



Genecept Assay® Report

Ordering Clinician: JIM STEVENSON, 123 Test boul., MONTREAL QC H3Z 2Y7

Patient:	Jon Johnson
Patient DOB:	1989-03-22
Ordering Clinician:	JIM STEVENSON
Sample Type:	Buccal
Panel Ordered:	Genecept Assay 2.0

Requisition Number:	2131dsdd
Accession ID:	101340
Sample Collection Date:	2017-05-05
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Electronically Signed By
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Literature Information Reviewed By
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How to read this Report

The information contained in this report is based upon research related to common genetic polymorphisms and their influence on behavior, psychiatric states and drug response. Interpretive comments focus only on psychotropic therapies. Implications related to non-psychotropic therapies may vary and are not considered in this report. These results are not intended to diagnose or make specific treatment recommendations. All images are for illustrative purposes only. The medications and treatments within this report are not intended to be comprehensive or prescriptive.

Personalized Consultation Available for Clinicians

Our Clinical Support Team is available to provide clinical interpretation of the biomarkers and translate the genetic test results to potential treatment strategies, as well as answer questions you may have concerning the report. This complimentary service is included with all Genecept Assay tests.

Contact us to arrange a consult at your convenience:

Phone: 888.988.1888
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References:

Please contact Dynacare to request a copy of the Literature Summary at DynacareNext@dynacare.ca or 888.988.1888.

RESULTS REPORT: Pharmacodynamic Gene Variations; Drug Target Sites



Use caution with related therapies



Therapeutic options



No known gene-drug interaction

GENE RESULT	THERAPEUTIC IMPLICATIONS	INTERACTION	CLINICAL IMPACT
<p>Serotonin Transporter (SLC6A4) L(G)/L(G) [Higher risk of non-response]</p>	<p>SLC6A4 is a presynaptic transmembrane protein responsible for serotonin reuptake</p> <ul style="list-style-type: none"> SSRIs act by blocking this transporter to produce a therapeutic response Higher risk of poor response, slow response or intolerance to SSRIs Potential for increased cortisol release in response to stress in S/S, L(G)/S or L(G)/L(G) patients Therapeutic options such as SNRIs or other non-SSRI antidepressants may be used if clinically indicated 	 	<p>Use caution with SSRIs</p> <p>Therapeutic options: SNRIs or non-SSRI antidepressants may be used if clinically indicated</p>
<p>Calcium Channel (CACNA1C) A/A [Increased risk of altered neuronal signaling]</p>	<p>CACNA1C is a subunit of L-type voltage gated calcium channels which is involved in excitatory signaling in the brain</p> <ul style="list-style-type: none"> Altered calcium signaling may be clinically associated with impairment of mood or cognition 		<p>Therapeutic options: atypical antipsychotics, mood stabilizers and/or omega-3 fatty acids may be used if clinically indicated</p>
<p>Serotonin Receptor 2C (5HT2C) C/C [Weight gain risk]</p>	<p>5HT2C is a receptor involved in the regulation of satiety</p> <ul style="list-style-type: none"> Atypical antipsychotics act by blocking this receptor Patients with the C/C genotype have risk of weight gain with atypical antipsychotics, however, this is the most common genotype Metformin, lorcaserin or other anti-obesity interventions may be beneficial to mitigate weight gain 	 	<p>Use caution with atypical antipsychotics</p> <p>Therapeutic options: metformin, lorcaserin or other anti-obesity interventions may be used if clinically indicated</p>
<p>Dopamine 2 Receptor (DRD2) C/DEL [Intermediate risk for poor response]</p>	<p>DRD2 is a receptor affected by dopamine in the brain</p> <ul style="list-style-type: none"> DRD2 is modulated by antipsychotic agents Higher risk of poor response and weight gain with antipsychotics due to reduced expression and receptor density Patients with a DEL allele may be at higher risk of opioid dependence 		<p>Use caution with antipsychotics and opioids</p>
<p>Catechol-O-Methyltransferase (COMT) Met/Met [Low activity]</p>	<p>COMT is an enzyme responsible for breakdown of dopamine in the frontal cortex of the brain</p> <ul style="list-style-type: none"> Risk for reduced COMT enzyme activity and a parallel ↑ in frontal cortex dopamine Met/Met patients may derive less executive function benefit from dopaminergic stimulants Met/Met patients with psychotic disorders may demonstrate an improved response to atypical antipsychotics compared to Val/Val patients Met/Met patients with psychotic disorders may experience cognitive improvement with atypical antipsychotics compared to Val/Val patients 	 	<p>Use caution with dopaminergic stimulants</p> <p>Therapeutic options: atypical antipsychotics may be used for psychotic-related disorders if clinically indicated</p>
<p>Methylenetetrahydrofolate Reductase (MTHFR) C677T: C/T A1298C: A/A [Intermediate activity]</p>	<p>MTHFR is an enzyme responsible for the conversion of folic acid to methylfolate which is a cofactor needed for serotonin, norepinephrine and dopamine synthesis</p> <ul style="list-style-type: none"> Risk for reduced MTHFR enzyme activity and reduced methylfolate production L-methylfolate supplementation of SSRIs and SNRIs show improved symptom reduction and medication adherence compared to SSRIs/SNRIs alone in Major Depressive Disorder L-methylfolate may be an effective monotherapy for patients with Major Depressive Disorder 		<p>Therapeutic options: L-methylfolate may be used if clinically indicated</p>
<p>Brain-derived Neurotrophic Factor (BDNF) Val/Met</p>	<p>BDNF is a protein involved in neuronal development and neural plasticity</p> <ul style="list-style-type: none"> Potential risk for increased depression symptoms, impaired working memory, and altered stress response Studies have shown that Met carriers may have less satisfactory response to SSRIs in Caucasians, but not Asians, however larger studies need to be conducted to confirm these findings Exercise has been linked to improvements in cognition, and recent studies show that Met allele carriers may demonstrate enhanced effects of exercise on working memory compared to Val/Val patients 		<p>Therapeutic options: increased levels of physical activity/exercise if clinically appropriate</p>
<p>Glutamate Receptor Kainate 1 (GRIK1) C/C [Likely to respond]</p>	<p>GRIK1 is an excitatory neurotransmitter receptor</p> <ul style="list-style-type: none"> Patients of European descent with the C/C genotype are more likely to respond to treatment with topiramate for chronic alcohol abuse and alcoholism compared to patients with the A allele 		<p>Therapeutic options: topiramate may be used for alcohol abuse if clinically indicated</p>



