DNA DRUGMAP: INHERITED THROMBOPHILIA :: FINAL REPORT

REPORT, SAMPLE			
PATIENT ID: FEMALE 42 YRS DATE OF BIRTH: 01/01/1972 ETHNICITY: UNKNOWN **ACCESSION: 0000-00000**		SPECIMEN	ORAL RINSE
		COLLECTED	05/27/2017
		RECEIVED	05/28/2017 10:22
		REPORTED	06/12/2017 13:35
		LOCATION	SAMPLE MEDICAL CLINIC
RELATED INFO		PHYSICIAN	ORDERING MD
PATIENT HISTORY	ANXIETY, DEPRESSION	REASON FOR TEST	

ORALDNA® LABS
Innovations in Salivary Diagnostics

7400 Flying Cloud Drive, Suite 150
Eden Prairie, MN 55344-3636
Phone: 855-323-0680
Fax: 952-942-0703
Medical Director: Ronald McGlennen MD
CLIA# 24D1033809
CAPLAP#: 7190878
Web Url: http://www.oraldna.com

DNA DRUGMAP™ PROFILE: INHERITED THROMBOPHILIA

List of Patient Medication(s): Effexor, olanzapine, *trazodone, *Flexeril, *Klonopin, Synthyroid

Category	Class	No Change in Dose	Prescribe with Caution	Avoid these Medications
Mood/Psychiatric	Antidepressants	doxepin desiprimine fluvoxamine nortriptyline ***trazodone** **Effexor** sertraline duloxetine mirtazapine paroxetine venlafaxine	*amitriptyline citalopram *levomilnacipran *fluoxetine escitalopram	*imipramine *clomipramine
Mood/Psychiatric	Anti-psychotics	aripiprazole **olanzapine** ziprasidone haloperidol pimozide *iloperidone	risperidone	
Pain Management	Muscle relaxant	carisoprodol		
Antiepileptic	Barbituate	*clonazepam ***Klonopin**	primidone	

(*) These medications are metabolized by more than one cytochrome p450 pathway and/or by alternative enzymatic pathways (e.g. 2B6, ACE, SCNN1A).

Pathologist Interpretation: The submitted sample reveals an Ultra Metabolizer (UM) phenotype for the pharmacogenetic markers CYP2C19. The effect of this phenotype is a marked increase (faster) rate of metabolism for common medications including selected treatments for depression, the platelet aggregation inhibitor clopridigrel and medications for the management of peptic ulcer disease. From the provided list of medications for this patient, none are metabolized by this enzymatic pathway. The additional pharmacogenetic markers, CYP2C9 and CYP2D6, as well as CYP3A4/5 each are predicted to be normal (Extensive) metabolizer phenotypes. For medications metabolized by these enzymatic pathways, including the psychoactive medications olanzaprine, Effexor and trazodone, please follow the manufacturer's recommended dosing when prescribing for this patient. A specific comment regarding olanzaprine, is focused on formulations involving the mixture of fluoxetine and olanzapine in that fluoxetine is a selective serotonin reuptake inhibitor and is metabolized by several cytochrome P450 enzymes with CYP2D6 being a major contributor. Olanzapine is an atypical antipsychotic metabolized by CYP2D6 and CYP1A2. Importantly, clearance of olanzapine is also influenced by smoking. There is also reported the genotyping results for a series of gene markers that separately effect the metabolism and mode of action of select medications. Based on the genotype for the gene marker ABCB1, (T/C), this patient may require a intermediate dose of opiates to achieve pain control. In the concern of management of depression or related psychiatric conditions, the combined genotype of the HTR2A and GRIK4 alleles predicts this patient to be likely of a normal response to serotonin-reuptake inhibitor medications. In the concern of the treatment of hyperlipidemia with simvastatin or related agents, this patient's genotype for SLCO1B1 (T/T) is predicted to be at normal risk for therapy-related myalgia. Clinical consultation regarding the pharmacogenetics of this medication may be indicated.

