

# 1. Progeria 101: Frequently Asked Questions

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## What is Hutchinson-Gilford Progeria Syndrome (HGPS or Progeria)?

Progeria is also known as Hutchinson-Gilford Progeria Syndrome (HGPS). It was first described in 1886 by Dr. Jonathan Hutchinson and in 1897 by Dr. Hastings Gilford.

Progeria is a rare, fatal, “premature aging” syndrome. It’s called a syndrome because all the children have very similar symptoms that “go together”. The children have a remarkably similar appearance, even though Progeria affects children of all different ethnic backgrounds. Although most babies with Progeria are born looking healthy, they begin to display many characteristics of accelerated aging by 18-24 months of age, or even earlier. Progeria signs include growth failure, loss of body fat and hair, skin changes, stiffness of joints, hip dislocation, generalized atherosclerosis, cardiovascular (heart) disease, and stroke. Children with Progeria die of atherosclerosis (heart disease) or stroke at an average age of 13 years (with a range of about 8-21 years). Remarkably, the intellect of children with Progeria is unaffected, and despite the physical changes in their young bodies, these extraordinary children are intelligent, courageous, and full of life.

*Genetic testing for Progeria can be performed from a small sample of blood (1-2 tsp) or sometimes from a sample of saliva.*

## What is PRF's history and mission?

The Progeria Research Foundation (PRF) was established in the United States in 1999 by the parents of a child with Progeria, Drs. Leslie Gordon and Scott Berns, and many dedicated friends and family who saw the need for a medical resource for the doctors, patients, and families of those with Progeria and for funding of Progeria research. Since that time, PRF has become a driving force for promoting advances in the field, including the historic discovery of the Progeria gene, and has developed a comprehensive network of programs (see *PRF Programs & Services*, section 20) to aid those affected by Progeria and those researchers who want to conduct Progeria research. PRF is the only non-profit organization worldwide solely dedicated to finding treatments and the cure for Progeria.

## What causes Progeria?

After an intense scientific search, the gene for HGPS was discovered in April 2003 by a group of researchers working together through The Progeria Research Foundation (PRF) Genetics Consortium, as well as by a French group of researchers. The gene responsible for HGPS is called LMNA (pronounced “lamin-a”). One tiny spelling mistake in the DNA sequence of LMNA is responsible for Progeria. This type of gene change is called a point mutation. The LMNA gene normally makes a protein called lamin A, which is an important protein for most cells of our bodies. Lamin A is found in the cell nucleus (the part of each cell that contains the DNA) and helps maintain the shape and function of the cell.

In Progeria, the LMNA mutation causes the gene to produce an abnormal Lamin A protein called **progerin**. In children with Progeria, many cells in the body – such as the blood vessels, skin, and bones – make progerin protein. As the children age, progerin builds up in these cells causing progressive disease. The discovery of this new protein called progerin has allowed us to understand why children with Progeria grow old before their time, and led us down a pathway to the first-ever drug treatment trials for Progeria (see *Drug Treatment Trials*, section 19). We also now know that everyone's body makes progerin, although in much lower amounts compared to children with Progeria. Therefore, by working to help children with Progeria, we may have discovered a brand new protein that affects heart disease and aging in all of us (See *Aging & Progeria*, section 18).

## How is Progeria diagnosed?

Progeria is best diagnosed by using both clinical examination and genetic testing. When a physician suspects that a child has Progeria, he or she may consult with a geneticist and/or genetic counselor about this possibility. Genetic testing in the United States should be performed through a CLIA-approved\* testing laboratory. Testing can be achieved through The PRF Diagnostic Testing Program, provided at no cost to families (see *PRF Programs & Services*, section 20). The genetic test is done by coordinating a blood sample submission by mail through home physicians, from anywhere in the world, to PRF. Once the blood sample is received, the test results are usually provided in 10 days to 4 weeks, depending on the extent of genetic testing that is required. Results are provided to families through home physicians, who can discuss results, answer questions, and provide a care plan with families in person. PRF is always available for questions and follow-up.

## Are there different types of Progeria?

In this handbook, we refer to the typical or classical HGPS as Progeria. Classical Progeria is caused by a particular genetic change in a particular location on the LMNA gene. Therefore, when we are searching only for classical Progeria, we test one section of the LMNA gene, and not the entire gene. There are other closely related genetic diseases that are called “progeroid laminopathies” or “progeroid syndromes”. These diseases can be more or less severe than classical Progeria, and they are typically even more rare than classical HGPS. When we are searching for progeroid syndromes, we test the entire LMNA gene.

The guidelines in this handbook are written for children with classical Progeria, because we know more about the disease process and treatment strategies for classical Progeria. Applying that knowledge to nonclassical progeroid syndromes can be helpful to families and home caretakers, but good judgment must be applied, since children with nonclassical progeroid syndromes will have different needs and problems.

\*Clinical Laboratory Improvement Amendments (CLIA) is a body of industry regulations ensuring quality laboratory testing.

## Is Progeria contagious or inherited?

HGPS is definitely not contagious, and is not usually passed down in families. The gene change is almost always a chance occurrence that is extremely rare. Children with other types of progeroid syndromes which are not HGPS may have diseases that are passed down in families. However, HGPS is a “sporadic autosomal dominant” mutation – sporadic because it is a new change in that family, and dominant because only one copy of the gene needs to be changed in order to have the syndrome.

For parents who have never had a child with Progeria, the chances of having a child with Progeria are 1 in 4 million. But for parents who have already had a child with Progeria, the chances of it happening again to those parents is much higher – about 2-3%. Why the increase? This is due to a condition called “mosaicism”, where a parent has the genetic mutation for Progeria in a small proportion of their cells, but does not have Progeria. Mosaicism occurs a small percentage of the time (2-3%) in many genetic diseases. If some of the parental eggs or sperm have the genetic mutation, then those parents could have another child with Progeria. Prenatal testing is available to look for the LMNA genetic change.