The Search to Tame Pseudoxanthoma Elasticum

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Pseudoxanthoma elasticum (PXE) results from putative mutations in the ABCC6/MRP6 gene and affects primarily the skin and eye. Affected individuals commonly present with skin papules and angioid streaks, breaks in Bruch's membrane frequently associated with retinal hemorrhage. Occasionally, individuals present with vascular signs and/or symptoms: gastrointestinal bleeding or intermittent claudication. The most frequent cause of morbidity and disability in PXE is reduced vision from disciform scarring from macular hemorrhage. Before the discovery of the gene, PXE was considered a prototypic connective tissue disorder. Now, however, there is some indication that it is in fact a metabolic condition, since ABCC6 is a membrane transport protein that is expressed primarily in the liver.

PXE International (a 501 (c) (3) organization) initiates, funds and conducts research; supports individuals affected by pseudoxanthoma elasticum and educates clinicians. Founded in 1995, the foundation was the first advocacy organization to manage its own repository and blood and tissue bank, the PXE International Blood and Tissue Bank. This has gone on to be a model for the Genetic Alliance BioBank. It is also the first organization to hold the patent on the gene associated with the condition. It has created a genetic test kit that will be submitted to the FDA for approval in 2006. It facilitates the PXE International Research Consortium, a consortium of a dozen labs around the world. At present, PXE International has hired a biochemical geneticist to conduct a clinical protocol at the Clinical Center at NIH.

Research Opportunities:

- Find the substrate transported by ABCC6 (MRP6)
- Elucidate the downstream effects of the mutations – protein, cellular processes
- Attempt genotype/subcellular phenotype correlations
- Clinical study of a variety of treatments for macular degeneration