Cytochrome p450 Markers: Genotype and Phenotype Results		
Gene Marker	**Result**	**Metabolic Phenotype**
CYP2C19	Alleles:*1/*17	Ultrarapid Metabolizer (UM)
CYP2C9	Alleles:*1/*2	Normal (Extensive) Metabolizer (NM)
VKORC1	Alleles:A/A	
CYP2D6	Alleles:*1/*2	Normal (Extensive) Metabolizer (NM)
CYP3A4	Alleles:*1/*1	Normal Enzymatic Expression
CYP3A5	Alleles:*3/*3	No Enzymatic Expression

Ancillary Pharmacogenetic Markers: Genotype and Phenotype Results		
Gene Marker	**Result**	**Metabolic Phenotype**
SLCO1B1 37041 T>C	Genotype:T/T	Normal Risk of Myalgia
ABCB1 3435 C>T	Genotype:T/C	Intermediate Requirement for Opiate Medications
GRIK4 STAR*D C>T	Genotype:T/C	Normal Response to SSRNI
HTR2A (-)1438 A>G	Genotype:A/A	Decreased Risk of SSRI Side Effects
HTR2A 102 T>C	Genotype:T/T	Higher Risk of Affective Disorders
HTR2A A>G	Genotype:A/G	Normal Response to SSRNI
HTR2A C>G	Genotype:C/C	

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Gene Markers of Inherited Thrombophilia: Genotype and Risk Assessment		
Gene Marker	**Result**	**Thrombophilia Risk**
Prothrombin (Factor II: G20210A) Mutation	G/G (No Mutation Detected)	Not increased
Factor V Leiden (FVL: G1691A) Mutation	G/G (No Mutation Detected)	
MTHFR 677 C>T	C/C (No Mutation Detected)	Normal
MTHFR 1298 A>C	C/C (Homozygous)	Normal

Interpretation:
This individual is normal (homozygous wild type) for the Prothrombin G20210A and Factor V Leiden G1691A mutations. Additionally this individual is normal (homozygous wild type) for the MTHFR C677T variant and is homozygous (two copies of the abnormal gene) for the MTHFR A1298C variant.

Comments:
Significance: The evaluation of thrombophilia involves the assessment of genetic risks and other risk modifiers.
Consider: In consideration of these normal results for the Factor V Leiden, Factor II/Prothrombin G20210A mutation, and MTHFR C677T the likelihood that this individual carries one of the common genetic markers of inherited thrombophilia is eliminated. If clinically indicated, testing for less common markers of thrombophilia such as the plasminogen activator inhibitor type 1 (PAI-1 4G/5G) may be useful. The MTHFR A1298C variant in absence of C677T is not considered significant. Genetic counseling regarding these results is available.

Thrombophilia Risk Assessment

Genetic Risk
Not increased *

Risk Modifiers	
Pregnancy	**3 times**
Oral Contraceptives	**8 times**
Hormone Replacement Therapy	**4 times**

* Risks are compared to that of the general population. These risks are not intended to be multiplied, but are independent variables and are further influenced by other medical and environmental factors.

DNA DRUGMAP™ PROFILE: GUIDELINES, GENOTYPE RESULTS AND METHODOLOGY

Dosing Guidelines

*Published and/or consensus dosing guidelines are not available for this patient's list of medications.

