



e-PKGene

Pharmacogenetics Database Background and Examples of Use

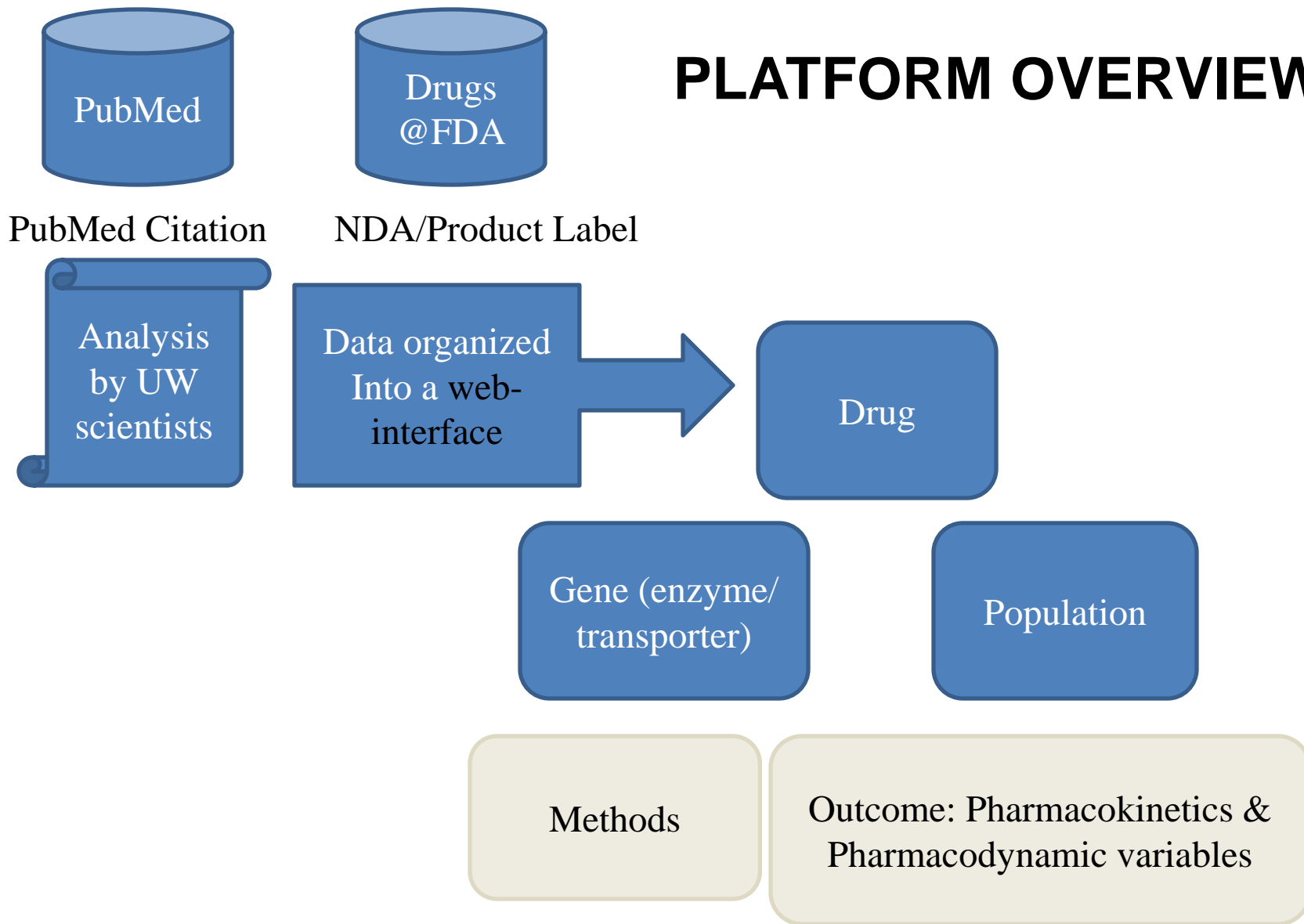
DIDB Program

Department of Pharmaceutics
School of Pharmacy
University of Washington



Background

PLATFORM OVERVIEW



e-PKGene Definitions

- **Articles** included in the e-PKGene database focus on drug exposure (AUC, Cl, C) in relation to pharmacogenetic variation. Studies can also include PD, clinical efficacy, and side effects.
- **Study:** set of assessments (PK, PD and safety) following the administration of a target compound to a well defined population.
- The **population** is usually divided into a “reference” group and an “impaired” group. The reference group usually consists of “extensive metabolizers” or carriers of two copies of the wild type allele of the gene of interest.

e-PKGene- Definitions

- e-PKGene defines each **variant allele** by one SNP which is unique to the allele. This SNP is identified as “diagnostic SNP”, but it is important to note that *the diagnostic SNP may not be responsible for the observed functional changes.*

Genetic characteristics for the most common CYP2D6 alleles (diagnostic Single Nucleotide Polymorphism)^{(1) (2)}
(4) (5) (6) (7) (8) (9) (10) (11) (12) (15) (16)

Allele Name	Diagnostic SNP		SNP position	Effect of Variation	Amino Acid Change NP_000097.2	rs number	Activity Score Model-B	Enzyme activity in vivo
	Gene M33388	NM_000106.4						
CYP2D6*1	none			“wild type” [reference]	NA		1	normal
CYP2D6*2	2850C>T 4180G>C	c.886T>C c.1457C>G	exon 6 exon 9	substitution (missense)	R296C T486S	rs16947 rs1135840	1	normal
CYP2D6*3	2549delA (also seen as 2637delA)	c.775delA	exon 5	frameshift (nonsense)	R259	rs4986774	0	none
CYP2D6*4	1846G>A (also seen as 1934G>A)	c.506-1G>A (IVS3 -1G>A)	intron 3	splicing defect (nonsense)	182ter	rs3892097	0	none
CYP2D6*5	whole gene deletion						0	none
