NNT Gene

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nicotinamide nucleotide transhydrogenase

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1. Introduction

The *NNT* gene provides instructions for making an enzyme called nicotinamide nucleotide transhydrogenase. This enzyme is found embedded in the inner membrane of structures called mitochondria, which are the energy-producing centers of cells. This enzyme helps produce a substance called NADPH, which is involved in removing potentially toxic molecules called reactive oxygen species that can damage DNA, proteins, and cell membranes. Nicotinamide nucleotide transhydrogenase is found throughout the body, but it is particularly abundant in the hormone-producing adrenal and thyroid glands, heart, kidneys, and fatty tissue.

2. Health Conditions Related to Genetic Changes

2.1. Familial glucocorticoid deficiency

At least 25 mutations in the *NNT* gene have been found to cause familial glucocorticoid deficiency. This condition is characterized by potentially life-threatening low blood sugar (hypoglycemia), recurrent infections, and skin coloring darker than that of other family members (hyperpigmentation). The features of familial glucocorticoid deficiency are caused by an inability of the adrenal glands to produce a group of hormones called glucocorticoids, which play a role in many functions in the body. *NNT* gene mutations account for approximately 10 percent of cases of this condition.

Most of the mutations that cause familial glucocorticoid deficiency change single protein building blocks (amino acids) in the nicotinamide nucleotide transhydrogenase enzyme. These mutations impair the enzyme's ability to produce NADPH, leading to an increase in reactive oxygen species in the adrenal glands. Over time, these toxic molecules can impair the function of adrenal gland cells and lead to the death of those cells (apoptosis), diminishing the production of glucocorticoids. A shortage of these hormones impairs blood sugar regulation, immune system function, and other cellular functions, leading to the signs and symptoms of familial glucocorticoid deficiency.

It is unclear why *NNT* gene mutations seem to only affect adrenal gland function. Researchers suggest that individuals with familial glucocorticoid deficiency caused by *NNT* gene mutations could develop problems in other tissues over time as reactive oxygen species exert their harmful effects.

3. Other Names for This Gene

- energy-linked transhydrogenase
- GCCD4
- NAD(P) transhydrogenase
- NAD(P) transhydrogenase, mitochondrial
- NADP transhydrogenase
- NADPH transferase
- nicotinamide adenine dinucleotide phosphate + transhydrogenase
- NNTM_HUMAN

- pyridine nucleotide transhydrogenase

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