Use caution with related therapies



Therapeutic options



No known gene-drug interaction

GENE RESULT	THERAPEUTIC IMPLICATIONS	INTERACTION	CLINICAL IMPACT
Sodium Channel (ANK3) C/T [Intermediate risk of altered neuronal signaling]	<i>ANK3 is a protein that plays a role in sodium ion channel function and is involved in excitatory signaling in the brain</i> <ul style="list-style-type: none"> A single T allele confers a modest increased risk for altered neuronal signaling, however this modest increased risk is unlikely to be clinically significant This genotype confers normal activity 		There are no known gene-drug interactions for this genotype
Melanocortin 4 Receptor (MC4R) C/C [Normal]	<i>MC4R is a receptor that plays a central role in the control of food intake</i> <ul style="list-style-type: none"> MC4R is involved in antipsychotic-induced weight gain This genotype confers normal activity 		There are no known gene-drug interactions for this genotype
Alpha-2A Adrenergic Receptor (ADRA2A) C/C [Normal response]	<i>ADRA2A is a receptor which plays an important role in neurotransmitter release</i> <ul style="list-style-type: none"> ADRA2A is involved in response to stimulants This genotype confers normal activity 		There are no known gene-drug interactions for this genotype
μ-Opioid Receptor (OPRM1) A/A [Normal response]	<i>OPRM1 is an opioid receptor which is affected by natural and synthetic compounds</i> <ul style="list-style-type: none"> OPRM1 is involved in response to opioids This genotype confers normal activity 		There are no known gene-drug interactions for this genotype