CYP2D6*6	1707 delT (also seen as 1795delT)	c.454del T	exon 3	frameshift (nonsense)	W152X	rs5030655	0	none

e-PKGene Definitions

- Assignment of **Impact**: The classification is assigned by the database editorial team to provide users with a contextual framework that rapidly highlight variants of interest. Based on a predefined cut-off given by the statistical analysis performed by the authors (statistical significance).

e-PKGene rules (Impact of Variant)

1: statistical analysis must be performed by the authors of the study

2: control group is genotype *wt/*wt and/or Extensive Metabolizers

➤ **Active parent compound**

- Change in AUC
- Change in CL
- Change in Concentration

➤ **Metabolites**

- Change in CL (formation)
- Change in AUC ratio
- Change in Concentration ratio



Examples of Queries

Example 1: Compound Search

Irinotecan

- Enter first letters of compound generic name OR first digits of compound CAS number
- Select the compound of interest

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure* 1,130 PubMed citations and 3 NDAs
Home Search Summaries DDB Logged in as: sophiea **Log Out**

Search

Compound	iri
Gene	irinotecan (camptothecin-11) CAS 97682-44-5 irinotecan metabolite M2 (APC)
Populations	glime piride CAS 93479-97-1 hydroxyglime piride (M1) CAS 127554-89-6 levosul piride CAS 23672-07-3

Search

Compound	976
Gene	irinotecan (camptothecin-11) CAS 97682-44-5 rabeprazole CAS 117 976 -89-3
Populations	

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Search Results

Links to PubChem and compound summary

University of Washington
e-PKGene Impact of Genetics on Drug Exposure
1,130 PubMed citations and 3 NDAs
Home Search Summaries DIB Logged in as: sophiea Log Out

Search Results

Irinotecan (camptothecin-11) - Prodrug

[PubChem](#) [Compound Summary](#)

Results (36 Articles)

