# When smooth muscle cells lack strength

**University of Tübingen team discovers how malformations of the blood vessels can occur in mice – yielding information with possible ramifications for retinal disease.**

The heart pumps blood through the vascular system, supplying cells with oxygen and energy Smooth muscle cells in the vessels finely regulate the blood flow. If they cannot perform their task, malformations and dilations of the vascular system may occur, according to a research team led by Professor Alfred Nordheim from the Interfaculty Institute of Cell Biology at the University of Tübingen, together with scientists from Tübingen, Münster and Uppsala, Sweden. Their new study, the result of experiments on an animal model, could be experimentally applied to a model of a specific retinal disease of the eye in premature infants, as it points to a potential new approach to treatment. The study has been published in Circulation Research.

In arterial and venous blood vessels, smooth muscle cells selectively contract and relax to regulate where more and where less blood flows. They also give the vascular network the strength it needs to withstand blood pressure. In an experiment, Alfred Nordheim and his team inactivated the gene for the serum response factor (SRF) in mice, which significantly regulates the cells' ability to contract. "This led to significant vasodilatation and vascular malformations in the blood vessels," Nordheim reported.

## Reduced blood flow

The malformations involve direct connections between arteries and veins, Nordheimer explained. "The arteries take a shortcut to the veins, bypassing tiny microvessels. Similar malformations are also known in certain rare blood vessel diseases in humans. Our team was able to show that such shortcuts cause the surrounding tissue to receive reduced blood flow." The lack of strength in the smooth muscle cells sometimes even led to ruptures in the vessels, Nordheim said.

## Side track to another disease

“This newly-gained knowledge also put us on the track of a completely different disease, called ischemic retinopathy. This is a retinal disease in premature infants, which in the worst case can lead to blindness," says the study's lead author Dr. Michael Orlich of Uppsala University. An overreaction in the growth of blood vessels leads to pathological changes in cells known as pericytes. "Among other things, the pathological pericytes produce contractile proteins, similar to smooth muscle cells," explains Orlich. "We had expected that the serum response factor also plays an important role here. In addition, we assumed that the symptoms of retinal disease would improve if the overreaction of the pericytes was reduced."

The research team tested its assumptions experimentally in mice in which a disease comparable to ischemic retinopathy had been induced. "When we specifically switched off the serum response factor in pericytes of these mice, the symptoms decreased," Orlich said, summarizing the results. This, he says, could form a potential approach for new treatments of ischemic retinopathies in humans.

**Publication**

Michael M. Orlich, Rodrigo Diéguez-Hurtado, Regine Muehlfriedel, Vithiyanjali Sothilingam, Hartwig Wolburg, Cansu Ebru Oender, Pascal Woelffing, Christer Betsholtz, Konstantin Gaengel, Mathias Seeliger, Ralf H. Adams, and Alfred Nordheim: Mural Cell SRF Controls Pericyte Migration, Vessel Patterning and Blood Flow. Circulation Research,
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## Further information

- Eberhard Karls University Tübingen