Neutralization of placental growth factor reduces retinal inflammation in diabetic animal models

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DESIGN OF THE STUDY. Therapeutic effect of placental growth factor (PlGF) inhibition on inflammation in different diabetic mouse models.

PURPOSE. The aim of this study was to test the efficacy of intravitreal (IVT) administration of an anti-PlGF antibody on inflammation in the diabetic Akimba and streptozotocin (STZ)-induced mouse model.

METHODS. The *in vivo* efficacy of a PlGF neutralizing antibody (5D11D4; 5.4 µg/eye) on retinal inflammation was tested in the diabetic Akimba and STZ-induced mouse model (n=7-16 mice/group). Repeated intravitreal (IVT) injections of 5D11D4, anti-VEGF or vehicle were started in 5 to 7 week-old Akimba mice, whereas in the mouse STZ model, injections were started at week 7 after diabetes onset. Retinal inflammation was measured by the quantification of isolectin B4 positive cells and F4/80 positive cells, 5 weeks post treatment in the Akimba mice and in the STZ model at week 8, respectively.

RESULTS. Repeated IVT administration of the anti-PlGF antibody significantly reduced the presence of inflammatory cells in both diabetic mouse models. In the Akimba mice, 5D11D4 significantly reduced the retinal presence of isolectin B4 positive cells by up to 86% as compared to vehicle-treated eyes ($p<0.001$). The number of F4/80 positive cells was significantly reduced in the mouse STZ model by 51% after PlGF inhibition, as compared to buffer-treated eyes ($p < 0.05$), whereas administration of a VEGF inhibitor did not have an effect ($p > 0.05$ *vs.* vehicle).

CONCLUSIONS. In this study, it is demonstrated that repeated administration of an anti-PlGF antibody significantly reduced retinal inflammation in different diabetic animal models. These findings might provide an additional benefit for anti-PlGF treatment and potentially make the DME/inflammatory–driven pathways in DR more susceptible to anti-PlGF therapy, as compared to anti-VEGF therapy.$