Refine Search By:

Gene	Population
ABCB1 (6)	Africans (1)
ABCC2 (3)	Asians (16)
ABCG2 (5)	Caucasians (9)
CES2 (1)	Children (2)
CYP3A5 (1)	Elderly (1)

[Clear Fields](#)

Irinotecan (camptothecin-11) (36)

Citations Impact of Variant

Showing 1 to 10 of 36 entries

Year	PMID	Title
2011	21740478	Genotype-directed, dose-finding study of irinotecan in cancer patients with UGT1A1*28 and/or UGT1A1*6 polymorphisms.
2011	21617725	Concurrence of UGT1A polymorphism and end-stage renal disease leads to severe toxicities of irinotecan in a patient with metastatic colon cancer.
2010	19771428	Additive effects of drug transporter genetic polymorphisms on irinotecan pharmacokinetics/pharmacodynamics in Japanese cancer patients.

- **Gene box:** number of citations for each polymorphic gene studied

- **Population box:** number of citations performed in a given population (ethnic, health status)

- **Citations:** list ordered chronologically

- **Links:** PubChem compound, compound summary, citation display

Link to citation display

Refine the search: by **Gene** and/or **Population**

e-PKGene *Impact of Genetics on Drug Exposure* 1,130 PubMed citations and 3 NDAs
Home Search Summaries DIBB Logged in as: sophiea Log Out

Search Results

Irinotecan (camptothecin-11) - Prodrug

[PubChem](#) [Compound Summary](#)

Results (36 Articles)

Refine Search By:

Gene	Population
CES2 (1)	Asians (10)
CYP3A5 (1)	Caucasians (8)
SLCO1B1 (6)	Children (2)
UGT1A1 (26)	Elderly (1)
UGT1A7 (3)	Europeans (3)

Clear Fields

Irinotecan (camptothecin-11) (36) > UGT1A1 (26) > Europeans (3)

Citations Impact of Variant

Showing 1 to 3 of 3 entries Search:

Year	PMID	Title
2009	19608554	Prolonged neutropenia after irinotecan-based chemotherapy in a child with polymorphisms of UGT1A1 and SLCO1B1.
2006	17185998	Irinotecan-induced diarrhea: functional significance of the polymorphic ABCC2 transporter protein.
1997	9402181	Severe CPT-11 toxicity in patients with Gilbert's syndrome: two case reports.

Show 10 entries First Previous 1 Next Last

Select gene and/or population of interest. This will:

1) Narrow the number of citations listed according to criteria of selection

1) Allows the access to **“Impact of Variant”** box

Specific additional search by key word, date or PMID

Reorder by ascending or descending years and PMIDs

Refine Search By:

Gene	Population
CYP3A5 (1)	Asians (10)
SLCO1B1 (6)	Caucasians (8)
UGT1A1 (26)	Children (2)
UGT1A7 (3)	Elderly (1)
UGT1A8 (1)	Europeans (3)

Clear Fields

Impact of Variant

Binary classification of genotypes/compound pairs based on PK differential observed across the various citations retrieved

Irinotecan (camptothecin-11) (36) > UGT1A1 (26) > Caucasians (8)

Citations		Impact of Variant	
Specific genetic variants have been investigated in only 5 of the 8 citations retrieved.			
UGT1A1*1/*28			
Yes	No	Yes	No
SN-38 (7-Ethyl-10-hydroxycamptothecin) 17185998	irinotecan (camptothecin-11) 17185998	SN-38 (7-Ethyl-10-hydroxycamptothecin) 15286088 15523087	17185998
	SN-38 glucuronide (7-ethyl-10-hydroxycamptothecin glucuronide) 15523087 17185998		
UGT1A1*28/*28			
Yes	No	Yes	No
SN-38 (7-Ethyl-10-hydroxycamptothecin) 15523087 16809730	irinotecan (camptothecin-11) 17185998		

Access to citation display

- Based on change of exposure between reference group (wild-type) and variant group
- Predefined cut-off: statistical analysis
- Based on Parent or metabolite(s) exposure

*Impact is assigned by the database team based on the following criteria: Impact=YES if the change in AUC, CL or Cmax is statistically significant (as determined by the study author). If changes are not statistically significant, the database team has assigned Impact=NO. Impact is assigned based on changes for the parent compounds, and metabolites.

