

CYTOCHROME P450 2D6 GENOTYPE FOR TAMOXIFEN HORMONAL THERAPY #87966

EXPLANATION: This assay has been enhanced by an addition of several polymorphisms (SNPs) to the list of potential findings. Also, effective with the detection of the additional SNPs, the individual SNP results will be reported along with the current interpretation field. This will require file definition changes.

NOTE: Specimen requirements and fees will remain unchanged.

CURRENT CPT CODE:

"Cytochrome P450 2D6 Genotype for Tamoxifen Hormonal
Therapy"
83892/Enzymatic digestion
83896/x14 Nucleic acid probe, each
83900/Amplification, target, multiplex, first 2 nucleic acid sequences
83912/Interpretation and report

"Rapid DNA Extraction"
83890

NEW CPT CODE:

"Cytochrome P450 2D6 Genotype for Tamoxifen Hormonal
Therapy"
83892/Enzymatic digestion
83900/Amplification, target, multiplex, first 2 nucleic acid sequences
83901/x2 Amplification, target, multiplex, each additional nucleic acid
83912/Interpretation and report
83914/x17 Mutation identification by enzymatic ligation or primer

"Rapid DNA Extraction"
83890

QUESTIONS: Contact your Mayo Medical Laboratories' Regional Manager
Shirley Pokorski, Mayo Medical Laboratories' Technologist Support
Telephone: 800-533-1710



TEST DEFINITION

5/15/2009

MML NAME/ORDER CODE CROSS-REFERENCE

CODE NAME

87966 CYP2D6 GENOTYPE - TAMOXIFEN THERAPY

MML MML TEST SETUP INFORMATION

ORDER CODE	EFF DATE	TC	TITLE	CHECKING NORMALS	PRINT NORMALS (# CODED)	PERFORM SITE *
87966	4/7/2009		CYP2D6 GENOTYPE - TAMOXIFEN THERAPY			MCR
			UNIT CODE ALWAYS MESSAGE - [ZIUO]			
			INVESTIGATIONAL USE ONLY			
			TRANSPORT TEMP : AMBIENT\FROZEN OK\REFRIG OK			
			45520 2D6 TAMOXIFEN PHENOTYPE INTERP			
			- - - - -			
			26775 2D6 TAMOXIFEN GENOTYPE STAR ALLELES			
			TEST CODE ALWAYS MESSAGE - [Z26775]			
			Z26775 SEE HTTP://WWW.CYPALLELES.KI.SE/CYP2D6.HTM FOR A FULL			
			DESCRIPTION OF CYP2D6 ALLELES.			
			- - - - -			
			26758 2D6T DUPLICATION			
			- - - - -			
			26759 2D6T DELETION			
			- - - - -			
			26760 2D6T -1584c>g (*2A)			
			- - - - -			
			26761 2D6T 100c>t (*10)			
			- - - - -			
			26762 2D6T 124g>a (*12)			
			- - - - -			
			30797 2D6T 138INST (*15)			
			- - - - -			
			26763 2D6T 883g>c (*11)			
			- - - - -			
			26764 2D6T 1023c>t (*17)			
			- - - - -			

MML TEST SETUP INFORMATION

ORDER CODE	EFF DATE	TC	TITLE	CHECKING NORMALS	PRINT NORMALS (# CODED)	PERFORM SITE *
87966	(CONTINUED)					
		26766	2D6T 1707TDEL (*6)			
		26767	2D6T 1758G>T/A (*8/*14)			
		26768	2D6T 1846G>A (*4)			
		26769	2D6T 2549ADEL (*3)			
		26770	2D6T 2613AGADEL (*9)			
		26771	2D6T 2850C>T (*2)			
		26772	2D6T 2935A>C (*7)			
		26773	2D6T 2988G>A (*41)			
		45521	2D6 TAMOXIFEN GENOTYPE INTERP			
		26776	2D6 TAMOXIFEN REVIEWED BY			

POSSIBLE RESULT VALUES INCLUDE : DENNIS J. O'KANE, PH.D., JOHN L. BLACK, M.D., LINNEA M. BAUDHUIN, PH.D., LORALIE J. LANG.
 TEST CODE ALWAYS MESSAGE - [Z87966A]

