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DPYD Fact Sheet

What is the *DPYD* Gene?

The *DPYD* gene provides the body with instructions for making an enzyme called dihydropyrimidine dehydrogenase. This enzyme is responsible for the breakdown of molecules called fluoropyrimidines. Fluoropyrimidines, such as 5-fluorouracil (5-FU) are drugs used as chemotherapies in the treatment of certain cancers.[i],[ii]

We all have variants/changes in our DNA; most of them don't cause any health-related problems, however, some affect the way our bodies metabolize certain drugs/supplements, and some are related to the development of certain health conditions. Roughly 2-8% of the population carry a genetic variation in the *DPYD* gene, which can affect an individual's ability to break down chemotherapy drugs like 5-FU[iii]. When the *DYPD* enzyme is not functioning properly, fluoropyrimidines can build up in the body and become toxic. This puts a person at increased risk of severe and sometimes fatal side effects, including fever, inflammation of the gastrointestinal tract, mouth, tongue and gums, vomiting, diarrhea and in severe cases heart, gastrointestinal bleeding and neurological conditions. This is referred to as Severe Fluoropyrimidine-Induced Toxicity (5-FU toxicity).[iv], [v], [vi]

What does having a *DPYD* variant mean for me and my family?

Genetic variants in *DYPD* are typically inherited from a parent. We all have 2 copies of the *DPYD* gene, and we inherit one copy from each parent. To be at risk for 5-FU-related toxicity, a person inherits one copy of a variant in *DYPD* from one parent. A variant in *DPYD* does not cause health problems on its own but puts a person at risk for severe toxicity when exposed to certain chemotherapies such as 5-FU or Capecitabine.

If two individuals who both have a *DPYD* variant have children together, they have a 25% chance to have a child who inherits both *DPYD* variants from each parent. An individual who inherits two copies of a *DPYD* gene variant can be at risk to have a condition called hereditary thymine-uraciluria which can include seizures, cognitive impairment/autism, language delay, brain abnormalities and developmental delays.[vii]

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Important Facts:

- Individuals with a *DPYD* variant should avoid use of fluoropyrimidines for cancer treatment or be treated with reduced starting doses of fluoropyrimidines (this depends on the specific *DPYD* variant present in that individual).
- A person with a *DPYD* variant who is considering pregnancy should consider having their partner tested for *DPYD* variants.
- Prenatal diagnosis options are available to couples who are both carriers of a *DYPD* variant to determine the *DPYD* genetic status of the fetus.
- Siblings and parents of a *DPYD* carrier are at 50% chance to carry the same *DPYD* variant.

How Can I Get More Information?

A referral to a genetic counsellor can help clarify individual risks and determine other at-risk family members who could benefit from predictive testing for the *DPYD* variant.

In Canada, genetic counselling is available at provincial genetic clinics by referral. Your healthcare provider can send a referral to Dynacare Genetics Specialty team at 450.901.3076. Our online referral form can be completed here. Alternatively, to locate a genetic clinic near you, visit the Canadian Association of Genetic Counsellors at www.cagc-accg.org.

Genetic Counselling Referral forms:

- Dynacare Pharmacogenomic Genetic Counselling Referral

[i] Food and Drug Administration: Highlights of prescribing information [fluorourcil]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/012209s040lbl.pdf Google Scholar

[ii] Food and Drug Administration: Highlights of prescribing information [Xeloda]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/020896s037lbl.pdf Google ScholarView F

[iii] Your Guide to Understanding Genetic Conditions - Dihydropyrimidine dehydrogenase deficiency NHI US National Library of Medicine, Accessed October 2018

[iv] Latchman J, Guastella A, Tofthagen C. 5-Fluorouracil toxicity and dihydropyrimidine dehydrogenase enzyme: implications for practice. Clin J Oncol Nurs. 2014 Oct;18(5):581-5. doi: 10.1188/14.CJON.581-585. PMID: 25253112; PMCID: PMC5469441.

[v] Johnson MR, Diasio RB. Importance of dihydropyrimidine dehydrogenase (DPD) deficiency in patients exhibiting toxicity following treatment with 5-fluorouracil. *Adv Enzyme Regul.* 2001;41:151–157. doi: 10.1016/S0065-2571(00)00011-X.

[vi] van Kuilenburg ABP. Dihydropyrimidine dehydrogenase and the efficacy and toxicity of 5-fluorouracil. *Eur J Cancer.* 2004;40(7):939–950. doi: 10.1016/j.ejca.2003.12.004.

[vii] Au KM, Lai CK, Yuen YP, Shek CC, Lam CW, Chan AY. Diagnosis of dihydropyrimidine dehydrogenase deficiency in a neonate with thymine-uraciluria. Hong Kong Med J. 2003 Apr;9(2):130-2. PMID: 12668826.