MedicalXpress

# Researchers identify transcription factors that regulate retinal vascularization

April 8 2013

The retina is a highly vascularized tissue, but too much or too little vascularization can lead to visual impairment and diseases such as familial exudative vitreoretinopathy or macular degeneration. In this issue of the *Journal of Clinical Investigation*, Alfred Nordheim and colleagues at Tuebingen University in Tuebingen, Germany, identified the DNA transcription factor SRF and its cofactors MRTF-A and MRTF-B as critical regulators of vascularization in the postnatal mouse eye.

LNormal functioning of the eye depends on a proper supply of blood to the retina. Light entering the eye passes through the cornea, the lens, and the vitreous body before reaching the retina, where it stimulates the nerves. If the retina contains too few or too many blood vessels – i.e., if it is under- or oversupplied with blood – a number of severe, often blinding eye diseases can develop.

An international group of researchers led by Professor Alfred Nordheim at the University of Tübingen's Interfaculty Institute for *Cell* Biology has found, using experiments on mice, that genes for blood vessel growth in the retina are "switched on" by a known factor – a protein called SRF. The scientists showed that by eliminating this factor, they could artificially induce a certain disease profile in newborn mice and a different one in adult mice. Their results, which are published now in The *Journal of Clinical Investigation*, offer important clues on the diseases afflicting human eyes and provide starting-points for the development of treatments for defective retinae and vitreous bodies.

Professor Alfred Nordheim's team has been examining the serum response factor (SRF) and its various functions for several years. SRF regulates the function of many genes in the genome of mice and men – thereby setting in motion distinct growth processes for organs. Experimenting on mice in the laboratory, the Tübingen researchers have developed sophisticated mechanisms to influence the activity of SRF and its co-factors in distinct types of cells and at defined time points when the organism reaches a certain developmental stage.

In the current study, the researchers switched off SRF in the blood vessels of mouse embryos, as well as in newborn and adult mice. As a result, the blood vessels in the retinae of the newborns were not fully developed. Their eye problems were very similar to certain hereditary forms of a disease affecting the retina and vitreous body in the human eye (vitreoretinopathy and Norrie disease). Children affected by it often go blind at an early age. In mice of adult ages, however, switching off SRF had the opposite effect – too many new blood vessels were formed in the retina, oversupplying it with blood. Doctors have made corresponding observations in elderly patients with a certain form of age-related macular degeneration (AMD), a disease which increasingly damages the retina and leads to vision loss. It is characterized by dilated blood vessels and the formation of excess blood vessels.

"I expected that SRF would play a role in the development of the vessel system, because it generally works to ensure the formation of cellular protrusions and new branched cellular structures in many organs, for instance in the nervous system and the vascular system," says Alfred Nordheim. But, he added, it was astonishing how closely the pathology of mice with switched-off SRF resembled that of human patients with particular eye diseases. "I think we have established a very good model with which we can investigate these diseases much more precisely," Nordheim says. It represents an important step for research into possible treatments, he adds.

**More information:** Endothelial SRF/MRTF ablation causes vascular disease phenotypes in murine retinae, *J Clin Invest*. doi:10.1172/JCI64201