We have many differences but are more alike than not

By Veronica Bonfiglio, Board Member

The various NBIA Disorders are like an alphabet soup – PKAN, MPAN, BPAN, PLAN, FAHN – each with their own distinguishing characteristics, but there’s a common link: all affected individuals have elevated iron in the basal ganglia and axonal spheroids.

I don’t come from a scientific background, and sometimes I have to wonder whether there are more differences or commonalities among the different forms of NBIA. I have concluded that we are all pieces of the same puzzle, making it essential that we see the big picture and NBIA’s various forms as pieces of the whole.

Let me explain, with help from the National Institutes of Health’s Genetic Home Reference website. If a gene’s instructions for making a protein are changed, a mutation can cause the protein to malfunction or to be missing entirely. When a mutation alters a protein that plays a critical role in the body, it can disrupt normal development and lead to illness and genetic disorders.

Even though the gene mutations are different, at present researchers think that people affected by any form of NBIA may end up on a common biological pathway.

Wikipedia explains that a biological pathway is a series of actions among molecules in a cell that leads to a certain product or a change in a cell. Such a pathway can trigger the assembly of new molecules, such as a fat or protein. Pathways can also turn genes on and off. Some of the most common biological pathways are involved in metabolism, the regulation of gene expression and the transmission of signals.

Allison Gregory, a genetic counselor with Dr. Susan Hayflick’s Lab at the Oregon Health and Science University, gave an example of shared biologic pathways in our NBIA disorders.

The protein in the PANK2 gene, which causes the PKAN form of NBIA, localizes to the mitochondria and is involved in the Coenzyme A pathway and lipid, or fat, metabolism. The gene c19orf12, which causes MPAN, codes for a protein that also localizes to the mitochondria, but we don’t yet know what the function of this gene’s protein is. The protein made by the gene PLA2G6, which causes PLAN, is also involved in lipid metabolism. Clearly, there are themes related to the function of the mitochondria and lipid metabolism. The problem is that we still don’t know “how they all hang together,” Gregory said.

Gregory says that the discoveries of PANK2, c19orf12, PLA2G6, WDR45 (BPAN), and FA2H (FAHN) help investigators when trying to identify other potential NBIA genes which may also be involved in mitochondrial function or lipid metabolism.

Gregory described the current state of knowledge about NBIA disorders as “having a handful of puzzle pieces but missing the majority. The ones we have don’t even hook together; we’re missing the ones that go in between.”

As a mom and NBIA board member, I have no doubt that we are all part of the same puzzle. If one piece is missing, we can’t solve it. As such, each piece is equally important to the others. For this reason, our board firmly believes that a breakthrough for all could come from studying any one of the identified forms, including those where the gene mutation has not yet been identified and are classified as Idiopathic NBIA.

That approach is good for research and good for our families who may experience isolation, stress and limited resources. We are stronger as individuals and as a group when we work together.

We have been able to develop international connections that have resulted in the creation of sister organizations in seven countries and the formation of the NBIA Alliance that advocates worldwide for all forms of NBIA. The European Union’s TIRCON research grant shows the power of collaboration between industry, research institutions and our patient advocacy organizations. The shared goal is to improve the lives of all those living with NBIA disorders.

Both our Scientific & Medical Advisory Board and the Board of Trustees are more convinced than ever: We can and will solve this puzzle together.