ostensibly healthy population. It had not been previously curated by ICSL or reported in the Human Gene Mutation Database (HGMD: prior to June 1st, 2018), and was therefore a candidate for classification through an automated scoring system. Utilizing variant allele frequency, disease prevalence and penetrance estimates, and inheritance mode, an automated score was calculated to assess if this variant is too frequent to cause the disease. Based on the score and internal cut-off values, a variant classified as benign is not then subjected to further curation. The score for this variant resulted in a classification of benign for this disease.

Variant Statistics:

Mutation Number	Gene	DNA change	Transcript ID	AF in patient	Nbr. Reads	Quality	Frequency globally	Maximal AF globally	Population with maximal AF
1	MASP2	c.1479C>T	ENST00000400897.3	61.40%	57	42	79.41%	86.64%	East
2	MASP2	c.1130T>C	ENST00000400897.3	42.86%	21	62	4.95%	20.90%	East
3	MASP2	c.891G>A	ENST00000400897.3	45.00%	20	56	5.79%	25.19%	African
4	MASP2	c.729C>T	ENST00000400897.3	51.52%	33	66	2.00%	26.48%	African
5	MTHFR	c.1305C>T	ENST00000376592.1	52.17%	46	59	97.55%	100.00%	FIN

Note: Quality Score: <10 is low quality; 10-20 is medium quality; >20 is high quality

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Relevant Articles:

Number	Name of Mutation	Pubmed ID	Title
1	MASP2 c.1479C>T (p.Ser493=)	19405982	Lack of association between polymorphisms of MASP2 and susceptibility to SARS coronavirus infection.
1	MASP2 c.1479C>T (p.Ser493=)	24033266	A systematic approach to assessing the clinical significance of genetic variants.
1	MASP2 c.1479C>T (p.Ser493=)	24632598	Association of MASP-2 levels and MASP2 gene polymorphisms with rheumatoid arthritis in patients and their relatives.
1	MASP2 c.1479C>T (p.Ser493=)	27596159	Association of polymorphisms in genes of factors involved in regulation of splicing of cystic fibrosis transmembrane conductance regulator mRNA with acute respiratory distress syndrome in children with pneumonia.
2	MASP2 c.1130T>C (p.Val377Ala)	17252003	Deficiency of mannan-binding lectin associated serine protease-2 due to missense polymorphisms.
2	MASP2 c.1130T>C (p.Val377Ala)	19234189	Polymorphisms in mannan-binding lectin (MBL)-associated serine protease 2 affect stability, binding to MBL, and enzymatic activity.
2	MASP2 c.1130T>C (p.Val377Ala)	19405982	Lack of association between polymorphisms of MASP2 and susceptibility to SARS coronavirus infection.
2	MASP2 c.1130T>C (p.Val377Ala)	22380611	Mutations of complement lectin pathway genes MBL2 and MASP2 associated with placental malaria.
2	MASP2 c.1130T>C (p.Val377Ala)	24632598	Association of MASP-2 levels and MASP2 gene polymorphisms with rheumatoid arthritis in patients and their relatives.
3	MASP2 c.891G>A (p.Ala297=)	19405982	Lack of association between polymorphisms of MASP2 and susceptibility to SARS coronavirus infection.
5	MTHFR c.1305C>T (p.Phe435=)	16439441	Racial or ethnic differences in allele frequencies of single-nucleotide polymorphisms in the methylenetetrahydrofolate reductase gene and their influence on response to methotrexate in rheumatoid arthritis.
5	MTHFR c.1305C>T (p.Phe435=)	18483346	Direct genotyping of single nucleotide polymorphisms in methyl metabolism genes using probe-free high-resolution melting analysis.
5	MTHFR c.1305C>T (p.Phe435=)	19493349	118 SNPs of folate-related genes and risks of spina bifida and conotruncal heart defects.
5	MTHFR c.1305C>T (p.Phe435=)	22241680	Deep sequencing study of the MTHFR gene to identify variants associated with myelomeningocele.
5	MTHFR c.1305C>T (p.Phe435=)	23300409	Chapter 7: Pharmacogenomics.
6	MTHFR c.665C>T (p.Ala222Val)	1522835	Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects.
6	MTHFR c.665C>T (p.Ala222Val)	7564788	Mutated methylenetetrahydrofolate reductase as a risk factor for spina bifida.
6	MTHFR c.665C>T (p.Ala222Val)	7647779	A candidate genetic risk factor for vascular disease: a common mutation in methylenetetrahydrofolate reductase.
6	MTHFR c.665C>T (p.Ala222Val)	7741859	Homocysteine metabolism in pregnancies complicated by neural-tube defects.

6	MTHFR c.665C>T (p.Ala222Val)	8542260	A genetic defect in 5,10 methylenetetrahydrofolate reductase in neural tube defects.