

# Ocriplasmin and muller glia

## Letter to editor

Stalsmans et al.,<sup>1</sup> published an article entitled of “Enzymatic Vitreolysis with Ocriplasmin for Vitreomacular Traction and Macular Holes” based on the two pivotal Phase-III clinical safety and efficacy studies of ocriplasmin. The overall clinical efficacy was encouraging and marked 40%-60% anatomic closures of macular holes without further surgery. Whilst taking a close look at the safety profile noted on FDA Ophthalmic Drug Advisory Committee Meeting Debriefing,<sup>2</sup> 5.6% patients experienced a vision decrease (2-3 line loss) during the first week post injection and slowly recovered over a six-month period, accordingly, a transit reduction of Electroretinogram (ERG) on both a-and b-wave amplitudes was remarkable.<sup>2</sup> By far, there seems no sound biological explanation to such adverse event. This letter is to shed light on Muller glia as the primary biologic interface between ocriplasmin and neurosensory retina.

Ocriplasmin is a proteolytic enzyme that digests laminin, fibronectin, and collagen IV. In the vertebrate retina, Muller glial terminals form the key component of vitreoretinal interface, namely Inner Limiting Membrane (ILM), of which laminin enriches its extracellular matrix. Moreover, Muller glia serves as “living optical fiber” and antenna that collects external light from cornea and transmits it through the neurosensory layer towards the photoreceptors, where the visual process and refinement begins.<sup>3</sup> When ocriplasmin is injected into the vitreous cavity, ILM acts as the very first biologic defense and drug delivery barrier. If the retina were overexposed to this enzyme, the integrity of Muller glia terminals will be first compromised. However, Muller glia is the only structure cell within the retina that has the ability to regenerate and regrow following injury, which may explain why such vision disturbance is reversible, gradual and time-dependent. From ERG point of view, Muller glial end-feet at retinal surface has high potassium conductance towards photoreceptors, which are the origin of a-wave of ERG. Muller glia may indirectly involve with b-wave.<sup>4</sup> If their end processes were enzymatically or surgically compromised, the potassium-driven electrical conduct towards photoreceptor might be hindered till a complete regrowth of its extracellular processes. The appreciation of Muller glia may also shed insight on patients who experienced of similar visual disturbance following surgical ILM peelings.<sup>5</sup>

In clinic, many ocular pathological conditions involve with basement membrane abnormalities, for which ocriplasmin may have a role. To introduce Muller glia into this context has strategic importance to further translational efficiency (dosing strategy) in potential new indications whilst adding a value to evidence-based patient outcome measures.

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## Conflicts of interest

Author declares that there is no conflict of interest.

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