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QS29

Study of the Retinochoroidal Circulation with Fluorescein Angiography in a Rodent Orthotopic Whole Eye Transplantation Model

Chiaki Komatsu, MD1, Jila Noori, MD1,2, Maxine R. Miller, MD1, Yong Wang, MD1, Touka Banae, MD1, Bing Li, MD1, Joshua Barnett, BS1, Wendy Chen, MD, MS1, Kira L. Lathrop, MAMS2,3, Ian A. Rosner, BS1, Wensheng Zhang, MD1, Mario G. Solari, MD1, Joel S. Schuman, MD4, Andrew W. Eller, MD2, Kia M. Washington, MD5,6

1University of Pittsburgh Medical Center, Department of Plastic Surgery, Pittsburgh, PA, USA, 2University of Pittsburgh Medical Center, Department of Ophthalmology, Pittsburgh, PA, USA, 3University of Pittsburgh, Swanson School of Engineering, Department of Bioengineering, Pittsburgh, PA, USA, 4New York University Medical Center, Department of Ophthalmology, New York, NY, USA, 5University of Pittsburgh Medical Center, Departments of Plastic Surgery, Ophthalmology, Orthopedic, Pittsburgh, PA, USA, 6VA Pittsburgh Medical Center, Pittsburgh, PA, USA

PURPOSE: Whole eye transplantation (WET) could potentially provide a viable optical system to people worldwide with irreversible vision loss. As a first step toward realizing this goal, we have developed an orthotopic model for whole eye transplantation in the rat. Given that viability of the retina is crucial to functional visual return, we evaluated the structural integrity of the retinochoroidal circulation after transplantation using fluorescein angiography (FA), which is the gold standard to evaluate retinal circulation.

METHODS: Brown Norway rats underwent syngeneic whole eye transplantation (n=4). Animals were examined at post-operative week 1. Wide-field FA images and fundus photographs were obtained to evaluate retinochoroidal blood flow. Ocular examinations were performed by an ophthalmologist with retina specialization to evaluate the anterior and posterior segments of the eye. A second group of naïve Brown Norway rats (n=3) served as controls.

RESULTS: FA imaging revealed that two of four rats had transplanted eyes that exhibited normal choroidal flush and arterial and venous filling patterns, normal optic disc appearances, normal retinal vessel caliber and no retinal vessel leakage comparable to the eyes of control animals. Taken together with the results of ocular exams and interpretation of fundus photographs, it was confirmed that there were no signs of retinal ischemia, vessel narrowing or arteritis/phlebitis present in the eyes of these animals. The remaining two of four rats with transplanted eyes showed normal choroidal, arterial and venous filling patterns and no signs of arteritis/phlebitis or vessel leakage, however attenuated retinal vessels were seen on color fundus photographs and FA imaging in the study eyes. Correlated with ocular exam results and evaluation of the retina as captured on fundus photographs, there appeared to be decreased retinal perfusion in these animals as compared to controls.

CONCLUSION: FA results have confirmed that retinochoroidal blood flow can be established after WET in a rat model. Two of the transplanted rats displayed no difference in retinochoroidal circulation as compared to the eyes of control animals. The remaining two rats with transplanted eyes appeared to have decreased retinal perfusion. In all rats, the pattern of vascular filling was normal, and the absence of vessel leakage indicates that the structural integrity of ocular blood vessels can be maintained after WET. The etiology of vascular attenuation and presumed decrease in retinal perfusion will be investigated in future studies.

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QS30

E2f1 Represses M1 And M2 Macrophages Transformation To Effect Wound Healing Process

Min Wu, PHD, MD, Hui Xiao, Master, Changchun Yang, Master, Zhen Yi, Master, Pei Deng, MD, Haiping Wang, MD, Ning Zeng, Phd, MD, Yiping Wu, Phd, MD

Tongji Hospital, Wuhan, China

PURPOSE: Wound healing is a complex process, which is classically divided into inflammation, proliferation and remodeling phases. Macrophages play a key role in wound healing. M1 macrophages mediate tissue damage and initiate the inflammatory response in the early stages of wound healing. M2 phenotype promotes wound healing via formation of a highly vascularized, cellular granulation tissue and scar tissues. The phenotype of polarized M1-M2 macrophage can, to some extent, be reversed in vitro and in vivo. It is not clear whether the mechanism of this switch involves the recruitment of circulating precursors or the reeducation of cells in situ. In our previous study, we found that E2F1-null (E2F1\(^{-}\)) mice have enhanced expression of macrophages in the border zone of the skin wound at day 7 post-surgery. However, whether E2F1 mediates the M1-M2 switch during the wound healing process is not known.

METHODS: Skin wounds were surgically induced in E2F1\(^{-}\) mice and the WT littermate. At 2th and 7th day after surgery, we detected the numbers of M1 and M2 macrophages in the border zone of the wound. Then we performed Western-blotting and RT-PCR to investigate the PPAR-\(\gamma\) protein and RNA expression in the wound tissue. And Co-IP was performed to check whether E2F1 interaction with PPAR-\(\gamma\).

RESULTS: In the border zone of the wound, E2F1\(^{-}\) mice had more M2 macrophages and less M1 macrophages at day 7 post-surgery. Surprisingly, at day 2, the M2 macrophages were also remarkably increased in the E2F1\(^{-}\) mice, which suggests a certain degree of transformation amongst the M1 and M2 phenotypes on the 2nd day. We know that PPAR-\(\gamma\) plays a key role in the M1-M2 switch. However, whether E2F1 interacts with PPAR-\(\gamma\) during the wound healing process is not known. We performed Co-IP and found that E2F1 indeed interacts with PPAR-\(\gamma\). Western-blotting and RT-PCR showed higher expression of PPAR-\(\gamma\) in the E2F1\(^{-}\) mice as compared to that in the WT mice.

CONCLUSION: E2F1 may repress PPAR-\(\gamma\) expression to affect M1-M2 macrophage switch that prevents skin wound healing.

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