RESULTS REPORT: Pharmacokinetic Gene Variations; CYP450 Drug Metabolism

GENE RESULT	THERAPEUTIC IMPLICATIONS	INTERACTION	CLINICAL IMPACT
CYP2C19 IM *1/*2 [Intermediate activity]	Intermediate metabolizer: ↑ risk of elevated serum levels and drug interactions <ul style="list-style-type: none"> A dose adjustment or alternate therapy may be necessary 		Use caution with medications metabolized by CYP2C19 See Drug Interaction Summary for details
CYP2D6 IM *4/*41 [Intermediate activity]	Intermediate metabolizer: ↑ risk of elevated serum levels, drug interactions, and ↓ production of active moieties <ul style="list-style-type: none"> A dose adjustment or alternate therapy may be necessary 		Use caution with medications metabolized by CYP2D6 See Drug Interaction Summary for details
CYP3A4 *1/*1 CYP3A5 *1/*3 Fast Metabolizer [High activity]	High activity metabolizer: ↑ metabolism of drugs leading to poorer efficacy due to ↓ serum levels. Possible adverse events associated with toxic metabolites <ul style="list-style-type: none"> A dose adjustment or alternate therapy may be necessary CYP3A activity is determined by the sum activity of the CYP3A family of genes; in adults the most influential are CYP3A4 and 3A5 		Use caution with medications metabolized by CYP3A4/5 See Drug Interaction Summary for details
CYP1A2 EM *1A/*1F [Normal activity and risk for induction in the presence of inducers]	<i>Variations in the CYP1A2 liver enzyme can result in altered drug metabolism and unexpected drug serum levels</i> <ul style="list-style-type: none"> This genotype confers normal activity This patient, however, in the presence of inducers, is at risk for induction of CYP1A2 which may increase metabolism due to the presence of the *1F allele (see the Genecept Assay Report Interpretation Guide for full list of inducers) 		There are no known gene-drug interactions for this genotype
CYP2B6 EM *1/*1 [Normal activity]	<i>Variations in the CYP2B6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels</i> <ul style="list-style-type: none"> This genotype confers normal activity 		There are no known gene-drug interactions for this genotype
CYP2C9 EM *1/*1 [Normal activity]	<i>Variations in the CYP2C9 liver enzyme can result in altered drug metabolism and unexpected drug serum levels</i> <ul style="list-style-type: none"> This genotype confers normal activity 		There are no known gene-drug interactions for this genotype

This is based upon a review of the literature that is suggestive of treatments which may be appropriate and those that may be used with caution or avoided. Clinicians should review the full prescribing information of treatments being considered and should make their own treatment decisions based upon their knowledge as it relates to the patient. The selection of any therapeutic option is at the sole discretion of the prescriber. The physician is a learned intermediary and should be making all decisions based on experience and knowledge as related to the patient. The prescriber is expected to be well versed in the adverse effects and monitoring parameters of any medications prescribed or recommended to patients. Medications in this report are listed in alphabetical order; listing of medications is not meant to imply comparable efficacy or safety. Brand names are listed for exemplary purposes only; additional brand names exist and Genomind does not endorse or support any particular product. All registered trademarks are the property of their respective owners.

Drug Interaction Summary:

This summary provides a listing of implications for psychotropic and pain medications specific to your patient's genetic profile