Citation Display: **Effects** page screen

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure* 1,130 PubMed citations and 3 NDAs
 Home Search Summaries DIDB Logged in as: sophiea Log Out

CITATION

PMID: 17185998 [PubMed](#)

Title: [Irinotecan-induced diarrhea: functional significance of the polymorphic ABCC2 transporter protein.](#)

Clinical pharmacology and therapeutics

Volume 81, Issue 1, Pages 42-9

Published 2007

FA de Jong, TJ Scott-Horton, DL Kroetz, HL McLeod, LE Friberg, RH Mathijssen, J Verweij, S Marsh, A Sparreboom

Comments:

In this study, none of the investigated ABCC2 SNPs (ABCC2 -1549G>A, -1019A>G, -24C>T, 1249G>A, IVS26 -34T>C, and 3972C>T) were found to be significantly associated with the investigated irinotecan pharmacokinetic parameters. ABCC2*2 haplotype is characterized by the variant -1019A>G alone. The presence of ABCC2*2 haplotype is defined by the authors as carrier of one or two ABCC2*2 (ABCC2 -1019AG or GG), whereas absence of ABCC2*2 haplotype is defined as non-carrier of ABCC2*2 (ABCC2 -1019AA).

Effects

Impact on Pharmacokinetics

Full Study Sets

Study 1	irinotecan (camptothecin-11) IV single 90-min infusion (350 mg/m2 or 600 mg/m2), once every 3 weeks		
UGT1A1 Gene Summary	68 Patients (reference) UGT1A1*1/*1 Caucasians Europeans	58 Patients UGT1A1*1/*28 Caucasians Europeans	8 Patients UGT1A1*28/*28 Caucasians Europeans
irinotecan (camptothecin-11) - Prodrug PubChem Compound Summary			
Δ CL (systemic-IV)		0.68%	-1.02%
Impact		No	No

Features:

- Links to PubMed, PubChem, gene and compound summary
- Comments (curator)

Effects: summary of the impact of variant(s) on parent compound PK in the different populations (based on ΔAUC, ΔCL, or Δconc)

Citation Display: Impact on Pharmacokinetics

CITATION

PMID: 17185998 [PubMed](#)

Title: [Irinotecan-induced diarrhea: functional significance of the polymorphic ABCC2 transporter protein.](#)

Clinical pharmacology and therapeutics

Volume 81, Issue 1, Pages 42-9

Published 2007

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Effects	Impact on Pharmacokinetics	Full Study Sets	
Study 1	irinotecan (camptothecin-11) IV single 90-min infusion (350 mg/m2 or 600 mg/m2), once every 3 weeks		
UGT1A1 Gene Summary	68 Patients (reference) UGT1A1*1/*1 Caucasians Europeans	58 Patients UGT1A1*1/*28 Caucasians Europeans	8 Patients UGT1A1*28/*28 Caucasians Europeans
irinotecan (camptothecin-11) - Prodrug PubChem Compound Summary			
CL (systemic-IV) (L/h) (Medians (Range))	29.5 (13.1 - 50.41)	29.7 (11.7 - 50.4)	29.2 (17.3 - 41.1)
Δ CL (systemic-IV) %		0.68	-1.02
SN-38 (7-Ethyl-10-hydroxycamptothecin) - active metabolite PubChem			
AUC ratio (metabolite/parent) (Medians (Range))	3 (1.08 - 7.35)	3.64 (1.88 - 24.5)	4.49 (2.4 - 8.1)
Δ AUC ratio (metabolite/parent) %		21.33	49.67*
Biliary Index (Medians (Range))	7.95 (1.92 - 27.1)	9.04 (0.97 - 24.5)	18.8 (7.1 - 34.3)
Δ Biliary Index %		13.71	136.48*
CL (systemic-IV) (L/h) (Medians (Range))	387 (199 - 1683)	316 (107 - 833)	266 (68.8 - 495)
Δ CL (systemic-IV) %		-18.35*	-31.27*
SN-38 glucuronide (7-ethyl-10-hydroxycamptothecin glucuronide)			
AUC ratio (metabolite/parent) (Medians (Range))	4.41 (1.26 - 12.2)	4.02 (1.84 - 36.3)	2.24 (1.38 - 3.97)
Δ AUC ratio (metabolite/parent) %		-8.84	-49.21*
CL (systemic-IV) (L/h) (Medians (Range))	57.6 (23.7 - 214)	53.8 (2.24 - 163)	69.6 (34.3 - 125)
Δ CL (systemic-IV) %		-6.6	20.83

