PABPN1 Gene

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poly(A) binding protein nuclear 1

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1. Introduction

The *PABPN1* gene provides instructions for making a protein that is found throughout the body. The PABPN1 protein plays an important role in processing molecules called messenger RNAs (mRNAs), which serve as genetic blueprints for making proteins. The PABPN1 protein attaches (binds) to the end of an mRNA molecule at a region called the polyadenine tail or poly(A) tail. Poly(A) tails consist of many copies of a molecule called adenine, which is one of the building blocks of RNA and its chemical cousin, DNA. Poly(A) tails protect the mRNA from being broken down and allow the mRNA to be transported within the cell. The PABPN1 protein helps add adenines to the poly(A) tail through a process called polyadenylation. PABPN1 also helps transport mRNA out of the nucleus and may be involved in regulating mRNA production and the breakdown of poor quality mRNA.

Near the beginning of the PABPN1 protein is an area where 10 copies of the protein building block (amino acid) alanine occur in a row. This stretch of alanines is known as a polyalanine tract. The role of the polyalanine tract in PABPN1 protein function is unknown.

2. Health Conditions Related to Genetic Changes

2.1. Oculopharyngeal muscular dystrophy

At least 20 different mutations in the *PABPN1* gene have been found to cause oculopharyngeal muscular dystrophy. This condition is characterized by muscle weakness that begins in adulthood and largely affects the eyelids, throat, shoulders, hips, and legs. The *PABPN1* gene mutations that cause this condition usually affect one of the two copies of the gene in each cell and result in a PABPN1 protein with an abnormally long (expanded) polyalanine tract that has 11 to 18 copies of alanine.

The age of onset and severity of the condition can be partly explained by the mutation. Most affected individuals have polyalanine tracts that are 13 alanines long and tend to develop muscle weakness in their sixties. Individuals with PABPN1 proteins that contain polyalanine tracts containing 16 to 18 copies of alanine often begin to experience muscle weakness in their forties or fifties. Individuals who have a polyalanine tract mutation containing 11 alanines tend to develop signs and symptom of the condition in their seventies. Some individuals have mutations in both copies of the *PABPN1* gene that lead to expanded polyalanine tracts. These individuals often develop muscle weakness in their thirties or forties and may have disturbances in nerve function (neuropathy) and neurological problems.

The extra alanines cause the PABPN1 protein to form nonfunctional clumps within muscle cells. These clumps (called intranuclear inclusions) accumulate and are thought to impair the normal functioning of muscle cells, eventually causing cell death. The loss of muscle cells over time most likely causes the muscle weakness seen in people with oculopharyngeal muscular dystrophy. In severe cases, it is likely that intranuclear inclusions affect nerve cells as well as muscle cells.

3. Other Names for This Gene

- OPMD
- PAB2
- PABP2
- PABP2_HUMAN

- poly(A) binding protein 2
- poly(A) binding protein II
- poly(A) binding protein, nuclear 1

References

1. Banerjee A, Apponi LH, Pavlath GK, Corbett AH. PABPN1: molecular function and muscle disease. FEBS J. 2013 Sep;280(17):4230-50. doi: 10.1111/febs.12294.
2. Cruz-Aguilar M, Guerrero-de Ferran C, Tovilla-Canales JL, Nava-Castañeda A,Zenteno JC. Characterization of PABPN1 expansion mutations in a large cohort ofMexican patients with oculopharyngeal muscular dystrophy (OPMD). J Investig Med. 2017 Mar;65(3):705-708. doi: 10.1136/jim-2016-000184.
3. Jouan L, Rocheford D, Szuto A, Carney E, David K, Dion PA, Rouleau GA. An 18alanine repeat in a severe form of oculopharyngeal muscular dystrophy. Can JNeurol Sci. 2014 Jul;41(4):508-11.
4. Richard P, Trollet C, Stojkovic T, de Becdelievre A, Perie S, Pouget J, EymardB; Neurologists of French Neuromuscular Reference Centers CORNEMUS and FILNEMUS. Correlation between PABPN1 genotype and disease severity in oculopharyngealmuscular dystrophy. Neurology. 2017 Jan 24;88(4):359-365. doi:10.1212/WNL.0000000000003554.