SCION GENOMICS

Preventative Screening.
Healthier Patients. Longer Life.

GeneDose™ Report User Guide

Genetic Summary

The **Genetic Summary** provides, in a three-column table format, a patient's results as per the gene panel(s) ordered by their health care provider. Specifically, the **Gene** tested, the genotype (**Result**) and the metabolic **Activity** of that genotype. The PGX panels at Scion Lab Services, LLC include:

PANEL NAME	NUMBER OF GENES TESTED
Full Panel	11
Cardiac Panel	8
Psychiatric Panel	4
Thrombosis Panel	3

See example to the right: the gene CYP2D6 was tested and the resulting genotype revealed that the patient is an Ultrarapid metabolizer, which impacts codeine and other analgesics like tramadol.

Genetic Summary

Gene	Result	Activity †
CYP2C19	*17|*17	Ultrarapid metabolizer
CYP2C9	*1|*1	Extensive metabolizer
CYP2D6	*1Ax2|*1A	Ultrarapid metabolizer
CYP3A4	*1A|*1A	Multiple statuses; see per-drug detail
CYP3A5	*1D|*1D; or *1A|*1A; or *1A|*1D	Extensive metabolizer

GeneDose Live™

GeneDose Live™ is a dynamic risk management tool available to health care providers after PGX genetic testing is completed. This online tool allows providers to add or remove information about a patient's medical conditions, lifestyle and medication regime and view, real-time, the impact on the Current Regimen Risk Chart. The tool link and log-in information are found on the first page of the report. It's simple to use, and the information provided makes it easy to alter as the patient's situation changes.

GeneDose Live

Individualized, additional therapeutic decision support information based on Bo Diddley's genetics, drug regimen, indications, demographics, and lifestyle indicators are available at GeneDose Live via this secured URL: http://checkdru.gs/

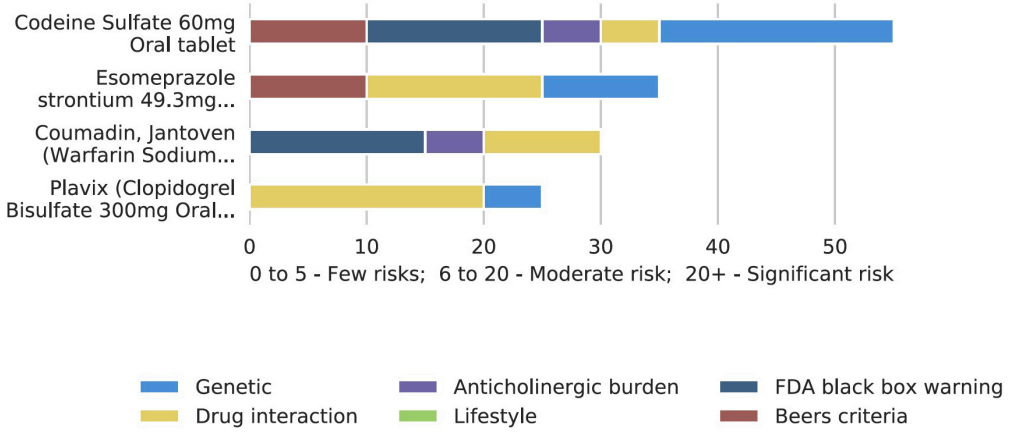
GeneDose Key: ARFFR6EJ9

Sample ID: 45443

Current Regimen Risk Chart

The **Current Regimen Risk Chart** is a schematic representation of various risk factors associated with the medication(s) in a patient's current regimen (independent of dose). The various risk factors considered are PGX DNA test results, drug interactions, anticholinergic burden, lifestyle, pregnancy, lactation and adverse drug reactions (also called the black box warning). For each medication, as listed on the y-axis, the risk factors that pose an increased risk are shown as colored horizontal bars. This risk chart demonstrates the potential impact of these risk factors in polypharmacy safety. The more colored bars, the more individual factors impacting that particular medication (accumulative impact is not known).

See example to the right: Codeine is impacted by the patient's genotype for CYP2D6, which is represented as a blue bar. The other risk factors for codeine are adverse drug reactions, drug interactions and anticholinergic burden.



Current Regime Risk Detail (by severity)

The **Current Regimen Risk Detail** lists the associated risk factors for each medication and the concomitant morbidity feature. Some medications have multiple risk factors while others may not have genetic or non-genetic risks associated. The risk factors included are PGX DNA test results, drug interactions, anticholinergic burden, lifestyle, adverse drug reactions (also called the black box warning) and whether or not there is pregnancy or lactation.

See Codeine example: More detailed information is provided regarding the risk factors. See adverse drug reactions and genetic warning. The warnings for drug interactions and anticholinergic burden are also presented in the report (not shown here).

