SERPINI1 Gene

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serpin family I member 1

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1. Normal Function

The *SERPINI1* gene provides instructions for making a protein called neuroserpin, which is a type of serine protease inhibitor (serpin). Serpins help control several kinds of chemical reactions by blocking (inhibiting) the activity of certain proteins. Neuroserpin inhibits the activity of an enzyme called tissue plasminogen activator (tPA), which plays a role in cell movement (migration), blood clotting, and inflammation.

As its name suggests, neuroserpin is involved in the development and function of the nervous system. This protein helps control the growth of nerve cells (neurons), particularly specialized extensions called axons that are required for the transmission of nerve impulses. Neuroserpin also plays a role in the development of synapses, which are the connections between neurons where cell-to-cell communication occurs. Synapses can change and adapt over time in response to experience, a characteristic called synaptic plasticity. Neuroserpin helps regulate synaptic plasticity, which suggests that it may be important for learning and memory.

2. Health Conditions Related to Genetic Changes

2.1. Familial encephalopathy with neuroserpin inclusion bodies

At least four mutations in the *SERPINI1* gene have been found to cause familial encephalopathy with neuroserpin inclusion bodies (FENIB). Each of these mutations changes a single protein building block (amino acid) used to make the neuroserpin protein. These changes result in the production of an abnormally shaped, unstable version of neuroserpin. Within neurons, defective neuroserpin proteins can attach to one another and form clumps called neuroserpin inclusion bodies or Collins bodies. These clumps disrupt the cells' normal functioning and ultimately lead to cell death. The gradual loss of neurons in certain parts of the brain causes progressive dementia in people with FENIB.

SERPINI1 mutations also reduce or eliminate the ability of neuroserpin to inhibit tPA in neurons. Researchers believe that unchecked activity of tPA may also contribute to the signs and symptoms of this condition.

Some *SERPINI1* mutations cause more severe forms of FENIB than others. The severity of the disease and its age of onset are correlated with the number of Collins bodies within neurons. One mutation, known as neuroserpin Syracuse, is associated with a moderate form of the disorder that causes a progressive decline in intellectual functioning beginning in a person's forties or fifties. This genetic change replaces the amino acid serine with the amino acid proline at position 49 in the neuroserpin protein (written as Ser49Pro or S49P).

Other *SERPINI1* mutations cause a more severe form of FENIB that is characterized by seizures and episodes of sudden, involuntary muscle jerking or twitching (myoclonus) in addition to dementia. These signs can appear as early as a person's teens. One of these severe mutations, called neuroserpin Portland, replaces the amino acid serine with the amino acid arginine at position 52 in the neuroserpin protein (written as Ser52Arg or S52R). Another mutation replaces the amino acid glycine with one of two other amino acids, glutamic acid or arginine, at protein position 392. (These mutations are written as Gly392Glu and Gly392Arg, respectively.) Children with one of these genetic changes experience a very severe form of the disorder that includes a combination of seizures and uncontrollable muscle jerks (myoclonic epilepsy) and delayed development.

3. Other Names for This Gene

- neuroserpin
- NEUS_HUMAN
- PI12
- protease inhibitor 12 (neuroserpin)
- serine (or cysteine) proteinase inhibitor, clade I (neuroserpin), member 1
- Serpin I1
- serpin peptidase inhibitor, clade I (neuroserpin), member 1

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