Johns Hopkins researchers find life in blood-starved retinas; shed light on vision loss

Like all tissues in the body, the eye needs a healthy blood supply to function properly. Poorly developed blood vessels can lead to visual impairment or even blindness. While many of the molecules involved in guiding the development of the intricate blood vessel architecture are known, only now are we learning how these molecules work and how they might affect sight.

Reporting in the Oct. 16 issue of *Cell*, researchers at the Johns Hopkins School of Medicine find that when some cells in the mouse retina are not properly fed by blood vessels, they can remain alive for many months and can later recover some or all of their normal function, suggesting that similar conditions in people may also be reversible.

"This finding is intriguing," says Jeremy Nathans, M.D., Ph.D., a professor of molecular biology and genetics, neuroscience and ophthalmology at Johns Hopkins and a Howard Hughes Medical Institute investigator. "It suggests that neurons in the retina can survive for an extended period of time even though they have been functionally silenced."

Three genes

Three genes - named Fz4, Ndp and Lrp5 - previously were suspected to be involved in blood vessel development in the human retina. Defects in any of these genes cause hypovascularization - a lack of sufficient blood vessels - in the retina. Similarly, eliminating any of these genes in mice can lead to hypovascularized retinas.

Mice lacking functional Fz4 have poor blood vessel growth in the retina and are blind, but it was not known whether the blood vessel deficiency was the cause of blindness or whether the absence of Fz4 leads to some other defect that causes blindness. The team found that Fz4 function is required only in blood vessels, where it senses a signal produced by the Ndp gene in other retinal cells.

Defect in electrical signalling found

When the team measured electrical responses in retinal cells of mice lacking Fz4, they found a defect in electrical signalling in the middle layer of the retina - the same region lacking blood vessels.

The researchers then bathed the Fz4 mutant retinas in oxygen and nutrients to mimic a normal blood supply, and measured electrical signalling in response to light. They found that when provided with oxygen and nutrients, the retinas were able to sense light and generate signals similar to those generated by normal retinas. The team suggests that in the absence of Fz4 the defective blood vessels provide the retinas with only enough oxygen and nutrients to keep the retinal cells alive, but not

enough for them to function normally to send electrical signals.

"If the human retina responds to a decrease in blood supply in the same way that the mouse retina responds, then these results may have relevance for those patients with vision loss due to vascular defects," says Nathans.

"In particular, these experiments suggest that if a region of the retina has been deprived of its normal blood supply, then completely or partially restoring that supply may also restore some visual function, even if this happens weeks or months later."

Source: Johns Hopkins Medical Institutions