Z87966A DIRECT POLYMORPHISM ANALYSIS FOR -1584C>G, 100C>T, 124G>A, 138INS T, 883G>C, 1023C>T, 1707T>DEL, 1758G>T, 1758G>A, 1846G>A, 2549A>DEL, 2613DELAGA, 2850C>T, 2935A>C, 2988G>A, CYP2D6 GENE DELETION, AND GENE DUPLICATION IS PERFORMED FOLLOWING PCR AMPLIFICATION. DIRECT DNA TESTING WILL NOT DETECT ALL THE KNOWN MUTATIONS THAT RESULT IN DECREASED OR INACTIVE CYP2D6. ABSENCE OF A DETECTABLE GENE MUTATION OR POLYMORPHISM DOES NOT RULE OUT THE POSSIBILITY THAT A PATIENT HAS AN INTERMEDIATE OR POOR METABOLIZER PHENOTYPE. BASED ON THE TEST SENSITIVITY AND CURRENTLY AVAILABLE CYP2D6 POLYMORPHISM CARRIER FREQUENCIES, PERSONS OF CAUCASIAN DESCENT WHO TESTED NEGATIVE FOR THE ABOVE POLYMORPHISMS WOULD BE ESTIMATED TO HAVE A LESS THAN 1.4% RESIDUAL RISK FOR CARRYING ONE OR MORE COPIES OF AN UNDETECTED POOR METABOLIZER ALLELE. THIS RESIDUAL RISK MAY BE HIGHER OR LOWER IN OTHER ETHNIC GROUPS. THE FREQUENCY OF POLYMORPHISMS CAUSING POOR METABOLISM IS HIGHEST IN THE CAUCASIAN POPULATION AND LOWER IN AFRICAN AMERICANS AND ASIANS. PATIENTS WITH AN EXTENSIVE (NORMAL) OR INTERMEDIATE METABOLIZER GENOTYPE MAY HAVE CYP2D6 ENZYME ACTIVITY INHIBITED BY A VARIETY OF MEDICATIONS, OR THEIR METABOLITES. BECAUSE ANTIDEPRESSANTS ARE OFTEN PRESCRIBED TO ALLEVIATE THE HOT FLASHES THAT ACCOMPANY TAMOXIFEN THERAPY, IT IS PARTICULARLY IMPORTANT TO UTILIZE AN ANTIDEPRESSANT THAT DOES NOT COMPROMISE

CYP2D6 ACTIVITY, WHICH COULD REDUCE TAMOXIFEN'S EFFICACY.
THE FOLLOWING IS A PARTIAL LISTING OF DRUGS KNOWN TO AFFECT
CYP2D6 ACTIVITY AS OF THE DATE OF THIS REPORT.
DRUGS THAT INHIBIT CYP2D6 SIGNIFICANTLY:
AMIODARONE, CIMETIDINE, COCAINE, DEXMEDETOMIDINE,
FLUOXETINE, PAROXETINE, PERAZINE, PERPHENAZINE,
PERGOLIDE, PIMOZIDE, QUINIDINE, SERTRALINE,
AND THIORIDAZINE.

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MML MML TEST SETUP INFORMATION

*PERFORMING SITE LEGEND

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MCR	MAYO CLINIC DPT OF LAB MED & PATHOLOGY	LAB DIRECTOR:	FRANKLIN R. COCKERILL, III, M.D.
	200 FIRST STREET SW		
	ROCHESTER, MN 55905		

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MML MESSAGES USED AS NORMALS
CODE TEXT

TOTAL OF 0 NORMALS CODES

*** END OF REPORT ***



TEST DEFINITION

2/11/2009

MML NAME/ORDER CODE CROSS-REFERENCE
CODE NAME

81769 RAPID DNA EXTRACTION

MML		MML TEST SETUP INFORMATION			PERFORM	
ORDER CODE	EFF DATE	TC	TITLE	CHECKING NORMALS	PRINT NORMALS (# CODED)	SITE *
81769	5/25/2007		RAPID DNA EXTRACTION			MCR
			TRANSPORT TEMP : AMBIENT\FROZEN OK\REFRIG OK			
			28357 COMMENT			

*PERFORMING SITE LEGEND

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MCR	MAYO CLINIC DPT OF LAB MED & PATHOLOGY	LAB DIRECTOR:	FRANKLIN R. COCKERILL, III, M.D.
	200 FIRST STREET SW		
	ROCHESTER, MN 55905		

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MML MESSAGES USED AS NORMALS
CODE TEXT

TOTAL OF 0 NORMALS CODES

*** END OF REPORT ***



LABORATORY SERVICE REPORT

1-800-533-1710

PATIENT NAME TESTING, JAMIE		PATIENT NUMBER		AGE 29	SEX F	ACCESSION # G9127092
ORDERING PHYSICIAN		CLIENT ORDER #			ACCOUNT # LIAISONS	
COLLECTION 05/14/09 02:41 P	RECEIVED 05/14/09 02:41 P	REPORT PRINTED 05/15/09 01:57 P		SPECIMEN INFORMATION DATE OF BIRTH:		
DATE	TIME	DATE	TIME			
Test Client Attn: Mayo Liaisons 200 First Street SW Rochester, MN 55905 507-284-8202						

TEST REQUESTED	HI LO	REF RANGE	PERFORM SITE *
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Rapid DNA Extraction

Comment	Genomic DNA was extracted.	MCR
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CYP2D6 Genotype - Tamoxifen Therapy

2D6 Tamoxifen		MCR
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Phenotype Interp

Predicted poor metabolizer

This patient has a genotype associated with a poor tamoxifen metabolizer phenotype. Patients who have this phenotype have significantly lower levels of the important tamoxifen metabolite, endoxifen. Postmenopausal women with this genotype are at increased risk of breast cancer recurrence when treated with tamoxifen as adjuvant therapy for early breast cancer. Other treatment options should be considered.

