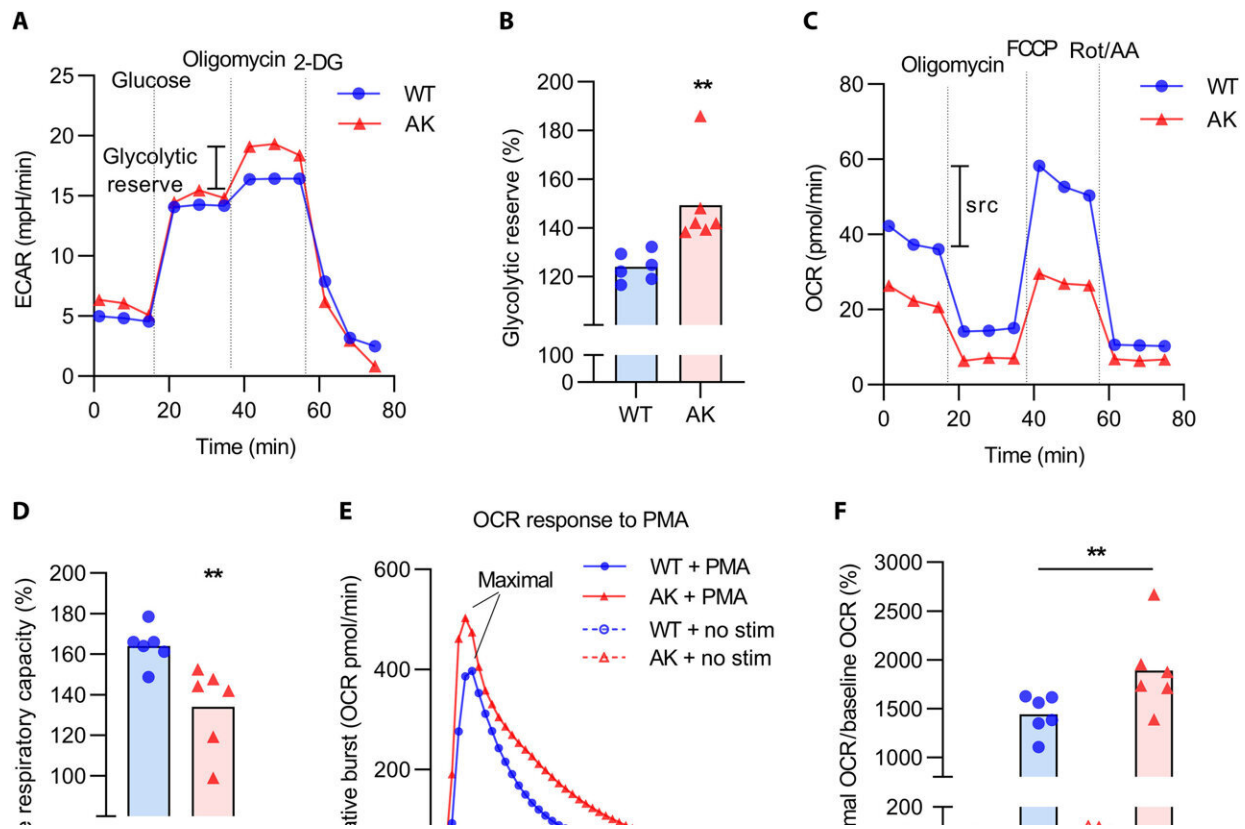


Research finds potential target for cardiovascular disease in diabetes

October 26 2023, by Valerie Goodwin



Phenotypic characterization of neutrophils in 24-week-old Akita mice. (A) Representative extracellular acidification rate (ECAR) curves assessing glycolysis. (B) Glycolytic reserve is the difference between glycolytic capacity and baseline glycolysis; mean for $n = 6$, ** P Science Advances (2023). DOI: 10.1126/sciadv.adj1019

More than 10% of the population in the United States has been diagnosed with diabetes according to the Centers for Disease Control and Prevention. About 7.5% of these diabetic patients will experience cardiovascular events like heart attack or stroke in their lives.

Research from rheumatologists, cardiovascular pharmacologists and nephrologists at the University of Michigan has found a potential target when it comes to preventing vascular dysfunction, the first step toward frank cardiovascular events such as heart attack or stroke, in patients with diabetes.

In a [study](#) published in *Science Advances*, University of Michigan researchers found that the overproduction of neutrophil extracellular traps is an important contributing factor to vascular dysfunction in diabetes.

Neutrophils are [white blood cells](#) that help the body fight against infections and are responsible for the production of NETs.

NETs are intended to act as first responders against various bacterial and viral infections, but they may also become overactive in chronic autoimmune or [inflammatory diseases](#) such as lupus or diabetes. When this happens, NETs can create problems for [blood vessels](#).

"An excess of NETs is a common contributing factor to inflammation in patients with autoimmune rheumatologic diseases. This is a major area of research in our laboratory directed by Jason Knight, M.D., Ph.D.," said Chao Liu, Ph.D., the first author and a research fellow in the Division of Rheumatology, Department of Internal Medicine.

The rheumatology team at the University of Michigan collaborated with Kevin Atkins, M.D., and Subramaniam Pennathur, M.D., in the division of nephrology to extend the research of NETs to diabetes.

"We noticed that others were finding a role for NETs in certain [diabetic complications](#) like retinal damage and problems with wound healing," said Liu.

"We wondered if this connection might also extend to vascular dysfunction, which is a topic we were well-positioned to explore based on our prior work."

In laboratory research, the team found that [diabetic mice](#) had an excess of NETs as expected. The mice also had blood vessel walls that did not relax normally making them more susceptible to forming the lipid plaques that lead to heart attack or stroke.

When the excess NETs were eliminated, the diabetic mice had much healthier appearing vessels that were essentially indistinguishable from healthy non-diabetic mice.

In patients with diabetes, factors like high glucose and [oxidative stress](#) appear to activate neutrophils to form excessive NETs.

"By treating the excess of NETs in diabetic patients, we think it is possible that we would be able to reduce vascular dysfunction and the complications that follow it," said Liu. "Finding a solution for vascular dysfunction could greatly improve the lives of [diabetic patients](#)."

Going forward, the team is hoping to study the role of neutrophils and NETs in all phases of diabetic vascular diseases, from [vascular dysfunction](#) to frank atherosclerosis with a goal of finding personalized and proactive treatments for patients with diabetes and likely beyond.

More information: Chao Liu et al, Inhibition of neutrophil extracellular trap formation alleviates vascular dysfunction in type 1 diabetic mice, *Science Advances* (2023). [DOI: 10.1126/sciadv.adj1019](https://doi.org/10.1126/sciadv.adj1019)

Provided by University of Michigan

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