#ret #incomplete

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1 | SNP. Project. Write-up.

Resources: [[KBxSNPPCR]] Instructions

1.0.1 | Part One

Outline

- basics
- function and regulation
- SNP effect

Writing!%%

1.0.2 | Part One!

The *COMT* gene, or catechol-O-methyltransferase, encodes the *COMT* enzyme which is responsible for breaking down neurotransmitters the brain's prefrontal cortex. More specifically, it acts as a catalyst for the transfer of a methyl group from S-adenosylmethionine to dopamine, epinephrine, and norepinephrine. This process, called O-methylation, leads to the degradation of the aforementioned neurotransmitters. The *COMT* enzyme also effects the metabolism of exogenous substances, but that is irrelevant for the mutation at hand citation. The *COMT* gene itself is 27.22kb long and located on chromosome 22q11.2 citation. It has ubiquitous expression in 27 tissues, including the placenta, the adrenal, and the lung citation. Val158Met, also known as rs4680, is a common missense mutation swapping a guanine for an adenine. It has the frequency G=0.510915, and thus, A=0.489085. Val158Met causes the *COMT* enzyme to be roughly 25% as effective compared to the wild type. Expression levels in mRNA, despite its reduced protein abundance, are not effected by Val158Met citation & citation. Thus, Val158Met must be located in a protein-coding region causing the *COMT* enzyme to have lower protein integrity, explaining the discrepancy between mRNA expression and protein expression. This lower protein integrity is most likely manifested as diminished thermostability of the enzyme citation. The higher level effect of this reduced enzyme efficacy is greatly debated, and linked to many different phenotypes. At a broad level, lower *COMT* activity leads to higher levels of catecholamines in the prefrontal cortex. The actual effect of these increased levels are not well understood. One proposed theory is the Warrior versus Worrier hypothesis, which outlines two groups of personality traits based upon the Val158Met mutation citation. The "Warrior" group, defined as the wild type group with lower levels of catecholamines like dopamine, are said to have an advantage in processing aversive stimuli. They are also said to have higher pain tolerance, be less prone to stress, less exploratory, and ect. However, many of these claims are not well defined and bordering on pseudoscience citation. The "Worrier" group, those with the mutation, are said to have an advantage in memory and attention tasks citation. The Val158Met mutation has also been linked to schizophrenia, but this claim is debated citation.

Citations: *(order of appearance)*

- NCBI COMT catechol-O-methyltransferase *Homo sapiens* (human)
- Chromosomal mapping of the human catechol-O-methyltransferase gene to 22q11.1——-q11.2
- Gene Expression – NCBI COMT catechol-O-methyltransferase *Homo sapiens* (human)
- Lack of Association between rs4680 Polymorphism in Catechol-O-Methyltransferase Gene and Alcohol Use Disorder: A Meta-Analysis
- Functional Analysis of Genetic Variation in Catechol-O-Methyltransferase (COMT): Effects on mRNA, Protein, and Enzyme Activity in Postmortem Human Brain
- Kinetics of human soluble and membrane-bound catechol O-methyltransferase: a revised mechanism and description of the thermolabile variant of the enzyme
- Warriors versus worriers: the role of COMT gene variants
- Self Decode rs4680
- The effect of rs1076560 (DRD2) and rs4680 (COMT) on tardive dyskinesia and cognition in schizophrenia subjects