What types of mutations might I have?

On the next page are listed the different types of mutations that patients may have in their gene for dysferlin. Each individual patient has one or two specific mutations, which can be found by gene mutation analysis (gene sequencing). Please read the document "Why should I get gene mutation analysis?" for information on why you should find out which specific mutations you have.

You should understand the answers to the following questions before reading about the different types of mutations:

What are proteins?
Proteins are large molecules that make up cells in the human body. There are two basic types of proteins. Some form the structure of cells – you can think of these proteins as building blocks that are put together to make cells. Others carry out certain functions within the cell – you can think of these proteins as small machines inside your body. The dysferlin protein is one of these machines, and scientists think that its job is to help fix any holes in the outer membrane (the outer wall) of the cell.

What do proteins look like?
All proteins—both building blocks and machines—are actually long ribbons that are folded up into three-dimensional shapes. Each long ribbon is a chain of connected links called amino acids. There are 20 different kinds of amino acids, each with a slightly different shape. The different kinds of amino acids are strung together in a specific sequence to form a protein ribbon. The exact sequence of these amino acids in the protein is very important for the protein to fold up correctly and to carry out its proper function in the cell.

What is DNA?
DNA (deoxyribonucleic acid) is the information storage system of the body. DNA is a code that contains instructions telling the cell how to make all of its proteins. There is a separate DNA code (a gene) corresponding to each protein that is made by the cell. For example, instructions for how to make the dysferlin protein are written down in DNA code in the dysferlin gene.

What does DNA look like?
Like proteins, DNA molecules are also long ribbons. But DNA ribbons don't act as machines, they just store instructions for making the protein ribbons. Each protein is a chain of amino acids, and each DNA molecule is a chain of connected links called nucleotides. There are four different nucleotides: adenine (A), thymine (T), guanine (G), and cytosine (C). Each set of three nucleotides is code for a specific amino acid. For example, if the DNA has the nucleotides adenine, then thymine, then guanine in a row (ATG), that is code for an amino acid called Methionine.

How is the DNA code used to make proteins?
Proteins are made by machines called ribosomes, which read the DNA code and translate it into a chain of amino acids to form a protein. The ribosome reads each set of three nucleotides in the DNA and determines which amino acids to attach together. The DNA also tells the ribosome when the protein is finished; i.e. when it should stop attaching new amino acids to the protein. Because the nucleotides are read in groups of three, it is important for the ribosome to know how to group the nucleotides. If they are grouped incorrectly, the ribosome will choose the wrong amino acids and the protein will not function.

Types of mutations

The DNA code sometimes has mistakes, called mutations, which cause defects in proteins. If there are mutations in the dysferlin gene, then the dysferlin protein will not be made correctly. Defects in the protein can be mild or severe depending on the type of mutation.

A MISSENSE mutation occurs when just one of the amino acids in the protein is wrong.
This mutation is caused by a mistake in one DNA nucleotide in the dysferlin gene. That one nucleotide is part of a set of three nucleotides that code for a specific amino acid. When the ribosome reads this particular set of three nucleotides, one of them is wrong and the ribosome selects the wrong amino acid for the protein. Missense mutations can range from very mild to severe, depending on where in the protein the affected amino acid is located and how important the affected amino acid is to the protein's function.

A SPLICE-SITE mutation occurs when a sizeable section of the protein is missing.
This mutation is caused by a mistake in the DNA that leads to a whole section of the protein being left out when the protein is made by the ribosome. In the case of dysferlin, this type of mutation usually means that 1-4% of the protein's amino acids are missing. Splice-site mutations can range from mild to severe, depending on which section of the protein is missing.

A FRAMESHIFT mutation occurs when all of the amino acids in the protein, after a certain point, are wrong.
This mutation is caused by an insertion or deletion of one or more nucleotides in the DNA. Because the ribosome makes the protein by reading sets of three nucleotides, inserting or deleting a nucleotide means that the ribosome can no longer correctly group the sets of three. Every set of three after the insertion/deletion is incorrectly grouped, so the ribosome picks the wrong amino acid for every set of three after this point in the protein. This is a severe defect because much of the protein is wrong and the protein cannot function correctly.

A NONSENSE or STOP mutation occurs when the protein chain stops prematurely.
This mutation is caused by a mistake in the DNA that tells the ribosome to stop attaching new amino acids to the protein. The ribosome stops too early and never even makes part of the protein. This is a severe defect because much of the protein is missing, so the protein cannot function correctly. It may be possible to correct this type of mutation, however, by using a molecular signal to tell the ribosome not to stop making the protein.