

Novel approach to treat proliferative vitreoretinopathy shows promise

October 31 2011

Proliferative vitreoretinopathy (PVR), or the formation of scar tissue within the eye, is a serious, sight-threatening complication in patients recovering surgical repair of retinal detachment. A new study conducted by investigators at the Schepens Eye Research Institute, the Department of Ophthalmology at Harvard Medical School, and the Massachusetts Eye and Ear Infirmary in Boston, published in the December issue of the *American Journal of Pathology*, suggests that a cocktail containing reagents to neutralize a relatively small subset of vitreal growth factors and cytokines may be an effective treatment.

"We found that a combination of 7 classes of growth factors and [cytokines](#) was essential for PVR to develop in an [animal model](#) of the disease," explains lead investigator Andrius Kazlauskas, PhD, of The Schepens Eye Research Institute and the Department of Ophthalmology, Harvard Medical School. "By neutralizing them, we prevented PVR-relevant signaling, and inhibited contraction of collagen gels containing primary [retinal pigment](#) epithelial cells derived from a human PVR membrane (RPEMs). These findings suggest a potential [therapeutic approach](#) to reduce the incidence of PVR in patients undergoing surgery to repair a detached retina."

In animal models, platelet-derived growth factor receptor α (PDGFR α) is associated with PVR and strongly promotes experimental PVR. Vitreal growth factors outside of the PDGF family promote an indirect route to activate PDGFR α . Importantly, indirectly activated PDGFR α engages a characteristic set of signaling events and cellular responses that are

tightly associated with PVR. This study sought to identify the factors that would induce those events, and develop therapeutic approaches to prevent patients from developing PVR.

Vitreous was obtained from normal rabbits or those in which PVR was either developing or stabilized. Normal vitreous was found to contain substantial levels of growth factors and cytokines, which change quantitatively or qualitatively as PVR develops. A set of nine growth agents was found to be most abundant and therefore most likely to contribute to PVR. Neutralizing a subset of these factors in rabbit vitreous eliminated their ability to induce PVR-relevant signaling and cellular responses. A single dose of neutralizing [reagents](#) effectively protected rabbits from developing [retinal detachment](#). "Our in vitro approach to characterize and neutralize vitreal bioactivity accurately predicted the efficacy of an in vivo therapy," notes Dr. Kazlauskas.

To identify growth factors likely to be driving PVR in humans, the investigators quantified the level of [growth factors](#) and cytokines from human donors that had either PVR, or a non-PVR retinal condition. Fourteen of the 24 agents quantified were present in large concentrations in PVR vitreous. Neutralizing just 7 of these prevented vitreous-induced activation of PDGFR α . Furthermore, the cocktail also suppressed the contraction of these cells in collagen. Therefore, the same neutralization strategy that prevented PVR in rabbits also prevented human PVR vitreous from inducing PVR-relevant responses. These results strongly suggest that a dose of neutralizing reagents may also protect humans from PVR.

"Although the outlook is encouraging, it would be useful to test the effectiveness of this treatment on alternate models of retinal detachment. It is also worth considering a combinatorial approach to therapy. For example, the antioxidant N-acetylcysteine (NAC) prevents retinal detachment in rabbits by blocking intracellular processes. A combined

therapy involving the neutralization approach presented here with NAC treatment would doubly-target PVR at the extracellular and intracellular levels," concludes Dr. Kazlauskas.

More information: The article is "A Novel Strategy to Develop Therapeutic Approaches to Prevent Proliferative Vitreoretinopathy," by Steven Pennock, Marc-Andre Rheaume Shizuo Mukai, and Andrius Kazlauskas ([doi: 10.1016/j.ajpath.2011.08.043](https://doi.org/10.1016/j.ajpath.2011.08.043)). It will appear in the American Journal of Pathology, Volume 179, Issue 6 (December 2011)

Provided by Elsevier Health Sciences

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