PROGERIA

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WHAT IS IT?

Progeria or Hutchinson-Gilford progeria syndrome

- extremely rare genetic disorder → appearance of premature aging in children

It strikes a child every 4-8 million births.

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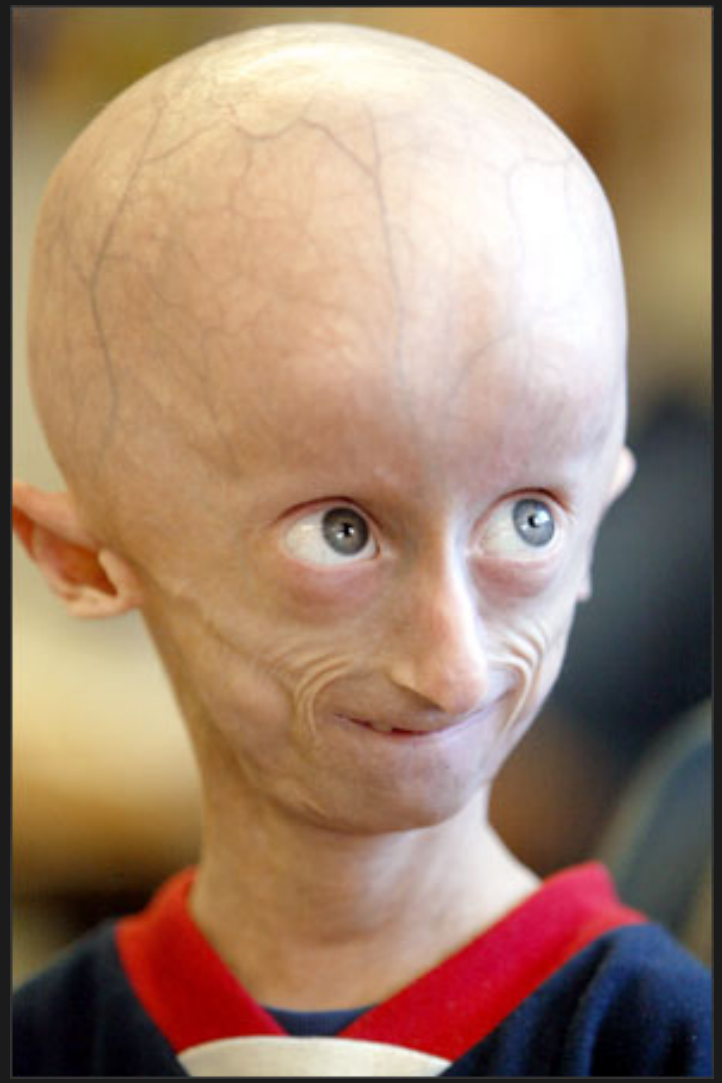
70 children in the world suffering from progeria

- There are a lot of form of Progeria, but the most known form is the Hutchinson-Gilford, from the name of the first doctors who studied this syndrome

SIGNS AND SYMPTOMS



Symptoms during the first months

Defects in the growth and localized scleroderma

After 18/24 months:

- Limited growth
- Hair loss
- characteristic appearance → little face with a slightly prominent jaw and pressed nose

Signs more marked over the years :

- wrinkled skin
- Arteriosclerosis
- kidney failure
- Loss of vision
- cardiovascular problems
- Scleroderma

Degeneration of the musculoskeletal system

Joint stiffness

Loss of body and muscle fat

Hip dislocation

Individuals usually maintain normal mental and motor development

Patients usually die within 20 years due to heart disease, heart attack or stroke

ETIOLOGY

CELL NUCLEUS → Delimitated by a nuclear envelope

NUCLEAR ENVELOPE

- Outer nuclear membrane
- Nuclear lamina
- Inner nucear membrane

Nuclear lamina → fibrous lattice formed by associations of laminae (fibrous proteins that aggregate to form more complex structures)

ETIOLOGY

7 types of laminae → 3 genes: A, B, C

Progeria = gene LMNA

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Overlaminate A

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At the end it presents cysteines that are prenylated by the addition of a working group

Unlike the " accelerated aging diseases " progeria it is not caused by defective DNA repair . Since these diseases cause changes in various aspects of aging , but never in all , they are often called " segmental progerias "

ETIOLOGY

Events in a normal somatic cell	Events in a cell with mutations
The LMNA gene encodes the pre-protein Lamin A	The LMNA gene codes for the protein Lamin A
Prelamin A has a farnesyl group attached at the end	Prelamin A has a Farnesyl group attached to the end
Farnesyl group of prelamin A is removed	Farnesyl group remained attached to prelamin A
Normal form, called "Lamin A"	Abnormal form of prelamin A, called "progerin"
Lamin A isn't anchored to the nuclear rim	Progerin is anchored to the nuclear rim
Normal shape of the nucleus	Abnormal shape of the nucleus

SEARCH

In recent years, researchers have made some very important discoveries that have enabled us to better understand the mechanisms that cause the disease .

2003

the discovery of the gene that causes progeria

Experimental therapies that slow the progression of the disease

"SCIENTIFIC MIRACLE"

SEARCH

2007/2009

Experiments with an inhibitor drug which should slow the progression of the disease

DUTY POINT ON PROGERIA

Problem

Genetic mutation in LMNA

Progressive accumulation of progeria

Nuclear cell loses its regular organisation

Nuclear DNA assumes a new spatial organisation

Nuclear DNA is more exposed to damage

The cell blocks his own cell cycle

Possible therapy

ATRA reduces the levels of progerin

Synergistic effect

Rapamycin reduces the levels of progerin

The cell takes up the cell cycle