Black box warning for Coumadin, Jantoven (Warfarin Sodium 10mg Oral tablet) and bleeding

Black box warning for Codeine Sulfate 60mg Oral tablet and psychological dependence

Black box warning for Codeine Sulfate 60mg Oral tablet and neonatal opioid withdrawal syndrome

Medication Summary

The **Medication Summary** provides information on the effect of panel variants on medications that are displayed by therapeutic drug class (for each specific specialty i.e., Cardiac, GI, ID, Pain…. etc.). Based on the patient's genetic profile, various classes of medications are categorized as Standard Precautions, Caution/Info and Change Recommended. These medications are those that are known to be impacted by specific variants and are not necessarily in the patient's current regime.

Example: See Codeine listed under Change Recommended (right column)

Pain			
Therapeutic Class	**Standard Precautions**	**Caution / Info**	**Change recommended**
	Meloxicam Piroxicam		
Opioids	Buprenorphine Fentanyl Oxycodone (CYP3A5)	Hydrocodone Oxycodone Tramadol	Codeine
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluvoxamine Sertraline	Fluoxetine Paroxetine	Citalopram Escitalopram

Medication Report Details

This section expands on the detail provided in the Medication Summary section. Medications potentially impacted by the genes tested are listed in column one and grouped by therapeutic class. The concomitant genotype is presented and explained in column two and the recommendations are listed in column three. If there is an impact on the treatment regimen the type of concern is listed in column four, such as ADR or Efficacy and finally in column five, the level of clinical evidence to support the recommendations such as strong, moderate or emerging.

See Codeine example to the right

Drug		Finding	Recommendation	Concern	Evidence
Opioids					
Buprenorphine (Butrans, Buprenex) *FDA drug label: Not established for PGx*	✓	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Codeine *FDA drug label: Actionable PGx*	⛔	CYP2D6: Ultra-rapid metabolizer. One allele showing normal function and one duplicated allele showing normal function.	Individuals with ultrarapid metabolizer status have increased formation of morphine following codeine administration; the resultant increased morphine plasma concentrations leads to higher risk of toxicity. For analgesia, select alternative drug (e.g. acetaminophen, NSAID, morphine; not tramadol or oxycodone).	ADR	
Fentanyl (Duragesic, Sublimaze) *FDA drug label: Not established for PGx*	✓	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Hydrocodone *FDA drug label: Not established for PGx*	⚠	CYP2D6: Ultra-rapid metabolizer. One allele showing normal function and one duplicated allele showing normal function.	Individuals with ultrarapid metabolizer status may be at an increased risk of adverse drug reactions and/or therapeutic failure. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions and/or symptoms of insufficient therapy.	ADR	
Oxycodone (Oxycontin) *FDA drug label: Not established for PGx*	ℹ	CYP2D6: Ultra-rapid metabolizer. One allele showing normal function and one duplicated allele showing normal function.	Individuals with ultrarapid metabolizer status are at risk of possible adverse drug reaction. Insufficient evidence to allow calculation of dose adjustment. Select alternative drug (not tramadol or codeine) or be alert to adverse drug events (e.g. nausea; vomiting; constipation; respiratory depression; confusion; urinary retention).	ADR	
Oxycodone (CYP3A5) (Oxycontin) *FDA drug label: Not established for PGx*	✓	CYP3A5: Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Thrombosis Profile

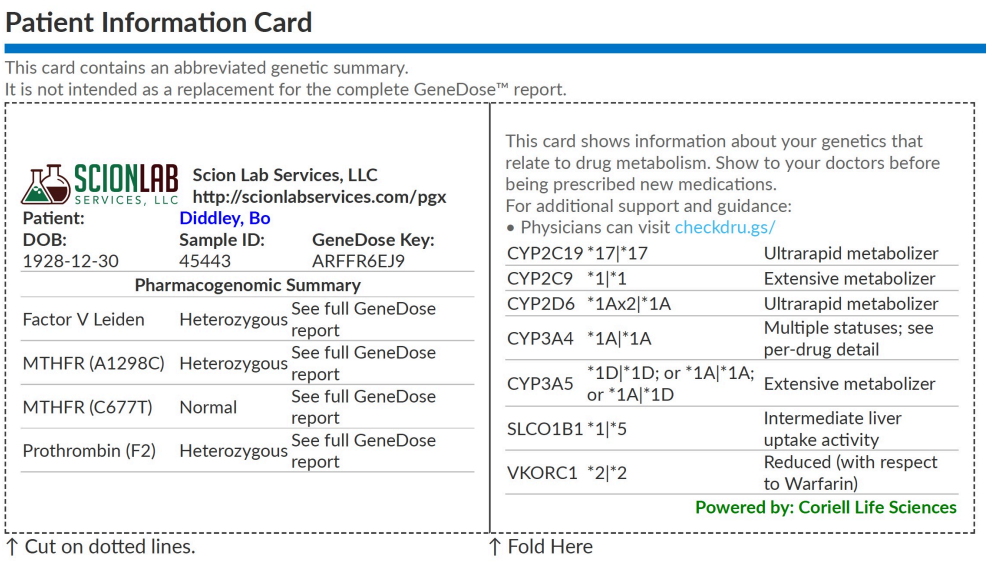
The **Thrombosis Profile** examines three genes: Prothrombin (*F2*), Factor V Leiden (*F5*) and the methylenetetrahydrofolate reductase gene (*MTHFR*). The presence of the *F2* gene variant (20210A) and the *F5* gene variant (1691A) are risk factors for venous thrombosis (*VT*). This risk may be further increased by the presence of at-risk *MTHFR* genotypes. *MTHFR* variant alleles alone do not predict a significant risk for venous thrombosis. Additional risk factors include estrogen therapy, oral contraceptive use, pregnancy and surgery.

