

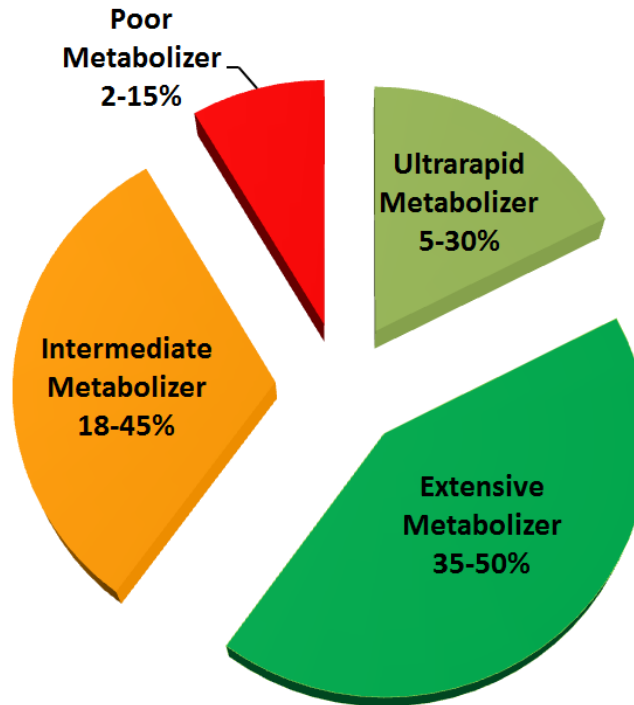
## Things To Remember:

- ⇒ CYP2C19 metabolizes clopidogrel from its inactive form to its active form in your body.
- ⇒ Too little or too much of the active form of clopidogrel can lead to side effects.
- ⇒ Some CYP2C19 forms caused by changes in the gene may affect the way your body responds to clopidogrel.
- ⇒ Depending on your genetic test results, your doctor may switch clopidogrel to another medication that is better for you.
- ⇒ Other medications may also affect your response to clopidogrel. 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
- ⇒ **Metabolism:** the breakdown of a drug
- ⇒ **Prodrug:** the inactive form of a drug which needs to be activated in the body before it can produce the desired effect.

## Breakdown of CYP2C19 Enzyme Activity in the General Population



*"One size does not fit all."*

**Translational Initiatives for Pharmacogenomics**  
*The Charles Bronfman Institute for Personalized Medicine*

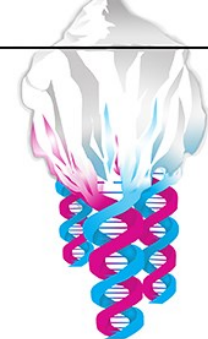
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Translational Initiatives in  
Pharmacogenomics

TIP



# Clopidogrel and CYP2C19



# Mount Sinai

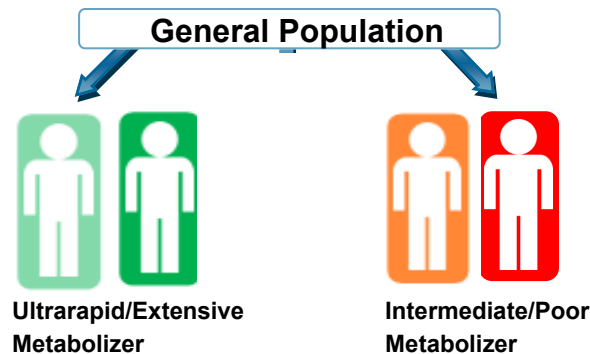


## Pharmacogenetics: *CYP2C19*

- ◆ 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 use 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.
- ◆ *CYP2C19* is an enzyme that is responsible for the metabolism of many commonly prescribed drugs such as clopidogrel. Changes in the *CYP2C19* gene leads to different forms of the *CYP2C19* enzyme; which affects the way your body breaks down ("metabolizes") the affected drugs.

### Clopidogrel (Plavix®)

- ◆ Clopidogrel is a medication used to prevent blood clots in patients with conditions such as strokes and heart attacks.
- ◆ Clopidogrel needs to be activated in the body to work (prodrug). *CYP2C19* is the enzyme that activates clopidogrel in the body.
- ◆ Changes in *CYP2C19* can lead to reduced amounts of active clopidogrel in the body. This can lead to serious side effects such as heart attacks, strokes and even death.



### Personalized Medicine at Mount Sinai

- ◆ The *CYP2C19* genetic test provides information about how fast or slow you metabolize and respond to clopidogrel.
- ◆ In Mount Sinai's pharmacogenetics program, your genetic test results including your *CYP2C19* results are added to the electronic medical records.
- ◆ If you are an **intermediate metabolizer** or a **poor metabolizer** of *CYP2C19*, your doctor will receive an alert when prescribing clopidogrel for you.
- ◆ This alert will tell the doctor to change to another medication that will be better for you. (see table below).

### *CYP2C19* enzyme forms and their effects on the breakdown of clopidogrel.

Classification	Protein activity	Clinical Relevance
<b>Ultrarapid Metabolizer</b>	Normal or increased activity of the enzyme	Normal to increased response to the drug, may be at increased risk for bleeding
<b>Extensive Metabolizer</b>	Normal enzyme activity	Normal response to the drug
<b>Intermediate Metabolizer</b>	Low activity of the enzyme leading to reduced amounts of active clopidogrel	Reduced response to the drug, may be at high risk of serious side effects
<b>Poor Metabolizer</b>	Lowest activity of the enzyme leading to very low amounts of active clopidogrel	Very reduced response to the drug, may be at highest risk for serious side effects.