Additional information on the dosing recommendation of specific medications is available at: http://www.pharmgkb.org

Genotyping Results	
CYP2C19	CYP2C19 rs12248560 (-)806 C>T: C/T CYP2C19 rs17884712 431 G>A: G/G CYP2C19 rs28399504 1 A>G: A/A CYP2C19 rs41291556 358 T>C: T/T CYP2C19 rs4244285 618 G>A: G/G CYP2C19 rs4986893 636 G>A: G/G CYP2C19 rs55640102 1473 A>C: A/A CYP2C19 rs56337013 1279 C>T: C/C CYP2C19 rs6413438 680 C>T: C/C CYP2C19 rs72552267 395 G>A: G/G CYP2C19 rs72558186 19294 T>A: T/T
CYP2C9/VKORC1	CYP2C9 rs1057910 1075 A>C:A/A CYP2C9 rs1799853 430 C>T:C/T CYP2C9 rs28371685 1003 C>T:C/C CYP2C9 rs28371686 1080 C>G:C/C CYP2C9 rs7900194 449 G>A:G/G CYP2C9 rs9332131 818delA:A/A VKORC1 rs17708472 A>G:G/G VKORC1 rs2359612 A>G:A/A VKORC1 rs7294 A>G:G/G VKORC1 rs8050894 C>G:G/G VKORC1 rs9934438 1173 C>T:T/T
CYP2D6	CYP2D6 rs1065852 100 C>T: C/C CYP2D6 rs1135822 1611T>A: T/T CYP2D6 rs1135823 1617G>T: G/G CYP2D6 rs1135824 1749A>G: A/A CYP2D6 rs1135840 4180 G>C: C/G CYP2D6 rs16947 2850 C>T: T/C CYP2D6 rs28371696 77G>A: G/G CYP2D6 rs28371706 1023 C>T: C/C CYP2D6 rs28371725 2988 G>A: G/G CYP2D6 rs35742686 2549delA: A/A CYP2D6 rs3892097 1846 G>A: G/G CYP2D6 rs5030655 1707delT: T/T CYP2D6 rs5030656 2615_2617delAAG: GAA/GAA CYP2D6 rs5030862 124 G>A: G/G CYP2D6 rs5030863 883 G>C: G/G CYP2D6 rs5030865 1758 G>T/G>A: G/G CYP2D6 rs5030867 2935A>C: A/A CYP2D6 rs59421388 3183 G>T: G/G CYP2D6 rs72549357 137_138insT: T/T CYP2D6 rs769258 31 G>A: G/G
CYP3A4/5	CYP3A4 rs12721627 554 C>G:C/C CYP3A4 rs12721629 1117 C>T:C/C CYP3A4 rs2242480 20239G>A:G/G CYP3A4 rs35599367 6 C>T:C/C CYP3A4 rs4986909 1247C>T:C/C CYP3A4 rs4987161 566 T>C:T/T CYP3A4 rs67784355 1088C>T:C/C CYP3A4 rs72552799 1389G>A:G/G CYP3A5 rs776746 6986 A>G:G/G
FII/FV/MTHFR	Prothrombin rs1799963 20210 G>A:Normal(G) : Normal(G) Factor V Leiden rs6025 1691 G>A:Normal(G) : Normal(G) MTHFR rs1801133 677 C>T:Normal(C) : Normal(C) MTHFR rs1801131 1298 A>C:Mutant(C) : Mutant(C)
Other	ABCB1 rs1045642 3435 C>T: T/C GRIK4 rs1954787 C>T: T/C HTR2A rs6311 (-)1438 A>G: A/A HTR2A rs6313 102 T>C: T/T HTR2A rs7997012 A>G: A/G HTR2A rs9316233 C>G: C/C SLCO1B1 rs4149056 37041 T>C: T/T

Methodology: Genomic DNA was subjected to amplification by methods of target enrichment, a version of nested patch PCR, then sequenced using a MiSeq. The resulting DNA sequences were analyzed using alignment and base call algorithms in the Kailos Blue software. This assay may not determine genotypic differences in the CYP2D6 *2 allele from other more rare CYP2D6 haplotypes. The patient report was created by the review of these analyzed data along with the selection of medical comment and recommendations via TeleGene, a proprietary laboratory information system of Access Genetics, LLC. Technical assay performed by Kailos Genetics, Huntsville, AL 855-323-0680.

Interpreter: Ronald McGlennen MD, FCAP, FACMG,ABMG

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