* Change is statistically significant (P<0.05) or Confidence interval outside equivalence boundaries.

- Overview of all PK parameters measured in each population groups reported in the citation

- for parent compound and metabolites

- statistical significance vs reference group.

Citation Display: Full Study Sets

Effects Impact on Pharmacokinetics **Full Study Sets**

Study 1 » irinotecan (camptothecin-11),
8 Patients
UGT1A1*28/*28

Population 8 Patients UGT1A1*28/*28 Caucasians Europeans Solid tumors	Design and Drug Administration Drug Administration: irinotecan (camptothecin-11) IV single 90-min infusion (350 mg/m2 or 600 mg/m2), once every 3 weeks Design: Single Dosing	Genotyping Method Pyrosequencing Alleles Tested For UGT1A1(TA)6 UGT1A1(TA)7 UGT1A1*28
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Pharmacokinetics

8 Patients UGT1A1*28/*28 Caucasians Europeans	irinotecan (camptothecin-11)	SN-38 (7-Ethyl-10-hydroxycamptothecin)	SN-38 glucuronide (7-ethyl-10-hydroxycamptothecin glucuronide)
AUC ratio (metabolite/parent) (Medians (Range))		4.49 (2.4 - 8.1)	2.24 (1.38 - 3.97)
Biliary Index (Medians (Range))		18.8 (7.1 - 34.3)	
CL (systemic-IV) (L/h) (Medians (Range))	29.2 (17.3 - 41.1)	266 (68.8 - 495)	69.6 (34.3 - 125)

Comments

AUC ratio (SN-38/irinotecan) = relative extent of conversion; AUC ratio (SN-38-glucuronide/SN-38) = relative extent of glucuronidation. The Biliary Index (unit not provided by the authors) of SN-38 is a surrogate measurement of SN-38 biliary excretion. It is calculated as [(AUC SN-38/AUC SN-38G) × AUC CPT-11].

Side Effects

8 Patients UGT1A1*28/*28 Caucasians Europeans	SN-38 (7-Ethyl-10-hydroxycamptothecin)
Side Effect Types	Diarrhea Neutropenia
Description	The presence of at least one UGT1A1*28 allele was associated with a 1.3-fold higher (CI: 0.53–3.13) occurrence of severe diarrhea, but this was not statistically significant (p=0.587). Likewise, no relationship between UGT1A1*28 genotype and the occurrence of neutropenia was detected (p=0.411).

