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## **Definitions**

- **Aryl Amine N-Acetyltransferase (NAT):** An enzyme that helps process certain chemicals in the body.
- **Alleles:** Different forms of a gene that can exist at a specific spot on a chromosome.
- **NAT110 and NAT111 Alleles:** Specific variants of the NAT1 gene that may affect enzyme activity.
- **Phenotype:** Observable traits or characteristics of an organism resulting from the interaction of its genetic makeup and the environment.
- **Recombinant Protein Expression Systems:** Laboratory methods used to produce proteins from genes inserted into bacteria, yeast, or mammalian cells.

## **Key Findings**

- The NAT110 and NAT111 alleles are considered "increased-activity" alleles compared to the NAT1\*4 reference allele.
- The NAT1\*10 allele is more common in East Asian populations.
- Studies show inconsistent results on the activity levels of NAT110 and NAT111 due to various experimental conditions and methodologies.
- Recent studies suggest that these alleles increase NAT1 activity through different mechanisms.

## **Introduction**

This minireview examines the functional expression of two genetic variants of the NAT1 gene, known as NAT110 and NAT111. These variants are thought to increase the enzyme's activity, but previous studies have shown inconsistent results. The review aims to provide clarity on how these alleles function and their impact on enzyme activity.

## **Main Content**

### **Background**

The NAT1 gene produces an enzyme that helps the body process various chemicals. Genetic differences in this gene can lead to variations in enzyme activity. The NAT110 and NAT111 alleles have been studied extensively, but results have varied.

### **NAT1\*10 Allele**

- **Description:** Defined by two specific changes in the DNA sequence.
- **Prevalence:** About 35-40% globally, higher in East Asian populations.
- **Studies:** Some show increased enzyme activity in tissues like the bladder, colon, liver, and blood cells, while others do not.
- **Mechanism:** Recent studies suggest the NAT1\*10 allele increases enzyme activity through enhanced protein translation.

#### **NAT1\*11 Allele**

- **Description:** Includes three related variants with several DNA sequence changes.
- **Prevalence:** About 1.8% globally, more common in Eurasian populations.
- **Studies:** Results are inconsistent, with some studies showing no significant effect on enzyme activity.
- **Mechanism:** Recent research indicates the NAT1\*11 allele may enhance protein translation efficiency.

#### **Mechanistic Insights**

- **Polyadenylation Signals:** Differences in the 3' untranslated region (UTR) of the NAT1 gene affect mRNA processing and stability.
- **Protein Translation:** Variants can influence the efficiency of protein production, impacting overall enzyme activity.

#### **Conclusion**

The NAT110 and NAT111 alleles are now recognized as "increased-activity" alleles, though their exact mechanisms of action differ. These findings help clarify previous inconsistencies and underscore the importance of considering genetic variability in enzyme activity studies. Understanding these differences can improve personalized medicine approaches, especially in drug metabolism and disease risk assessment.

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