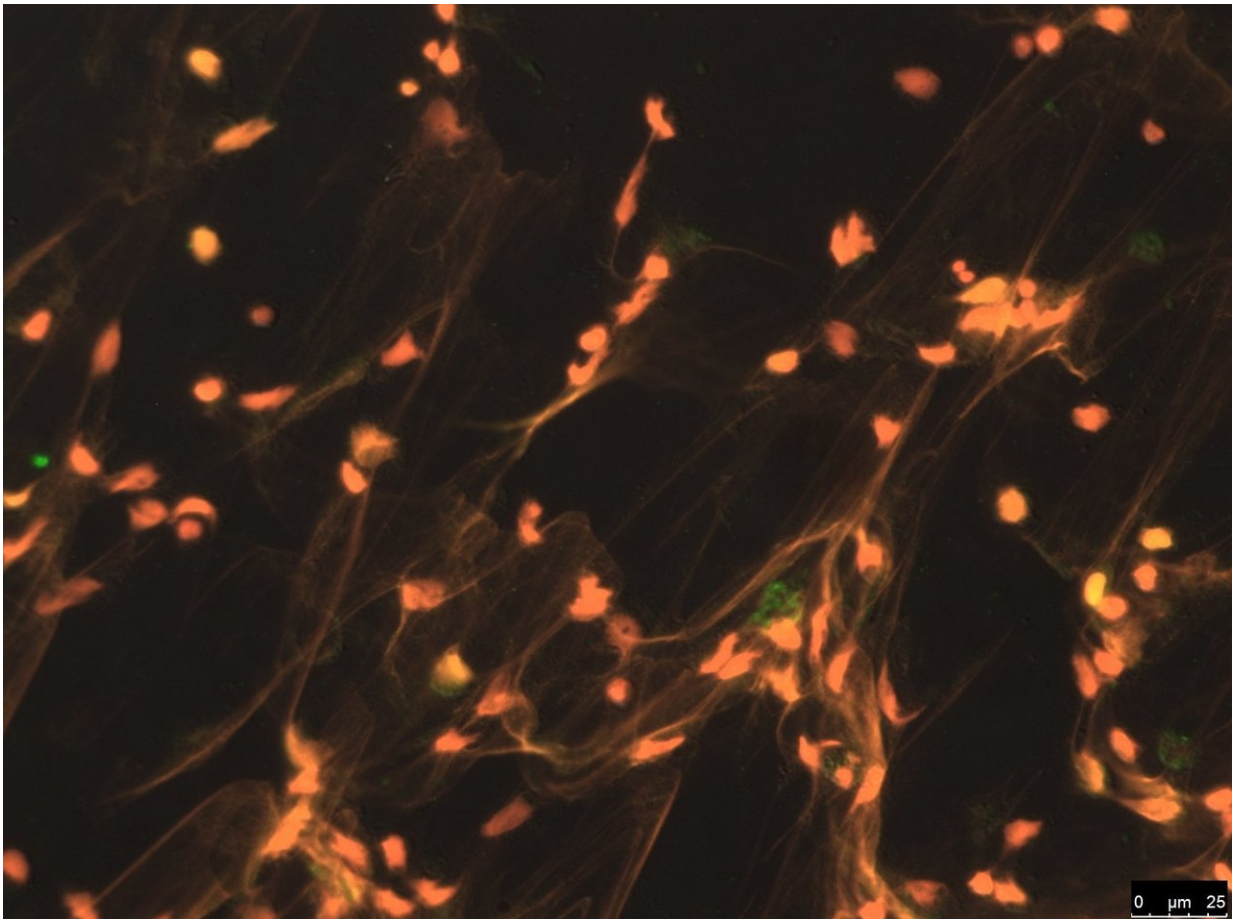


New treatment approach for autoimmune disorder

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Formation of extracellular structures from white blood cells, after stimulation with ANCA autoantibodies. Credit: A. Schreiber

Researchers from Charité—Universitätsmedizin Berlin have been able to

improve their understanding of the key mechanism involved in the pathogenesis of a serious autoimmune disease. For the first time, researchers were able to demonstrate a close link between the activation of programmed cell death, complement system activation, and organ damage in patients with systemic inflammation of blood vessels caused by ANCA antibodies. Results from this research have been published in the journal *Proceedings of the National Academy of Sciences*.

ANCA-associated vasculitis is a systemic disease characterized by the body's immune system attacking structures inside [white blood cells](#), causing inflammation within small [blood vessels](#). The kidneys are commonly involved in vasculitis, which can lead to [acute renal failure](#), but the condition can also affect the lungs and other organs.

Conventional treatment is based on suppressing the immune system. This treatment method stops disease progression, but is associated with severe side effects.

So what is the chain of events responsible for producing this disease? A team of researchers, led by PD Dr. Adrian Schreiber and Prof. Dr. Ralph Kettritz, were able to show that the process is triggered by the activation of a programmed form of cell death (necroptosis) within the body's white blood cells.

Antibodies that target the body's own proteins (auto-antibodies) attach themselves to certain components of white [blood cells](#). This activates necroptosis, which results in the formation of neutrophil extracellular traps (NETs)—complex networks of extracellular fibers composed of DNA. The team of researchers discovered that these NET structures play a role in the activation of the complement system (part of the immune system), thereby contributing to the development of the disease. Using a variety of genetically modified animal models and a pharmacological model, the researchers were able to show that necroptosis is one of the key mechanisms of pathogenesis in the development of severe vasculitis,

which is also associated with severe renal involvement.

"The specific pharmacological inhibition of [programmed cell death](#) may one day constitute a new approach to the treatment of ANCA vasculitis," says PD Dr. Schreiber. "The first clinical studies are underway, testing whether the inhibition of necroptosis may be suitable for general application. Looking ahead, we hope that, based on our data, it will be possible to develop a new treatment for ANCA vasculitis."

More information: Adrian Schreiber et al, Necroptosis controls NET generation and mediates complement activation, endothelial damage, and autoimmune vasculitis, *Proceedings of the National Academy of Sciences* (2017). [DOI: 10.1073/pnas.1708247114](https://doi.org/10.1073/pnas.1708247114)

Provided by Charité - Universitätsmedizin Berlin

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