Progeria

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ABSTRACT

Progeria has medicinal properties that mimic premature aging. Although mutations are thought to be responsible for the syndrome, the mechanism of action is not yet clear. Progeria research has gained momentum, especially in the last two decades, because there are opportunities to find clues about aging in general and in other path physiological conditions. Various clinical models have been developed in Vivo and Vitro to understand the cellular and molecular basis of a number of clinically controversial rare genetic diseases within the Progeria Syndrome (PS) range. According to the latest clinical studies, the pharyngeal transmission inhibitor Lonafernab is an effective "drug of hope" for Hutchinson-Gulford progeria syndrome (HGPS) and is believed to cause weight gain and cardiovascular disease in children with progeria. And it helps improve the skeleton. If I succeed in progeria research it may seem like the beginning of a new era and so it is a good time to review the progress of research in this field, molecular aspects, experimental models, promising drug remedies and better understanding of PS and its effects. Can be highlighted.

Keywords: Progeria, Prelamine A, Lamin A, HGPS, Morphulinus,

1 Introduction

Progeria is a very rare genetic disease, one of many progeria syndromes, in which age-like symptoms occur at a very young age. The word progeria is derived from the Greek word "pro" which means "previously" or "previous time" and "geras" means "old age". People born with progeria usually live to be in their twenties. It is a genetic disorder that is rarely inherited because it occurs as a new mutation and carriers usually do not survive and reproduce. The term progeria applies strictly to any disease characterized by symptoms of premature aging and is often used in the same way, but Hutchinson-Gilford progeria syndrome (HGPS) 2 is more common. A rare genetic disorder characterized by premature aging. Signs and symptoms vary by age and severity, but are usually much more consistent. Babies with HGPS usually appear normal at birth. In the first year, growth is significantly inhibited. Facial features can be identified by the inverted chin, a narrow nostril, and the nose. Exercise and intellectual development are common. Deaths usually occur between the ages of 6 and 20 due to complications of severe atherosclerosis, such as heart disease (myocardial infection) and stroke. The average age is about 13 years.

2 Prevalence

The prevalence of this condition is very low, affecting 1 in 8 million people. Researchers are very interested in Progeria because it can represent a normal aging process. The disease was first described by Jonathan Hutchinson in 1886. It was also independently described by Hastings Gilford in 1897. This condition was called Hutchinson-Gilford Progeria syndrome. An estimated 400 children worldwide are infected with the disease (Progeria Research Foundation).

3 Causes of Progeria

The causes of progressive liver disease are slow. There is no significant change in endocrine function, but the growth hormone response is normal. Some researchers attribute this to the loss of collagen and elastin in the skin. Some have suggested that HGPS is due to poor metabolism of vitamin E. Mutations in LMNA, the gene encoding lamina A, were reported in 2003.The only gene associated with HGPS and found in 90% of cases. History has shown that the main symptoms of HGPS patients are related to mutations in the LMNA gene. Typically, the LMNA gene encodes a structural protein called prelamin A. The forensic functional groups are connected to the structural carboxyl terminals. The forensic group allows the pre-Lemna A to temporarily stick to the edge of the base. Once the protein is bound, the pharyngeal group is removed. If this forensic group is not removed, the protein is permanently attached to the atomic edge. If there is no pharyngeal group, then the whole layer A is called layer A. The forensic group causes the prelamin A to temporarily stick to the edge of the base. When the protein binds, the pharyngeal group is removed. If this forensic group is not removed, the protein is permanently attached to the atomic edge. Without the pharyngeal group, the entire layer A is called layer A.

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Steps into a regular cell	Steps into the cell with progeria
Farnesyl group is extract from prelamin A.	Farnesyl group belongs to prelamin A.
Lamin A is the normal form.	Progerin is an abnormal version of prelamin A.
The nuclear rim is not attached to Lamin A.	The nuclear rim is where Progerin is tethered.

4 Clinical Manifestation

Early sickness includes scleroderma and local involvement of the skin. Additional conditions appear as the baby progresses the limits of growth, the loss of hair loss and some of the features of the face (small face and chin, closed nose) are clear. Clinical findings for Hutchinson's Gulford Progeria Syndrome (HGPS) include facial and skeletal abnormalities, and skin and hair abnormalities. People with this condition often have smaller and weaker bodies, such as older people. Internal growth is not affected. Some age-related conditions do not develop, but symptoms develop 8 to 10 times faster than normal. In particular, patients show no risk of neurodegeneration or cancer. Physical "fruit and tear" conditions associated with aging, such as cataracts (due to UV exposure) and osteoarthritis (due to mechanical wear and tear) do not usually occur.