Medication	Primary metabolizing enzyme(s)	Use as Directed	Therapeutic Options	Use with Caution		
		No known gene-drug interactions	Options which may be used if clinically indicated	CYP450		
				Serum levels may be ↑ [reduced dose may be required]	Serum levels may be ↓ [increased dose may be required]	Increased risk for adverse events or poor response
Antidepressants			SLC6A4			SLC6A4
SSRIs	Citalopram (Celexa®)	2C19, 3A4/5, 2D6		✓		✓
	Escitalopram (Lexapro®)	2C19, 2D6		✓		✓
	Fluoxetine (Prozac®)	2D6, 2C9		✓		✓
	Fluvoxamine (Luvox®)	2D6, 1A2		✓		✓
	Paroxetine (Paxil®)	2D6		✓		✓
	Sertraline (Zoloft®)	MultiCYP [11]				✓
SNRIs	Desvenlafaxine (Pristiq®)	--	✓			
	Duloxetine (Cymbalta®)	1A2, 2D6		✓		
	Levomilnacipran (Fetzima®)	3A4/5			✓	
	Venlafaxine (Effexor®) [1]	2D6, 2C19			Prodrug[1]	
Other	Bupropion (Wellbutrin®) [1]	2B6	✓			
	Mirtazapine (Remeron®)	2D6, 3A4/5, 1A2			Indeterminate[2]	
	Trazodone (Desyrel®, Olepto®)	3A4/5		✓		✓
	Vilazodone (Viibryd®)	3A4/5		✓		✓
	Vortioxetine (Trintellix®)	2D6		✓		
TCAs	Amitriptyline (Elavil®)	2D6, 2C19		✓		
	Clomipramine (Anafranil®)	2D6, 2C19, 1A2		✓		
	Desipramine (Norpramin®)	2D6		✓		
	Doxepin (Sinequan®)	2D6		✓		
	Imipramine (Tofranil®)	2D6, 2C19, 1A2		✓		
	Nortriptyline (Pamelor®)	2D6		✓		
	Trimipramine (Surmontil®)	2D6, 2C19, 3A4/5		✓		
MAOIs	Phenelzine (Nardil®)	--	✓			
	Selegiline (Eldepryl®, Emsam®)	2B6	✓			
	Tranylcypromine (Parnate®)	--	✓			
Mood Stabilizers/Anticonvulsants			CACNA1C, GRIK1			
	Carbamazepine (Tegretol®)	3A4/5		✓	✓	
	Gabapentin (Neurontin®, Gralise®)	--	✓	✓		
	Lamotrigine (Lamictal®)	--	✓	✓		
	Lithium (Lithobid®, Eskalith®)	--	✓	✓		
	Oxcarbazepine (Trileptal®)	--	✓	✓		
	Pregabalin (Lyrica®)	--	✓	✓		
	Topiramate (Topamax®)	--	✓	✓		
	Valproate (Depakote®, Depakene®)	2C9	✓	✓		

*See last page for drug interaction summary footnotes

Drug Interaction Summary:

This summary provides a listing of implications for psychotropic and pain medications specific to your patient's genetic profile

Medication	Primary metabolizing enzyme(s)	Use as Directed	Therapeutic Options	Use with Caution		Increased risk for adverse events or poor response
		No known gene-drug interactions	Options which may be used if clinically indicated	CYP450		
				Serum levels may be ↑ [reduced dose may be required]	Serum levels may be ↓ [increased dose may be required]	
Atypical Antipsychotic						5HT2C, DRD2
Aripiprazole (Abilify®)	2D6, 3A4/5			✓		✓ [4]
Asenapine (Saphris®)	1A2					✓ [4]
Brexpiprazole (Rexulti®)	2D6, 3A4/5			Indeterminate[2]		✓ [4]
Cariprazine (Vraylar®)	3A4/5				✓	✓ [4]
Clozapine (Clozaril®)	1A2, 2D6, 3A4/5			✓		✓ [4]
Lurasidone (Latuda®)	3A4/5				✓	✓ [4]
Olanzapine (Zyprexa®)	1A2					✓ [4]
Paliperidone (Invega®)	--					✓ [4]
Quetiapine (Seroquel®)	3A4/5				✓	✓ [4]
Risperidone (Risperdal®)	2D6			✓		✓ [4]
Zeldox (Geodon®)	--					✓ [4]
Typical Antipsychotic						DRD2
Chlorpromazine (Largactil®, Thorazine®)	2D6			✓		✓ [4]
Fluphenazine (Prolixin®)	2D6			✓		✓ [4]
Haloperidol (Haldol®)	2D6, 3A4/5			Indeterminate[2]		✓ [4]
Loxapine (Loxitane®)	MultiCYP [11]					✓ [4]
Perphenazine (Trilafon®)	2D6			✓		✓ [4]
Pimozide (Orap®)	2D6, 3A4/5			✓		✓ [4]
Promethazine (Phenegan®)	2D6			✓		✓ [4]
Thiothixene (Navane®)	1A2					✓ [4]
Trifluoperazine (Stelazine®)	1A2					✓ [4]
Anxiolytic						
Alprazolam (Xanax®)	3A4/5				✓	
Buspirone (Buspar®)	3A4/5				✓	
Chlordiazepoxide (Librium®)	3A4/5				✓	
Clonazepam (Klonopin®)	3A4/5				✓	
Clorazepate (Tranxene®)	--	✓				
Diazepam (Valium®)	2C19, 3A4/5			Indeterminate[2]		
Hydroxyzine (Vistaril®)	--	✓				
Lorazepam (Ativan®)	--	✓				
Oxazepam (Serax®)	--	✓				
Propranolol (Inderal®)	2D6, 1A2, 2C19			✓		
Temazepam (Restoril®)	--	✓				
Dopaminergic Stimulants Agents						COMT
Amphetamine-Dextroamphetamine (Adderall®, Evekeo®, Dyanavel®, Adzenys®)	2D6			✓		✓
Dextroamphetamine (Dexedrine®, Procentra®, Zenzedi®)	--					✓
Lisdexamfetamine (Vyvanse®)	--					✓
Methylphenidate (Ritalin®, Concerta®, Daytrana®, Metadate®)	--					✓

