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Registered Charity UK No 1111075

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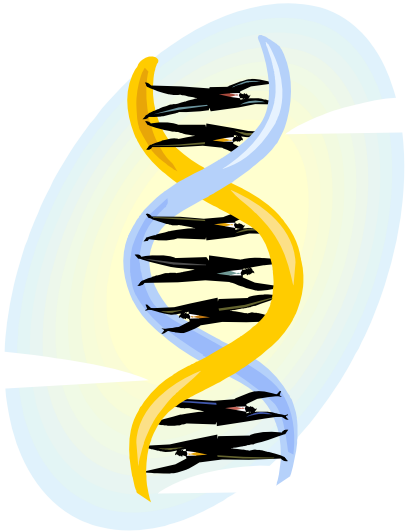
Síndrome Linfoproliferativo Ligado al Cromosoma X

Terapia génica y XLP



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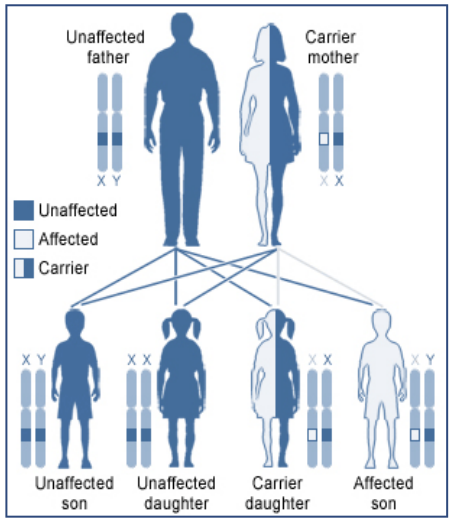
Inside the cells

Introducción

Hoy se está hablando mucho de la terapia génica, que ofrece el potencial de toda una gama nueva de tratamientos avanzados para un gran número de trastornos médicos y remedios a muchas enfermedades, habiéndose alcanzado exitosos resultados en ciertos campos, a la vez que decepcionantes fracasos en otros. El propósito de este prospecto es el de esbozar de qué forma quienes padecen del síndrome linfoproliferativo ligado al cromosoma X (XLP) podrían beneficiarse potencialmente de esta ciencia emergente, y cómo podría funcionar en concreto para el XLP.

Inheritance

The inheritance of XLP follows an "X-linked" (or "sex-linked") recessive pattern, in which females can be carriers of a *SH2DIA* mutation but only males will have the disease. Because females have two copies of the X-chromosome, they also have two copies of every gene on the X-chromosome. Because *SH2DIA* mutations are very rare, a female who inherits one chromosome carrying a mutation of the gene for XLP from one parent will almost always inherit a normal X-chromosome from the other parent. In all XLP mothers who carry a *SH2DIA* mutation on one of their two X-chromosomes, the normal *SH2DIA* gene on the other X chromosome provides enough *SH2DIA* function to prevent any disease. For this reason, a *SH2DIA* mutation in a female is termed a "recessive" mutation. In other words, although the female who carries a recessive *SH2DIA* mutation can pass the abnormal *SH2DIA* gene on to her children, she will not show any symptoms of XLP because of the protective effect of the normal *SH2DIA* gene on the other X-chromosome.



Unlike females who carry two copies of *SH2DIA* on their matched X-chromosomes, males have only one copy of the *SH2DIA* gene because they have only one X-chromosome. This is because a male who inherits from his mother an X-chromosome with one *SH2DIA* gene inherits from his father a shorter Y chromosome that lacks a copy of the *SH2DIA* gene. With no normal *SH2DIA* gene on the Y-chromosome to compensate for a *SH2DIA* mutation inherited on the mother's X-chromosome, all males with a *SH2DIA* mutation will have clinical signs of XLP.

When a mother is a carrier of a *SH2DIA* mutation on one of her two X-chromosomes, there is a 50% chance in any pregnancy that she will pass the X-chromosome with the *SH2DIA* mutation onto the child. If the child who inherits the *SH2DIA* mutation is a girl, she will be a carrier of XLP, and, like her mother, be able to pass the *SH2DIA* mutation on to her own children. However, also like her mother, she will not show symptoms of XLP. If the child is a boy, there is a 50% chance he will inherit *SH2DIA* mutation and have XLP and a 50% chance he will inherit only the X chromosome with the normal *SH2DIA* gene and, therefore, not have XLP. If the male inherits the *SH2DIA* mutation and has XLP, all of his daughters will be carriers, but none of his sons will have XLP. This is because the X-and Y-chromosomes are the sex-determining chromosomes, and all children who inherit his Y-chromosome (with no *SH2DIA* gene) from him will be boys, and all children who inherit the X-chromosome with a *SH2DIA* mutation will be girls. A genetic counsellor can assist families in understanding these potential outcomes.

Possible pregnancy outcomes:

A new mutation:

When a *SH2DIA* mutation for XLP cannot be detected in either parent, this is considered a new mutation. New mutations can be sporadic or they can be a result of "gonadal mosaicism." Gonadal mosaicism is the rare occurrence of a genetic mutation in a proportion of the eggs or sperm of an individual as a result of a random mutation that occurs during the development of eggs and sperm. The individual does not have any signs of the disorder, and the mutation would not be detected by a blood test because it is in only the egg or sperm cells. However, if one of the egg or sperm cells is used to conceive a child, that child will have the mutation in all cells.

Definitions:

o **DNA** (Deoxyribonucleic acid) is the molecule that carries genetic information.

o **Cell:** The smallest unit of living organism from which all tissues are made. Except for mature red cells, all cells contain complete copies of all 46 chromosomes. Cells are highly variable and specialize into many different types of cells and tissues, but all cells must at some stage use genes as instructions to make essential proteins.

o **Chromosome:** The genetic structure of cells that contains the DNA. Each chromosome is a single strand of DNA that encodes from hundreds to thousands of separate genes. All 23 pairs of chromosomes reside in the cell nucleus.

o **Gene:** The physical and functional unit of heredity located in a specific position on a particular chromosome. Most human genes are given a letter name, such as "*SH2DIA,*" and written by convention in italics.

o **Mutation:** A heritable change in the structure of a gene.