Understanding the Genetics

There are many lipodystrophy conditions, all of which share similarities as well as having many differences. Here I will try to explain the genetics and hereditary behind these rare conditions. Our genetic fingerprint is packaged into 46 chromosomes – 22 pairs plus the X and Y (sex determining) chromosomes. Each chromosome pair carries information pertaining to a particular phenotype (outward characteristic). This information is coded in what we call genes. So there are two copies of every gene, each called an allele – one on each chromosome in a pair. Our individuality is governed by which genes we inherit from our parents. Of our 22 pairs of chromosomes, one from a pair is inherited from our mother and the other from our father. In the same way our X and Y (sex) chromosomes are inherited, one from each parent – although X and Y are not strictly a pair as there are many differences between them. Many different gene expression patterns govern the outward characteristics that result from our unique combination of genes. For example: A dominant characteristic needs only one allele (one gene copy from the chromosome pair) to be positive for that trait in order for it to be expressed. A recessive characteristic needs two alleles (copies) to be positive for that trait in order for it to be expressed. An autosomal (dominant/recessive) characteristic simply means the gene is one of those encoded on the 22 pairs of chromosomes (not the X/Y). A sex linked (dominant/recessive) characteristic means the gene is one of those encoded by the sex chromosomes, X and/or Y.

Familial Partial Lipodystrophy, Type 2; (Dunnigan Type); FPLD2

FPLD of the Dunnigan type can be caused by a number of distinct but similar mutations in the gene that codes for a protein called lamin A/C (LMNA). FPLD2, or more accurately, the mutation that gives rise to the condition, is passed on through autosomal dominant inheritance. That means its inheritance is not connected to gender, and only one ‘mutant’ copy of the gene is required for the condition to present itself, i.e., passed on from one, but not both parents. A person, who does not have FPLD2 himself or herself, cannot pass it on to the next generation. Familial Partial Lipodystrophy, Type 1; (Kobberling Type); FPLD1 Suggested autosomal dominant inheritance, although the faulty gene has not yet been discovered/characterised.

Familial Partial Lipodystrophy, Type 3; FPLD3

FPLD3 is caused by a mutation in the gene that encodes a protein called PPARg (Peroxisome Proliferator Activated Receptor Gamma), and shows autosomal dominant inheritance.

Congenital Generalized Lipodystrophy, Type 2; CGL2; Berardinelli-Sepi CGL2

CGL2 is caused by a mutation in the gene that codes for a protein called Seipin (also known as BSCL2), and shows autosomal recessive inheritance. That means two mutant copies of the gene are required for the condition to present itself, i.e., one passed on from each parent (they themselves may only be carriers, having only one mutant copy of the gene).

Congenital Generalized Lipodystrophy, Type 1; CGL1; Berardinelli-Sepi CGL1

CGL1 is caused by a mutation in the gene encoding a protein called AGPAT2 (1-acylglycerol-3-phosphate O-acyltransferase-2), and shows autosomal recessive inheritance.

Acquired Lipodystrophies

Acquired lipodystrophies appear to have no genetic basis and may have been triggered by various environmental factors.

I hope this information helps to answer some questions I know a few of you have regarding inheritance and your children etc. If you have any questions or require further details about the lipodystrophy conditions listed here, or any not mentioned, I would be more that happy to help. Feel free to send me a private message on the forum.

Becky

* With thanks to author Rebecca Sanders for use of information.