

Lupus Update with Dr. Robert Katz

Can identifying the genetic cause of lupus improve treatment?

A few weeks ago, lupus was in the news thanks to Australian scientists who identified the possible genetic cause of lupus in a 10 year old girl. As you know, research indicates there is a genetic component to lupus that requires a trigger like injury, illness or stress. Identifying the genetic cause of lupus was exciting because it can determine a treatment targeting the cause. If we can identify abnormal chemical proteins related to genetic mutations, we might have a way of neutralizing the abnormal proteins that result from these mutations.

First, let me tell you about genetics. The human genome contains all of the genes in a person's DNA and consists of roughly 180,000 genetic sequences called exons. The exons are sequences from the DNA of a person that is transcribed into ribonucleic acid (RNA). Thus, exons are the protein coding region of the genome.

About 1 percent of the total genetic sequences are made up by these exons. Though they are a small fraction of all the genetic sequences, mutations in the exome are thought to contain most of the mutations that have a large effect on different diseases – including lupus.

In the case of the 10 year old girl, the cause was an increased amount of a particular molecule called interferon-alpha being produced. In this case, if one could give biologic therapy to antagonize the interferon alpha protein, therapy would be individualized and more effective.

Sequencing of the entire human genome, specifically in lupus patients, has identified several genes that are associated with a modest risk for developing lupus. None of the genes appear to have a direct relationship to the severity of the disease. The recent advances in whole exome sequencing are enabling the identification of mutations that underlie certain genetic disorders, and this allows for the possible development of specific antagonists to abnormal proteins produced in these individuals.

This Australian study demonstrates the use of exome sequencing in identifying the genetic basis of autoimmune disease on an individual, personalized basis.