

Things To Remember:

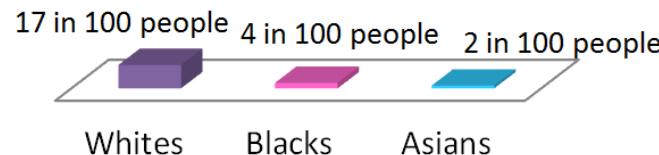
- ⇒ *CYP2C9* metabolizes warfarin in the body. *VKORC1* also affects the warfarin level in the body.
- ⇒ Some *CYP2C9* and *VKORC1* forms caused by changes in the genes may affect the way your body responds to warfarin.
- ⇒ Genetic testing results help your doctor in choosing the initial warfarin dose. However, careful monitoring of INR is still required.
- ⇒ Other medications may also affect your response to warfarin. Therefore, it is important to let your physician know all the medications that you are taking so that any potential interactions may be avoided.

Glossary

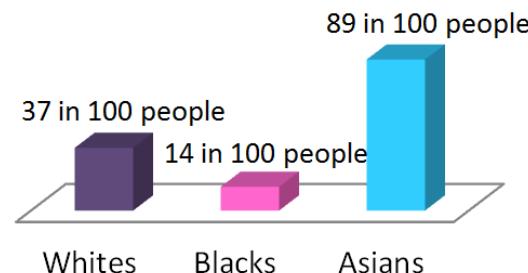
- ⇒ **Active drug:** the form of drug which produces an effect after it enters the body
- ⇒ **Enzyme:** a protein that breaks down a drug
- ⇒ **General population:** a group of people made up of different races/ethnicities
- ⇒ **INR (International Normalized Ratio):** a test used in patients taking warfarin to see if the blood is too thin or too thick
- ⇒ **Metabolism:** the breakdown of a drug

Breakdown of *CYP2C9* Enzyme And *VKORC1* Protein Activities In the General Population

At least one change in *CYP2C9* gene



At least one change in *VKORC1* gene



"One size does not fit all."

Translational Initiatives for Pharmacogenomics
The Charles Bronfman Institute for Personalized Medicine

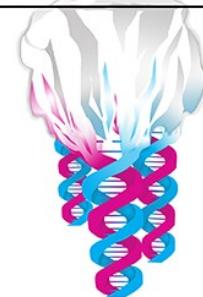
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Translational Initiatives in Pharmacogenomics

TIP



Warfarin,
CYP2C9, and
VKORC1



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Pharmacogenetics: CYP2C9, and VKORC1

- ◆ Pharmacogenetics is the study of how your genes affect the medications you take.
- ◆ Genes are the instruction manuals contained in each person's body.
- ◆ The instructions the body receives from the genes is what controls how we look, how to grow, and how we function.
- ◆ They also contain instructions for how to make enzymes, which are proteins the body uses to break down or "metabolize" what we take in, including medications.
- ◆ Changes in some genes may result in different instructions for how to make the enzymes. This could result in the body having a different form of the enzyme that may metabolize medications differently.
- ◆ CYP2C9 is an enzyme that is responsible for the metabolism of many commonly prescribed drugs, such as warfarin.
- ◆ VKORC1 is a protein that regulates Vitamin K level in the body, which affects the warfarin level, making blood too thin or too thick.
- ◆ Changes in the CYP2C9 and VKORC1 genes lead to different forms of CYP2C9 enzyme and VKORC1 protein; which affect the way your body responds to warfarin.

Warfarin (Coumadin®)

- ◆ Warfarin is a medication used to thin blood to prevent various conditions such as stroke or blood clots.
- ◆ Changes in CYP2C9 and VKORC1 can lead to increased amount of active warfarin in the body and reduced clotting activity. This can lead to side effects such as bleeding.

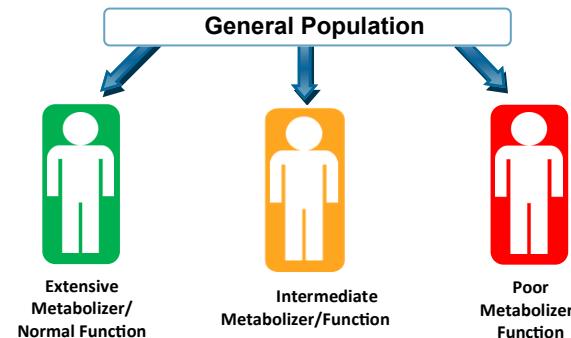


Table: CYP2C9 and VKORC1 forms and their effects on the breakdown of warfarin

		*alleles for CYP2C9 (*1 has normal protein activity; *2 and *3 have decreased protein activity)					
		*1/*1	*1/*2	*1/*3	*2/*2	*2/*3	*3/*3
VKORC1	Normal Function						
	Intermediate Function						
	Poor Function						
Classification		Protein activity				Clinical Relevance	
		Normal activity of the enzyme and normal clotting activity				Expected blood thinning effect	
		Low activity of the enzyme (increased amounts of active warfarin) and less clotting activity				May have higher risk of bleeding	
		Lowest activity of the enzyme (very high amounts of active warfarin) and very little clotting activity				May have highest risk of bleeding	

Personalized Medicine at Mount Sinai

- ◆ The CYP2C9 and VKORC1 genetic tests provide information that helps to estimate the dose of warfarin needed to reach the desired blood thinning effect.
- ◆ In Mount Sinai's pharmacogenetics program, your genetic test results including your CYP2C9 and VKORC1 results are added to the electronic medical records.
- ◆ Depending on your genetic test results, your doctor will receive an alert when prescribing warfarin for you.
- ◆ This alert will tell the doctor to doses that you will need, based on your genetic test results, to prevent clotting and avoid bleeding. (see tables below)