Research uncovers key to understanding cause of lupus

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S. Ansar Ahmed (left), immunolgy professor and head of the Virginia-Maryland Regional College of Veterinary Medicine's Department of Biomedical Sciences and Pathobiology, and Rujuan Dai, a research scientist at the veterinary college, published research that can potentially impact future diagnosis and treatment of lupus, an immune illness affecting more than five million people worldwide. Credit: Virginia Tech Photo

Potentially impacting future diagnosis and treatment of lupus, an immune illness affecting more than 5 million people worldwide, researchers at the Virginia-Maryland Regional College of Veterinary Medicine at Virginia Tech have likely uncovered where the breakdown in the body's lymphocyte molecular regulatory machinery is occurring.

Rujuan Dai, research scientist, and her colleagues in the veterinary college's Department of Biomedical Sciences and Pathobiology, have

discovered a "common set of dysregulated miRNAs in murine lupus models." The research, which appears in the Dec. 13, 2010, issue of the scientific journal PLoS One, was funded in part by the Lupus Foundation of America.

Lupus is a chronic autoimmune disease of connective tissue that causes the body's immune system to become hyperactive and attack normal, healthy tissue. This results in symptoms such as inflammation, swelling, and possible damage to joints, skin, kidneys, blood, the heart, or lungs.

In an effort to better understand epigenetic factors in the causes of lupus, researchers at the veterinary college focused on microRNA (miRNA), seeking to determine potential impairments of genetic regulation. These small RNAs control gene expression by directly regulating specific target messenger RNAs via inhibition of their translation or inducing their degradation.

"Micro RNAs perform these duties in an orderly fashion," said S. Ansar Ahmed, professor of immunology and head of the Department of Biomedical Sciences and Pathobiology at the college. "White blood cells use miRNA to regulate antibodies and other proteins in response to infection or any kind of assault."

The researchers chose three strains of autoimmune-prone mice that have different background genomes and manifest lupus-like disease at different ages. For example, one mouse strain began developing lupus-like disease around 3 months of age, and another mouse strain developed severe lupus much later, at 9 months of age.

Findings show that all three lupus strains manifest a common dysregulated pattern of miRNAs despite differences in their background genes. Importantly, this expression of miRNAs became evident only at an age when the mice manifest lupus.

The identification of these common miRNAs presents a new way of understanding lupus development. The researchers at the veterinary college believe these studies will potentially open a new approach for diagnosis and treatment of the illness by altering lupus-specific miRNAs in lymphocytes.

"In the short term, we want to use our better understanding of the disease to develop a tool in the form of molecular markers for early, reliable diagnosis," said Ahmed. The long-term goal, Ahmed added, is to offer entirely new therapeutic approaches, such as manipulation of lupus-related miRNA, to correct pathological conditions.

Having identified signature miRNA changes in lupus disease, the next step for the researchers is to prove they can really switch off the disease.

"If we can do this in a mouse model and then to cure other animals, hopefully it can one day be done in humans. This is long-range research but modern technology is narrowing the time it takes from mouse to human — speeding translation," said Ahmed.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0014302

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