- Displays data captured for a study in **one population of interest**

- May include:
- Population description
 - Study design/dosing regimen
 - Phenotyping/Genotyping Methods
 - Alleles tested for

- **Pharmacodynamic and/or side effects** when these assessments are performed

Other Search Criteria

Search by Gene

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure* 1,130 PubMed citations and 3 NDAs

Home Search Summaries DIDB Logged in as: sophiea [Log Out](#)

Search

Compound

Gene

Populations **ABCB1**
ABCC1
ABCC10
ABCC2
ABCC4

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Search by Population

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure* 1,130 PubMed citations and 3 NDAs

Home Search Summaries DIDB Logged in as: sophiea [Log Out](#)

Search

Compound

Gene

Populations

Asians
Caucasians
Middle Eastern
Non-Caucasians
Pooled Asians
Yupik (Alaska Native)

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Example 2: Search by gene - SLC01B1

- Curser in the gene box: drop box with the whole gene list by default

The screenshot shows the e-PKGene search interface. At the top, it says "University of Washington" and "e-PKGene Impact of Genetics on Drug Exposure". There are 1,130 PubMed citations and 3 NDAs. The user is logged in as "sophia". The search bar has three tabs: "Home", "Search", and "Summaries". The "Search" tab is active. The search form has three fields: "Compound" (with placeholder "Compound name or CAS number"), "Gene" (with a cursor), and "Populations". A dropdown menu is open under the "Gene" field, showing a list of genes: ABCB1, ABCC1, ABCC10, ABCC2, ABCC4, ABCG2, ALDH3A1, CES2, CYP1A2, and CYP1B1.

- Type first letters of gene and select gene of interest

The close-up shows the search form with the "Gene" field containing "SLCO". The dropdown menu is open, showing the following options: **SLCO1A2**, **SLCO1B1**, **SLCO1B3**, and **SLCO2B1**.

SLCO1B1 Search

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure*
 1,130 PubMed citations and 3 NDAs
 Home Search Summaries DIDB Logged in as: sophiea Log Out

Search Results

SLCO1B1

[Gene Summary](#)

Results (65 Articles)

Refine Search By:

Compound	Population
pitavastatin (5) pitavastatin lactone (3) <b style="background-color: #90EE90;">pravastatin (11) pravastatin + RMS-416 (2) pravastatin lactone (1)	African-American (1) Americans (1) Asians (5) Blacks (1) Caucasians (5)

[Clear Fields](#)

- **Refine search:** select a **compound** and/or **population**

- “Clear Field” to perform a new search

SLCO1B1 (65) > pravastatin (11)

Citations | Impact of Variant

Showing 1 to 10 of 11 entries Search:

Year	PMID	Title
2009	19833260	The SLCO1B1*5 genetic variant is associated with statin-induced side effects.
2008	18408565	The effect of SLCO1B1*15 on the disposition of pravastatin and pitavastatin is substrate dependent: the contribution of transporting activity changes by SLCO1B1*15.
2007	18641915	Pharmacokinetic interaction between pravastatin and olmesartan in relation to SLCO1B1 polymorphism.
2007	17622941	Effect of drug transporter genotypes on pravastatin disposition in European- and African-American patients.

- **Citation list** displays only citations studying the compound in the population selected

SLCO1B1 Search

Pravastatin and Asians selected

List of citations refined

Impact box opens

SLCO1B1

[Gene Summary](#)

Results (65 Articles)

Refine Search By:

Compound	Population
pitavastatin (5)	African-American (1)
pitavastatin lactone (3)	Americans (1)
pravastatin (11)	Asians (5)
pravastatin + RMS-416 (2)	Blacks (1)
pravastatin lactone (1)	Caucasians (5)

[Clear Fields](#)

SLCO1B1 (65) > pravastatin (11) > Asians (5)

Year	PMID	Title
2008	18408565	The effect of SLCO1B1*15 on the disposition of pravastatin and pitavastatin is substrate dependent: the contribution of transporting activity changes by SLCO1B1*15.
2007	18641915	Pharmacokinetic interaction between pravastatin and olmesartan in relation to SLCO1B1 polymorphism.
2006	16678545	Effects of organic anion transporting polypeptide 1B1 haplotype on pharmacokinetics of pravastatin, valsartan, and temocapril.
2004	15681900	A novel variant allele of OATP-C (SLCO1B1) found in a Japanese patient with pravastatin-induced myopathy.
2003	12811365	Polymorphisms of OATP-C (SLC21A6) and OAT3 (SLC22A8) genes: consequences for pravastatin pharmacokinetics.