2D6 Tamoxifen	3/3	MCR
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Genotype Star Alleles

See <http://www.cypalleles.ki.se/cyp2d6.htm> for a full description of CYP2D6 alleles.

2D6T Duplication	NO DUP	MCR
2D6T Deletion	NO DEL	MCR
2D6T -1584c>g (*2A)	C/C	MCR
2D6T 100c>t (*10)	C/C	MCR
2D6T 124g>a (*12)	G/G	MCR
2D6T 138inst (*15)	WT	MCR
2D6T 883g>c (*11)	G/G	MCR
2D6T 1023c>t (*17)	C/C	MCR
2D6T 1707tdel (*6)	T/T	MCR
2D6T 1758g>t/a (*8/*14)	G/G	MCR
2D6T 1846g>a (*4)	G/G	MCR
2D6T 2549adel (*3)	del/del	MCR

* Perform Site Legend on last page of report

PATIENT NAME TESTING, JAMIE	ORDER STATUS Final	COLLECTION DATE AND TIME 05/14/09 02:41 P
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LABORATORY SERVICE REPORT

1-800-533-1710

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DATE	TIME	DATE	TIME			
Test Client Attn: Mayo Liaisons 200 First Street SW Rochester, MN 55905 507-284-8202						

TEST REQUESTED	HI LO	REF RANGE	PERFORM SITE *
2D6T 2613agadel (*9)	WT		MCR
2D6T 2850c>t (*2)	C/C		MCR
2D6T 2935a>c (*7)	A/A		MCR
2D6T 2988g>a (*41)	G/G		MCR
2D6 Tamoxifen			MCR

Genotype Interp

This patient has two copies of null CYP2D6 alleles. Additional descriptions of the effects of the star alleles on CYP2D6 function are found in the Mayo Test Catalog (<http://www.mayomedicallaboratories.com/test-catalog/>).

2D6 Tamoxifen

Dennis J. O'Kane, Ph.D.

MCR

Reviewed by

Direct polymorphism analysis for -1584C>G, 100C>T, 124G>A, 138insT, 883G>C, 1023C>T, 1707T>del, 1758G>T, 1758G>A, 1846G>A, 2549A>del, 2613delAGA, 2850C>T, 2935A>C, 2988G>A, CYP2D6 gene deletion, and gene duplication is performed following PCR amplification. Direct DNA testing will not detect all the known mutations that result in decreased or inactive CYP2D6. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has an intermediate or poor metabolizer phenotype. Based on the test sensitivity and currently available CYP2D6 polymorphism carrier frequencies, persons of Caucasian descent who tested negative for the above polymorphisms would be estimated to have a less than 1.4% residual risk for carrying one or more copies of an undetected poor metabolizer allele. This residual risk may be higher or lower in other ethnic groups. The frequency of polymorphisms causing poor metabolism is highest in the Caucasian population and lower in African Americans and Asians. Patients with an extensive (normal) or intermediate metabolizer genotype may

* Perform Site Legend on last page of report

PATIENT NAME TESTING, JAMIE	ORDER STATUS Final	COLLECTION DATE AND TIME 05/14/09 02:41 P
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LABORATORY SERVICE REPORT

1-800-533-1710

PATIENT NAME TESTING, JAMIE		PATIENT NUMBER		AGE 29	SEX F	ACCESSION # G9127092
ORDERING PHYSICIAN		CLIENT ORDER #				ACCOUNT # LIAISONS
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DATE	TIME	DATE	TIME			
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TEST REQUESTED	HI LO	REF RANGE	PERFORM SITE *
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have CYP2D6 enzyme activity inhibited by a variety of medications, or their metabolites. Because antidepressants are often prescribed to alleviate the hot flashes that accompany tamoxifen therapy, it is particularly important to utilize an antidepressant that does not compromise CYP2D6 activity, which could reduce tamoxifen's efficacy. The following is a partial listing of drugs known to affect CYP2D6 activity as of the date of this report.

Drugs That Inhibit CYP2D6 Significantly:

Amiodarone, cimetidine, cocaine, dexmedetomidine, fluoxetine, paroxetine, perazine, perphenazine, pergolide, pimozide, quinidine, sertraline, and thioridazine.

Investigational Use Only

* PERFORMING SITE

MCR	Mayo Clinic Dpt of Lab Med & Pathology 200 First Street SW Rochester, MN 55905	Lab Director: Franklin R. Cockerill, III, M.D.
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PATIENT NAME TESTING, JAMIE	ORDER STATUS Final	COLLECTION DATE AND TIME 05/14/09 02:41 P
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Specimen receipt and report times are in CST/CDT

REPRINT

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