The following are other sign & symptoms:

- Skin and hair: Skin changes can occur at birth. Key features include shiny, supple skin. With light fat, wrinkles may appear on the skin. The patient is physically weak. Exposure to bright sunlight can cause skin hyper pigmentation with irritation. Complete hair loss on all parts of the body with skin, eyes and skin
- Musculoskeletal anomalies: The limbs are slender and have few muscles. The joints are prominent. Bending the knee joint can cause malfunctions. The patient walks slightly abnormally. Your chest will be pear-shaped. The face resembles that of an old man, with wide eyes and large ears. The incisors fall off quickly.
- Illness and death in people with HGPS is primarily the result of coronary arteries and coronary atherosclerosis, and at least 90% of deaths are directly related to complications of progressive atherosclerosis.
- Complications of heart disease include myocardial infarction and heart attack. In most cases, the cause of death is a heart attack

5 Diagnosis

Symptoms and signs such as skin changes, abnormal growth, and hair loss are diagnosed accordingly. Genetic testing for mutations in LMNA can confirm the diagnosis of Progeria. Because symptoms are so noticeable, your paediatrician may see them during regular check-ups. See your paediatrician if your child has changes that look like symptoms of progeria. She will check your baby's hearing and vision, measure heart rate and blood pressure, and compare your baby's height and weight with other children of her age. If a paediatrician is involved later, parents may need to see a geneticist who can confirm the diagnosis with blood tests.

6 Differential Diagnosis

Another syndrome of premature aging, also known as thrill-mimicking progesterone syndrome, must be different from progesterone. Neonatal progesterone syndrome occurs at birth and includes Weidmann-Lutinstratch syndrome, Hallermann-Streiff syndrome, and D-Barcy syndrome. Others, such as meningococcal dysplasia or cocaine syndrome, may be present in newborns but are diagnosed later. Werner syndrome and acupuncture may also be associated with HGPS

7 Treatment

- There is no effective treatment.
- Most treatment focuses on reducing complications with coronary artery bypass grafting or low-dose aspirin.
- Experiments have been performed to treat growth hormone.
- Efforts have also been made to use morphine to reduce progesterone production. The mutant pre-MRNA used the antisense morphine-oligonucleotides specifically directed against the mutant axon 11-axon 12 junction.

Low-dose aspirin: Daily aspirin may be prescribed to help prevent heart attacks and strokes. Children should only take aspirin under close medical supervision as it can have serious side effects.

8 current therapeutic strategies

Because HGPS impacts so many organ systems and cellular functions, it will almost certainly necessitate a mix of treatments. Fortunately, several medicines have been developed in the last five years that can assist patients. When it comes to developing medicines for the treatment of diseases, there are three main areas of focus:

- Complete post-translational processing inhibition in progesterone.
- Progesterone production is reduced, and the negative effects of progesterone are reduced.

As previously stated, farnesyltransferase inhibitors are the only medication that has proven benefit in patients, with a 1.6-year rise in age. They act by preventing progesterone from fornicating. Lonafarnab was tested in vitro and later in vivo with outstanding results. After the translation,

several editing locks were tested, but none had the same strong effect. In vivo models of the condition, inhibiting isoprenylcysteine carboxylmethyltransferase (ICMT), which inhibits carboxymethylation during prelamin-A processing and prevents the targeting of CAAX proteins to cell membranes, has shown promise. However, it has not yet been detected or reported. In vivo application. Following that, scientists began exploring for strategies to lower progesterone levels. Aurolimus, a rapamycin derivative that increases progesterone clearance, is the closest medicinal application for broad use. Both rapamycin and aurolysis significantly improved the cellular phenotype in cellular models. The efficacy of a combination of Lonafarnib and Aurolimus is being tested in the second phase of an ongoing clinical investigation (ClinicalTrials.gov identifier: NCT02579044). The primary school will close in December 2020. In medical research, some substances have been demonstrated to lower progesterone levels. All forms of trans-retinoic acid, sulforaphane, and calcitriol are among them (the active hormonal form of vitamin D). Everyone must now be evaluated in a mouse model of the disease to see if they can have the same effects in humans. The development of CRISPR treatment has sparked renewed interest in genetic approaches to reducing progesterone production. From a genetic standpoint, HGPS is a fantastic disease to cure because a single point alteration greatly improves the disease. As a result, a lot of research is being done to improve this element.

9 Conclusion

Progress has been made in understanding the mechanism of HGPS and its probable consequences on physical ageing since the genetic basis of the illness was discovered over a decade ago. The buildup of incorrectly processed lamina a protein, progesterone, appears to mediate a wide range of negative effects on HGPS patients' cells, according to the findings of various researches. Much advancement in basic research has led to the development of possible therapeutics, resulting in multiple clinical studies for HGPS patients, particularly in the last few years. It was thought that by targeting the biosynthesis routes of isoprenoid and cholesterol, these medicines may lessen the clinical course of HGPS. In clinical studies, however, the medications are unable to target the secret spice location. As a result, extra approaches may be required. Finally, a better knowledge of the mechanisms of HGPS could lead to a reduction in the degenerative processes seen in HGPS and the development of potential therapeutics for age-related disorders.

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