*See last page for drug interaction summary footnotes

Drug Interaction Summary:

This summary provides a listing of implications for psychotropic and pain medications specific to your patient's genetic profile

Medication	Primary metabolizing enzyme(s)	Use as Directed	Therapeutic Options	Use with Caution		
		No known gene-drug interactions	Options which may be used if clinically indicated	CYP450		Increased risk for adverse events or poor response
				Serum levels may be ↑ [reduced dose may be required]	Serum levels may be ↓ [increased dose may be required]	
Miscellaneous Stimulants; NRIs; α2-Agonists						
Atomoxetine (Strattera®)	2D6			✓		
Clonidine (Kapvay®)	2D6			✓		
Guanfacine (Intuniv®)	3A4/5				✓	
Modafinil (Provigil®)	3A4/5				✓	
Alternative/Complementary			CACNA1C, MTHFR			
L-methylfolate (Deplin®, EnLyte®)	--	✓	✓			
Omega-3-Fatty Acids	--	✓	✓			
Sleep Modulator						
Eszopiclone (Lunesta®)	3A4/5				✓	
Ramelteon (Rozerem®)	1A2	✓ [6]				
Suvorexant (Belsomra®)	3A4/5, 2C19				✓	
Starnoc (Sonata®)	3A4/5				✓	
Zolpidem (Ambien®)	3A4/5				✓	
Pain						DRD2
Non-opioid analgesics						
Acetaminophen (Tylenol®)	--	✓				
Celecoxib (Celebrex®)	2C9	✓				
Diclofenac (Voltaren®, Cataflam®)	2C9	✓				
Flurbiprofen (Ansaid®)	2C9	✓				
Ibuprofen (Advil®, Motrin®)	2C9	✓				
Ketorolac (Toradol®)	--	✓				
Meloxicam (Mobic®)	2C9	✓				
Naproxen (Aleve®, Naprosyn®)	1A2, 2C9	✓ [6]				
Piroxicam (Feldene®)	2C9	✓				
Opioids						
Alfentanil (Alfenta®)	3A4/5				✓	✓ [12]
Codeine [1]	2D6			Prodrug[1]		✓ [12]
Fentanyl (Duragesic®)	3A4/5				✓	✓ [12]
Hydrocodone [1]	2D6			Prodrug[1]		✓ [12]
Hydromorphone (Dilaudid®)	--					✓ [12]
Meperidine (Demerol®)	2B6, 3A4/5				✓	✓ [12]
Methadone (Dolophine®, Methadose®)	3A4/5, 2B6				✓	✓ [12]
Morphine (MS Contin®, Kadian®)	--					✓ [12]
Oxycodone (Oxycontin®)	2D6, 3A4/5			Indeterminate[2]		✓ [12]
Tapentadol (Nucynta®)	--					✓ [12]
Tramadol (Ultram®)	2D6, 3A4/5			✓		✓ [12]
Miscellaneous			5HT2C			
Baclofen (Lioresal®)	--	✓				
Buprenorphine (Butrans®)	3A4/5				✓	
Buprenorphine/Naloxone (Suboxone®)	3A4/5				✓	
Cyclobenzaprine (Flexeril®)	1A2	✓ [6]				
Metformin (Glucophage®)	--	✓	✓			
Methocarbamol (Robaxin®)	--	✓				
Naltrexone (Revia®, Vivitrol®)	--	✓				
Tizanidine (Zanaflex®)	1A2	✓ [6]				

