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EXPERT OPINION

Pharmacotherapy for treatment of retinal vein occlusion

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Dear Editor

We congratulate Sarao *et al*. for their article entitled 'Pharmacotherapy For Treatment Of Retinal Vein Occlusion (RVO)' [1]. The authors presented an update and a brief review on the current treatment modalities and promising alternatives for RVO. We would like to mention about matrix metalloproteinase (MMP)-9 as a potential future target.

MMP-9 is involved in the breakdown and re-modeling of extracellular matrix in multiple physiological and pathological processes such as angiogenesis, wound healing, cell migration, and etc. Studies about the role of MMP-9 in retinal vascular disorders are few. It has been demonstrated that MMP-2 and MMP-9 may trigger apoptosis of retinal capillary cells, mitochondrial dysfunction and neovascularization in diabetic retinopathy. Grieshaber *et al*. revealed the role of MMP-9 to optic disc and peripapillary retinal hemorrhages [2].

In ischemic stroke or intracerebral hemorrhage, there is an extensive expression of MMP-9 that is related to excitotoxicity, apoptosis, neural damage, hemorrhagic transformation and blood-brain barrier disruption that results in tissue edema. We hypothesize that MMP-9 may be a possible cause of retinal edema similar to stroke. Bertelmann *et al*. have demonstrated the elevation of intravitreal functional plasminogen in eyes with central and branch RVO and correlated with the extent of blood–retina barrier damage [3]. This pathological process could be mediated by MMP-9 similar to stroke. Meanwhile, Tuuminen *et al*. recently found that intravitreal levels of MMP-9 is significantly elevated in patients with RVO patients [4]. In regard to data mentioned above, we assume that MMP-9 can be considered as a rational target for RVO treatment. The inhibition of MMP-9 interfere with degradation of basement membrane and related intimal hyperplasia. This inhibition contributes in the prevention of vascular stenosis [5]. So targeting MMP-9 may be protective as well.

Declaration of interest

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Author's response

We appreciate the comments made by Dr. Abdullah Ilhan *et al*. to our paper "Pharmacotherapy for treatment of retinal vein occlusion (RVO)" [1] and are pleased to reply.

The aim of our review was to cover current aspects of the management of RVO. Therefore, our discussion was limited to pharmacological agents of immediate clinical applicability. However, an interesting point has been raised. It is well-known that many agents interfering with the multiple stimuli of the complex pathogenesis of RVO are currently under investigation and, as pointed out, MMP-9 is an extracellular proteolytic enzyme implicated in various endothelial cell functions, including proliferation, differentiation, and angiogenesis and it might have a crucial role in the pathogenesis of macular edema due to RVOs [2]. Still, the importance of MMP-9 in pathological manifestations of RVO has not been completely investigated yet. Tuuminen *et al*. found high intravitreal levels of MMP-9 only in eyes affected by RVO with ischemic complications [3]. We strongly agree that targeting MMP-9 may have some role in the treatment of RVO and for sure deserves further investigation.

Declaration of interest

P Lanzetta has worked as a consultant for Alcon, Allegran, Bausch & Lomb, Bayer, Novartis and Roche. The authors have no other relevant affiliations or financial involvement with any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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