Anti-PLGF treatment as a potential alternative therapy for diabetic retinopathy

Etienne I, Van Bergen T, Jonckx B, Feyen J H M.

ThromboGenics NV, Leuven, Belgium

Introduction. Diabetic Retinopathy (DR) is the leading cause of vision impairment among working-age adults. Despite encouraging results in improving vision, anti-VEGF agents may be associated with potential side-effects, such as neurotoxicity. Therefore, there is a need for alternative therapies for DR. In this study, the effect of 5D11D4, an antibody against murine placental growth factor (PlGF), was investigated on retinal ganglion cells (RGC) density in a diabetic mouse model. Previous studies already showed the inhibitory effect of this antibody on inflammation, leakage and angiogenesis.

METHODS. The anti-PlGF antibody was intravitreally administered at 7 weeks after diabetes onset and was compared to anti-VEGFR-2 antibody and PBS in the diabetic streptozotocin mouse model (STZ; n=30/group). At 8 weeks after diabetes onset, eyes were enucleated, dehydrated and cut into serial 7µm paraffin sections. The effect on RGC density was investigated by Brn3a mouse monoclonal antibody immunostaining. The background stain caused by the endogenous mouse IgG was decreased by using the MOM kit (Labconsult), which allows to perform the stain in one day. Metamorph software (Leica) was used to count the RGC density on 250 µm on either side of the optic nerve head.

RESULTS. The RGC number in STZ diabetic mice was significantly lower compared to non-diabetic mice (12.8 ± 1.0 versus 15.7 ± 0.8, respectively, P=0.04). After anti-PlGF treatment the RGC density in the diabetic mice was not significantly different from PBS-treated eyes, whereas anti-VEGFR-2 injection significantly reduced RGC density with 20% versus buffer (P=0.04).

CONCLUSIONS. It has been reported that PlGF-neutralization is able to affect different hallmarks in preclinical DR model. This study shows that PlGF-inhibition preserves the RGC density under diabetic conditions in contrast to VEGFR-2 neutralization. Clinical trials have been initiated to evaluate the therapeutic potential of anti-PlGF treatment in patients presenting diabetic macular edema.

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