

Enzyme keeps antibodies from targeting DNA and driving inflammation in lupus

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Failure of an enzyme to break down DNA spilling into the bloodstream as cells die may be a major driver of inflammation in lupus. This is the finding of a study in both mice and human patients led by researchers at NYU Langone Medical Center and published online June 9 in the journal *Cell*.

The study revolves around the constant, healthy turnover of [mammalian cells](#), which die, break up and have their parts, including DNA, recycled. Researchers found that an enzyme, DNASE1L3, normally digests the DNA within small particles issuing from disintegrating [cells](#), thereby preventing [lupus](#).

Without DNASE1L3 to prevent its buildup, accumulating DNA triggers immune cells to produce proteins called antibodies that glom onto and remove the DNA. Such antibodies, when attached to DNA in complexes, get lodged in the walls of arteries and in tissues to cause inflammation that damages blood vessels, skin, joints and the kidneys as part of the most severe type of lupus, [systemic lupus erythematosus](#) (SLE).

"Our study reveals a new mechanism that could be harnessed for biological therapies for lupus and other autoimmune diseases, where the immune system mistakenly targets the body's own cells," says senior study author Boris Reizis, PhD, professor of Pathology and Medicine at NYU Langone.

Specifically, the study authors were able re-create lupus disease processes, including the formation of antibodies to DNA and kidney inflammation, by engineering mice that lacked the gene for DNASE1L3.

"We also confirmed that human patients with a missing or malfunctioning DNASE1L3 gene had an abundance of circulating DNA and developed antibodies to it, and that such [antibodies](#) were also

present in most forms of lupus," says Reizis. "This opens up a potential avenue for a new treatment, including the possibility of administering DNASE1L3 as a drug."

The need to find new treatments is urgent, adds Reizis, because there have been few advances in the treatment of lupus in 50 years, and the drugs used traditionally are poorly tolerated.

Provided by New York University School of Medicine

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