*See last page for drug interaction summary footnotes

DRUG INTERACTION SUMMARY FOOTNOTES

- [1] **Prodrug or highly active metabolite** - requiring activation by the liver; CYP450 IMs/PMs may experience lower efficacy due to reduced conversion to the active metabolite and higher levels of the parent drug; CYP450 UMs may experience increased conversion of the parent drug, and higher levels of the active metabolite
 - [2] **Indeterminate** - Gene-drug interaction may exist, however indeterminate due to varied impact of multiple CYP450 enzymes, unknown clinical significance of a rare variation, or genotype was unable to be determined
 - [4] This medication is listed to use with caution due to a DRD2 variation which may lead to side effects and non-response with antipsychotics
 - [6] This patient has a variation in CYP1A2 which may lead to increased metabolism of this drug **in the presence of CYP1A2 inducers**, use caution; see the Genecept Assay Report Interpretation Guide for information related to CYP1A2 inducers
 - [11] **MultiCYP** - This drug is metabolized by multiple CYP450 enzymes, each having a minor effect on the drug's overall metabolism; abnormal activity in any one CYP450 enzyme is unlikely to be clinically significant for this drug
 - [12] Opioids are not contraindicated, although, patients with a DRD2 variation may be more likely to develop opioid dependence; use with caution
- *References for the drug interaction summary are available upon request

TEST METHODOLOGY

This test was developed and performance characteristics were validated by Genomind. It has not been cleared or approved by the US Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. Genomind performed the testing using standard and custom TaqMan reagents for all variants except for one, which was performed by PCR. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions.

Test Methodology Limitations: Factors influencing the amount and quality of DNA extracted include but are not limited to the amount of buccal cells extracted, patient oral hygiene, collection technique, and the presence of dietary or microbial sources of nucleic acids and nucleases. DNA quality and quantity are subject to matrix dependent influences. PCR inhibitors, extraneous DNA and nucleic acid degrading enzymes are all factors which must be considered in the evaluation of assay results. Some SNP assays are problematic due to multiple base repeats and other sequence aberrations which may hinder proper amplification and analysis. The gel based PCR assay is not sensitive enough to detect low expressed signals. DNA purity can influence the assay. SLC6A4 contains many polymorphisms and the assay was developed and validated as per the current available scientific information.

Variants tested include SLC6A4 rs25531 and 5-HTTLPR; CACNA1C; ANK3; 5HT2C; MC4R; DRD2; COMT; ADRA2A; MTHFR C677T and A1298C; BDNF; OPRM1; GRIK1; CYP1A2 *1C, *1D, *1E, *1F and *11; CYP2B6 *5, *6, and *7; CYP2C9 *2, *3, *4, *5, *6, *8, *11, *13, and *27; CYP2C19 *2, *3, *4, *5, *6, *7, *8, *9, *10, and *17; CYP2D6 *2, *3, *4, gene deletion (*5), gene duplication, *6, *7, *8, *9, *10, *11, *12, *14, *15, *17, *29 and *41; CYP3A5 *3, *6, *7; and CYP3A4 *22.

Testing performed by Genomind, Inc.
 2200 Renaissance Blvd, Suite 100 King of Prussia, PA 19406
 CLIA#39D2088097 David Robbins, PhD, DABCC, MT (AAB), Lab Director For Genomind, Inc.

LITERATURE REFERENCES

Gene	References
SLC6A4	1-24
CACNA1C	25-55
ANK3	26,28,30,35,37,46-49,56-64
5HT2C	7,65-75
MC4R	74,76-82
DRD2	83-87
COMT	88-117
ADRA2A	118-125
MTHFR	126-138

Gene	References
BDNF	139-161
OPRM1	162-172
GRIK1	173-177
CYP1A2	72,178-206
CYP2B6	178-182,199,203,207-220
CYP2C9	178-182,186,203,207,221-232
CYP2C19	7,178-182,199,203,207,216,222-224,231-244
CYP2D6	7,72,178-183,186,199-200,203,207,222-224,231-232,235,245-266
CYP3A4/5	7,72,178-183,186,199-200,203,207,216,267-269