Showing 1 to 5 of 5 entries

Search:

Show 10 entries

First Previous 1 Next Last

SLCO1B1

[Gene Summary](#)

Results (65 Articles)

Refine Search By:

Compound	Population
pitavastatin (5)	African-American (1)
pitavastatin lactone (3)	Americans (1)
pravastatin (11)	Asians (5)
pravastatin + RMS-416 (2)	Blacks (1)
pravastatin lactone (1)	Caucasians (5)

[Clear Fields](#)

SLCO1B1 (65) > pravastatin (11) > Asians (5)

SLCO1B1*15/*15		
Yes	No	
pravastatin + RMS-416	18641915	
pravastatin	12811365	
	18408565	
	18641915	
RMS-416 (3'-alpha-isopravastatin)	18641915	

Specific genetic variants have been investigated in only 4 of the 5 citations retrieved.

SLCO1B1*1A/*1A		
Yes	No	
		pravastatin
		12811365

Summaries

available in PDF format for **Drugs** and **Genes**

University of Washington
e-PKGene *Impact of Genetics on Drug Exposure*
 1,130 PubMed citations and 3 NDAs
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Summaries

Summary Title	Gene	Compound
ABCB1 (P-gp / MDR1) Polymorphism	ABCB1	
ABCG2 (BCRP) Polymorphism	ABCG2	
CYP2B6 Polymorphism	CYP2B6	
CYP2C19 Polymorphism	CYP2C19	
CYP2C8 Polymorphism	CYP2C8	
CYP2C9 Polymorphism	CYP2C9	
CYP2D6 Polymorphism	CYP2D6	
CYP3A5 Polymorphism	CYP3A5	
SLCO1B1 (OATP1B1) Polymorphism	SLCO1B1	
UGT1A1 Polymorphism	UGT1A1	
Atomoxetine		atomoxetine
Clopidogrel		clopidogrel
Cyclosporine		cyclosporine
Irinotecan		irinotecan (camptothecin-11)
Repaqlinide		repaqlinide
Rosuvastatin		rosuvastatin
Tamoxifen		tamoxifen
Warfarin		warfarin

- PDF summaries for Genes and Drugs

- Direct access to gene results or compound results

Example of Drug Summary: Tamoxifen

ePKGene Summary May 2010

Tamoxifen

Background: Metabolism and Pharmacokinetics

```

graph TD
    Tamoxifen -- "CYP3A4/5  
CYP2C9" --> N-desmethyltamoxifen
    N-desmethyltamoxifen -- "CYP2D6" --> Endoxifen
    Endoxifen -- "CYP3A4/5" --> 4-hydroxytamoxifen
    4-hydroxytamoxifen -- "CYP2D6" --> Endoxifen
    Endoxifen -- "UGTs" --> UGTs
    4-hydroxytamoxifen -- "UGTs" --> UGTs
    
```

Tamoxifen is a prodrug that requires metabolic activation to active metabolites 4-OH tamoxifen and 4-OH-N-desmethyltamoxifen (endoxifen) (1). Both CYP2D6 and CYP3A4 play a role in this activation. Loss or decrease of CYP2D6 function by genetic polymorphism may be associated with poorer clinical outcome compared with patients that have normal or ultrarapid metabolizer status (2).

1 Borges S, Desta Z, et.al. *Clinical Pharmacology & Therapeutics* (2006) **80**, 61–74
2 Kiyotani K, Mushiroda T, et. al. *J Clin Oncol.* (2010) **28**, 1287-93.

