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First time genome editing made possible on cells lining blood vessel walls

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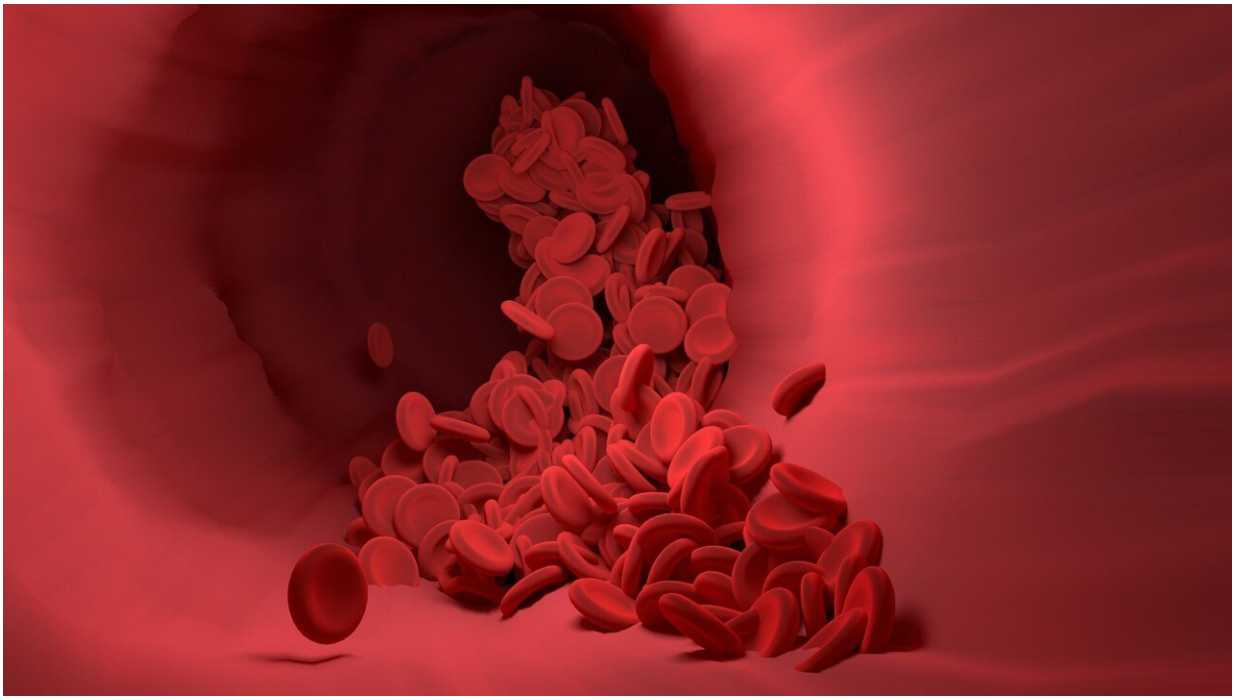

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The lab of Youyang Zhao, Ph.D., from Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of Chicago developed a unique nanoparticle to deliver genome editing technology, including CRISPR/Cas9, to endothelial cells, which are cells that line blood vessel walls. This is the first time that vascular endothelial cells could be reached for genome editing, since the usual way to deliver

CRISPR/Cas9—through a virus—does not work for this cell type. Findings were published in the journal *Cell Reports*.

"The nanoparticle we developed is a powerful new delivery system for genome editing in vascular endothelial cells, and could be used to treat many diseases, including acute respiratory distress syndrome from severe COVID-19," said senior author Dr. Zhao from Lurie Children's. "With this nanoparticle we can introduce genes to inhibit vascular injury and/or promote vascular repair, correct gene mutations and turn genes on or off to restore normal function. It also allows us to edit multiple genes at the same time. This is an important advance for treating any disease caused by endothelial dysfunction."

Endothelial dysfunction is at the root of many diseases, such as coronary artery disease, stroke, bronchopulmonary dysplasia and pulmonary artery hypertension. Dr. Zhao explained that genome editing in endothelial cells could even treat cancers by cutting off the blood supply to the tumor or blocking cancer metastasis.

At this stage, Dr. Zhao and colleagues achieved excellent results in a mouse model. The nanoparticle carrying CRISPR/Cas9 plasmid DNA was introduced via a one-time IV injection and required a few days to be effective. Preclinical testing will be necessary before clinical trials can begin.

"Our nanoparticle delivery system for genome editing and transgene expression also is a huge advance for cardiovascular research," added Dr. Zhao.

More information: Xianming Zhang et al, Robust genome editing in adult vascular endothelium by nanoparticle delivery of CRISPR-Cas9 plasmid DNA, *Cell Reports* (2022). DOI: 10.1016/j.celrep.2021.110196

Provided by Ann & Robert H. Lurie Children's Hospital of Chicago