National Human Genome Research Institute

Mouse Model of Hutchinson-Gilford Progeria Syndrome and Vascular Abnormalities

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KEY WORDS

Hutchinson-Gilford Progeria Syndrome, Arteriosclerosis, Aging, LMNA Gene, Lamin A

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PATENT-PENDING TECHNOLOGY AVAILABLE FOR LICENSING

SUMMARY

Children with Hutchinson-Gilford progeria syndrome (HGPS) suffer from acceleration of certain aging symptoms, mainly cardiovascular disease that generally leads to death from myocardial infarction and/or stroke. The cause of HGPS has been discovered to be a de novo point mutation in lamin A (LMNA). The LMNA gene has three protein products: lamin A, lamin C, and lamin Adelta10, which are components of the nuclear lamina. De novo mutation 1824 C to T (also called G608G) creates a splice donor site that results in a mutant LNMA protein called progerin. Progerin cannot be properly post-transcriptionally modified and causes alterations in nuclear structure and function.

NHGRI researchers have generated a transgenic mouse model of HGPS. This mouse carries a bacterial artificial chromosome (BAC) with the G608G mutated form of human LMNA. It also retains a normal form of mouse LMNA. A control mouse with wild-type human LMNA is also available. The mice are C57BL/6 animals that lack the external phenotype seen in human progeria, but have vascular abnormalities resembling the human syndrome. Specifically, the animals show progressive vascular smooth muscle cell loss in large arteries and replacement with proteoglycan and collagen (indicating progressive vascular calcification).

POTENTIAL COMMERCIAL APPLICATIONS

This mouse model can be used to further understand the vascular pathology of progeria and to study potential therapies. It can also be used to investigate symptoms of, and therapeutic treatments for, other cardiovascular and aging disorders, especially those that involve atherosclerotic lesions and vascular calcification.

RELATED ARTICLES

Varga, R. et al., Progressive Vascular Smooth Muscle Cell Defects in a Mouse Model of Hutchinson-Gilford Progeria Syndrome, 103 Proc Natl Acad Sci U S A 3250 (2006). http://www.pnas.org/content/103/9/3250.full.pdf

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