·Letter to the Editor·

# Comment on roles of tissue plasminogen activator and its inhibitor in proliferative diabetic retinopathy

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**Dear Sir,**

We congratulate Wu *et al* [1] for their study entitled "Roles of tissue plasminogen activator and its inhibitor in proliferative diabetic retinopathy". The authors investigated the effects of tissue plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI) in the pathogenesis of proliferative diabetic retinopathy (PDR). The authors reported that t-PA and PAI are involved in the pathogenesis of PDR.

Matrix metalloproteinases (MMPs) take part in the breakdown and re-modelling of extracellular matrix in various physiopathological mechanisms such as wound healing, cell migration, and angiogenesis. It has been proved that MMP-9 and MMP-2 might lead to retinal capillary cell apoptosis, neovascularization and mitochondrial dysfunction in diabetic retinopathy. Another effect of MMPs is the induction of vascular leakage by degradation of occludin, the tight junction protein, followed by disruption of the overall tight junction complex [2]. In short, MMPs are involved in neovascularization and the blood-retina barrier breakdown.

There is evidence that plasmin activates some MMPs subtypes in collagen gel contraction and capillary tube regression[3]. t-PA has been used for stroke (clot breakdown) and in retinal vein occlusion (enzymatic vitreolysis). However, t-PA was shown to be useful only in the first 3h after the cerebrovascular occlusion [4]. It activates MMPs that take part in the pathogenesis of blood-brain barrier damage and tissue edema [5]. With regard to the similarities between central nervous system and retina, we assume that roles of t-PA and its inhibitor in PDR may be mediated by MMPs similar to stroke. Therefore, targeting MMPs together with t-PA and PAI might be more efficient in the treatment.

The study reflects the levels of t-PA, PAI and vascular endothelial growth factor (VEGF) in PDR. PDR is usually accompanied by complications such as retinal ischemia, vitreoretinal tractions, epiretinal membranes or other fibrovascular changes that can trigger wound healing processes. While t-PA, PAI and VEGF have significant roles in inflammation and wound healing the alterations of their levels might be attributed to those wound healing processes but not the PDR pathogenesis. This may be accepted as a limitation of the study that aimed to explore the triggering and/or contributing effects of t-PA and PAI in the pathogenesis of PDR.

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