THE LAYMAN'S VIEW OF WHAT IS FA AND HOW DOES THAT AFFECT FA RESEARCH? Rev 3

"Most of us know that DNA is a sequence of codes arranged as genes. A new one-cell child gets to choose one of two genes from each of the parents of all the gene sets in the DNA. In FA usually both parents have one malfunctioning FA gene so the child has a 1 in 4 chance to choose both bad genes and therefore have FA.

The FA gene's code is for the production of a protein called Frataxin (named after the FA disorder) which has a section that uses repeats of the body's basic building block chemicals GAA. The GAA code normally repeats about 5 - 35 times but most FA'ers have 150 – 1700 GAA repeats. So when the RNA (what I call the "cook") tries to decode the Frataxin DNA (what I call the "recipe") to make Frataxin proteins the message gets confused when it comes to the GAA repeats and the body does not produce enough Frataxin. (In about 4% of FA'ers point mutations or exon deletions may cause the malfunction. I do not deal with that phenomena here.) There is some evidence that the more repeats you have the less Frataxin that is produced and the faster one progresses, but there are other variables that researchers don't yet understand that makes this assumption unreliable. It doesn't necessarily happen that way.

Now let's look at how Frataxin is used and what's going wrong in the linkage of nerve cells that carries the electrical signals between the brain and the muscles. In FA the signals are less strong and arrive late.

Frataxin is found in the mitochondria of each nerve cell. The mitochondrion is the energy production part of a nerve cell. Part of the energy production in the mitochondrion comes from iron and sulfur, and Frataxin assists in the formation of iron-sulfur lattices. These lattices are then processed through the mitochondrion "energy factory" that creates the energy, ATP, which powers our bodies. If there is not enough frataxin in the mitochondria, some of the iron and sulfur is left sitting around in the cells and they do not get turned into energy. When the mitochondrion "factory" does not run at full efficiency it gets sick. It also generates a high level of oxygen-based "free radicals" which then wreak havoc on our cells and add to the increasing sickness and eventual death of the nerve cells linking the brain to the muscles. Some of the excess unused trapped iron bonds to the free radicals forming a toxic iron oxide which also hurts the mitochondrion and nerve cell.

Now one can understand why FA'ers have increasing trouble with their balance and walking; these increasingly sick mitochondria and nerve cells that form the electrical "wire" from brain to muscles and from sensory nerves back to the brain have increasing trouble carrying the signal back and forth.

Now with your new understanding let's talk about the coming FA treatments!

One of the treatment approaches is to develop super strong anti-oxidants that will go into the mitochondria and neutralize some of the free radicals that are causing so much harm. Examples are Idebenone, Pioglitazone and OX1.

Another is to put "grease" into the energy factory to help it run more efficiently on less Frataxin. Examples are A-0001 and EPI-743.

A third treatment aims to help the existing Frataxin last/live longer. That's EPO.

A fourth treatment would put additional Frataxin in the mitochondria. That's "TAT Frataxin".

And finally another treatment approach is to encourage the RNA to read the DNA better and produce more Frataxin. That is the treatment called HDAC Inhibitors.

Beyond these treatments someday are gene and stem cell therapies to replace or fix the bad genes. FA gene therapy is being researched. Stem cell research is in its infancy and is not nearly ready for human subjects.