Thrombosis Profile

Tested Genes (Alleles)	Genotype	Predicted Phenotype	Clinical Guidance
Prothrombin (F2)	Heterozygous	Variant alleles detected. It is important for individuals possessing this allelic variant to understand the clinical risks and the genetic implications of their result. Patients should be counseled by their physician or genetic counselor	Individuals carrying both the Factor V Leiden and prothrombin 20210G>A mutations have an approximately 20-fold increased risk of having a venous thrombosis than individuals without either mutation. Between 1% and 10% of symptomatic carriers of the Factor V Leiden mutation also carry the prothrombin 20210G>A mutation. These individuals have a 50- to 80-fold relative risk of thrombosis as compared to homozygotes for the Factor V Leiden mutation.
Factor V Leiden	Heterozygous		
MTHFR (A1298C)	Heterozygous		
MTHFR (C677T)	Normal		

Patient Information Card

The **Patient Information Card** provides each patient with a copy of their genetic results from the PGX panel(s) ordered by their health care provider. This wallet-size card is meant to be carried by the patient and shared with all present and future health care providers.



Patient Information Card

This card contains an abbreviated genetic summary.
It is not intended as a replacement for the complete GeneDose™ report.

SCIONLAB SERVICES, LLC

Scion Lab Services, LLC
http://scionlabservices.com/pgx

Patient:	**Diddley, Bo**	
DOB:	**Sample ID:**	**GeneDose Key:**
1928-12-30	45443	ARFFR6EJ9

Pharmacogenomic Summary

Factor V Leiden	Heterozygous	See full GeneDose report
MTHFR (A1298C)	Heterozygous	See full GeneDose report
MTHFR (C677T)	Normal	See full GeneDose report
Prothrombin (F2)	Heterozygous	See full GeneDose report

This card shows information about your genetics that relate to drug metabolism. Show to your doctors before being prescribed new medications.
For additional support and guidance:
• Physicians can visit checkdru.gs/

CYP2C19	*17|*17	Ultrarapid metabolizer
CYP2C9	*1|*1	Extensive metabolizer
CYP2D6	*1Ax2|*1A	Ultrarapid metabolizer
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CYP3A5	*1D|*1D; or *1A|*1A; or *1A|*1D	Extensive metabolizer
SLCO1B1	*1|*5	Intermediate liver uptake activity
VKORC1	*2|*2	Reduced (with respect to Warfarin)

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ApoE Genotype Information

The **ApoE* gene produces the protein, apolipoprotein E which is involved in the packaging of cholesterol and other fats to be transported through the bloodstream. There are different alleles of this gene, however, the *ApoE ε2* allele is associated with an increased risk of type III hyperlipoproteinemia. Untreated affected individuals are at 5-10 times (NORD) more likely to develop cardiovascular disease as compared to the general population risk (0.02%). Individuals that are found to have two copies of the *ApoE ε2* allele have a 10-15% risk to develop symptoms of III hyperlipoproteinemia. Since the vast majority of individuals (>90%) with type III hyperlipoproteinemia have two *ApoE* ε2 genes, additional genetic, environmental, or hormonal factors play a role in the development of the disorder. Such as hypothyroidism, diabetes, obesity, or age. (NORD, OMIM)

*NOTE: Only *ApoE ε2 genotype information is provided.*

ApoE Genotype Information*

Gene	Apolipoprotein E (*ApoE*)
Allele Tested	ε2

RESULTS

Genotype Result	No *ApoE ε2* alleles detected

Methodology

Genetic analysis of the *ApoE* gene was performed using allele-specific PCR. The zygosity of *ApoE ε2* alleles is based on genotyping results from SNPs rs429358 and rs7412 (NCBI reference IDs).

Phenotype

Insufficient information to assess risk.

Clinical Guidance

Many factors play a role in the development of cardiovascular disease (CVD). Such factors include genetic, environmental, hormonal factors, the presence of other disorders (e,g., hypothyroidism, diabetes), obesity or age. This test does not identify or rule out all potential genetic risks for CVD.

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www.scionlabservices.com/pgx.htm