Pharmacokinetics/Pharmacodynamics Summary for Tamoxifen

Max % Change by CYP2D6 Genotype/Phenotype (6 studies evaluated)

			Homozygous EM or *1/*1		*10/*10		*4/*4		Heterozygous EM		Homozygous Variant (PM)		Ultra-rapid (UM)	
			Control	Range	Range	Range	Range	Range	Range	Range				
PK	Tamoxifen	Css	Control	31	* 3.7	* -22.4	* -27.5	-1.1 to -27.4	-8.9	* 7.8	* -14.7	* 7.8	* -14.7	
	N desmethyl tamoxifen	Css	Control	**	**	**	**	1.6	* 11.1	5.2 to 11.1	17.5	* -14.7	* -14.7	
	4-OH tamoxifen	Css	Control	-10.7	-1.9 to -10.7	-46.4	-22.6 to -46.4	-25.3	* -12.6	-1.7 to -12.6	-12.1	* 1.7	* 1.7	
	Endoxifen	Css	Control	-9	* -60.3	* -74.4	* -75.3	-5.2 to -75.6	-56.2	-27.5 to -56.2	-11.5	* -11.5	* -11.5	
PD	Not Available													

* Single study ** Not studied **BOLD**=statistically significant

Homozygous EM= assigned based on genotype to include *X/*Y (X=1, 2, 1xN, 41, Y=1, 2, 35, 1xN, 2xN, 41)

Heterozygous EM= assigned based on genotype to include one allele with compromised activity (10, 4, 5, 6)

Homozygous PM= assigned based on genotype to include two alleles with compromised activity (3,4, 5, 9, 10, 17, 21, 41)

Ultrarapid UM=assigned based on genotype to include *1/*2x2

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Background:
Summary of drug disposition characteristics

Maximum changes in exposure found in the literature for a given drug and a given genotype

Example of Gene Summary: CYP2D6

CYP2D6 Gene Polymorphism Summary

Official Full Name: cytochrome P450, family 2, subfamily D, polypeptide 6
Alias Names: RP4-669P10.2, CPD6, CYP2D, CYP2D@, CYP2DL1, MGC120389, MGC120390, P450-DB1, P450C2D, P450DB1
CYP2D6 Location: chromosome: 22; Location: 22q13.1
Gene Reference: M33388
Gene Identification Number: 1565
gene information from NCBI dbSNP database(Entrez Gene) ⁽¹⁾

Definitions

Single nucleotide polymorphism (SNP)⁽³⁾

A single nucleotide polymorphism (SNP) is a variation occurring in the DNA when a single nucleotide — A, T, C, or G — differs between a paired chromosomes in an individual. SNPs are the most common genetic variations in humans.

CYP2D6 allele classification⁽⁵⁾⁽⁶⁾

➤ The CYP2D6*1 allele is the **wild-type** allele (it has no SNP) and encodes an enzyme with **normal activity**. It defines the **Extensive Metabolizers** status and is considered as the “Reference” allele.

Allele Name	Diagnostic SNP		SNP position	Effect of Variation	Amino Acid Change NP_000097.2	rs number	Activity Score Model-B	Enzyme activity in vivo
	Gene M33388	NM_000106.4						
CYP2D6*1	none			“wild type” [reference]	NA		1	normal
CYP2D6*2	2850C>T 4180G>C	c.886T>C c.1457C>G	exon 6 exon 9	substitution (missense)	R296C T486S	rs16947 rs1135840	1	normal

Relation Genotype/Phenotype

It is important to note that phenotypes displayed in the citations are the ones the authors assigned to their

Activity Score	>2	2	1 < AS < 2	0 < AS ≤ 1	0
Phenotype	Ultrarapid Metabolizers (UMs)	Extensive Metabolizers (EMs)	Slow Extensive Metabolizers (SEMs)	Intermediate Metabolizers (IMs)	Poor Metabolizers (PMs)

- General description of Gene
- Definitions
- Classification of alleles
- Genetic description for some alleles
- Relation Genotype/Phenotype (when available)
- Frequencies by ethnicity
- References



For Comments and Questions

Contact DIDB Program at didbase@uw.edu