Poster
#472-P

Development and Validation of STZ-Induced Diabetic Retinopathy Models for Therapeutic Evaluation

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Introduction

Diabetic retinopathy affects about 35% of diabetic patients and is a leading cause of adult blindness, significantly impacting quality of life and healthcare costs. Developing robust animal models for research and therapeutic development is challenging due to the need to replicate human pathophysiology and ensure reproducibility. In this study, we developed diabetic retinopathy models using Streptozotocin (STZ)-induced diabetic animals and tested a reference agent to evaluate therapeutic potential.

Methods & Experimental Design

Diabetic retinopathy model was developed using STZ-induced type I diabetic mice. A single intraperitoneal (i.p.) injection of STZ (150 mg/kg; Sigma, S0130-1G) was administered for the induction of diabetes on Day 1. Aflibercept (25 mg/kg, Eylea, Bayer) was intraperitoneally injected once a week from the 4th week after STZ modeling (Day 28). In-life and terminal readouts including retinal thickness by Optical Coherence Tomography (OCT), retinal function by electroretinography (ERG), retinal pathology by CD45 immunohistochemistry (IHC) analysis, and scanning-laser ophthalmoscopy were performed.

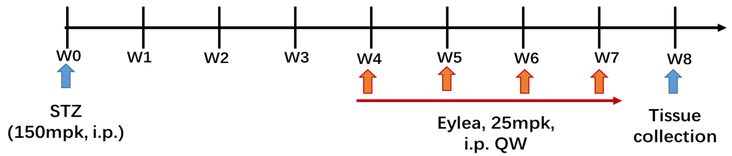

Figure 1. Time schedule of model development and treatment. Model C57BL/6J mice were fasted overnight, then weighed and administered a single intraperitoneal (i.p.) injection of streptozotocin (STZ, 150 mg/kg). On Day 7, the model mice is randomly divided into 2 groups according to fasting blood glucose and body weight (G2 model group & G3 positive drug group), and G3 was given i.p. Aflibercept (25 mg/kg; Eylea) once a week from the 4th week after STZ modeling (Day 28).

Results

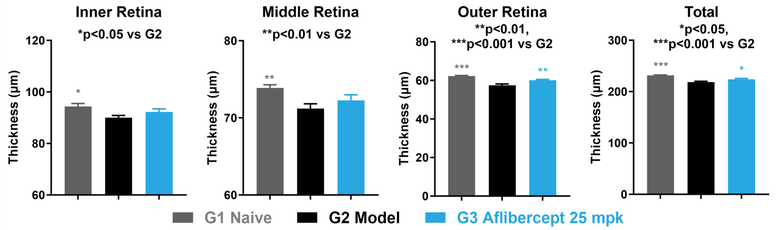

Figure 1. Inner, middle, outer and total retina thickness of mice from naïve (G1), model (G2), and Aflibercept-treated (G3) groups. Data are presented as Mean±SEM (G1 n=16, G2 n=12, G3 n=8). Data are analyzed by one-way ANOVA followed by Dunnett's multiple comparison tests.

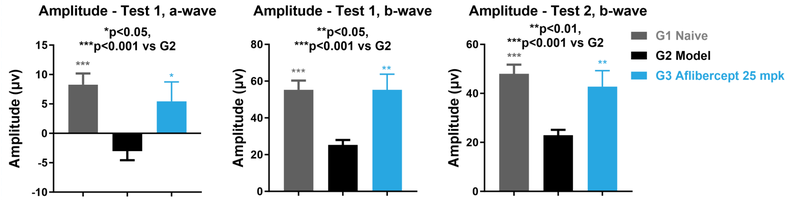

Figure 2. Amplitude of ERG a-waves and b-waves of mice from naïve (G1), model (G2), and Aflibercept-treated (G3) groups. Data are presented as Mean±SEM (G1 n=16, G2 n=12, G3 n=8). Data are analyzed by one-way ANOVA followed by Dunnett's multiple comparison tests.

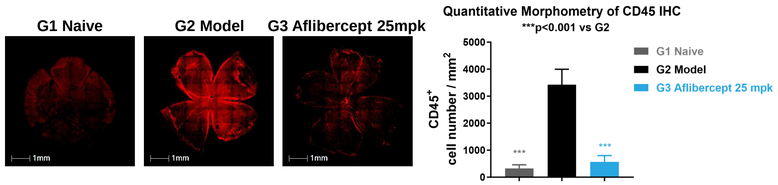

Figure 3. Representative CD45 IHC images (left) and CD45⁺ area quantifications (right) of retinas from naïve (G1), model (G2), and Aflibercept-treated (G3) mice. Data are presented as Mean±SEM (n=6/group). Data are analyzed by one-way ANOVA followed by Dunnett's multiple comparison tests.

Results

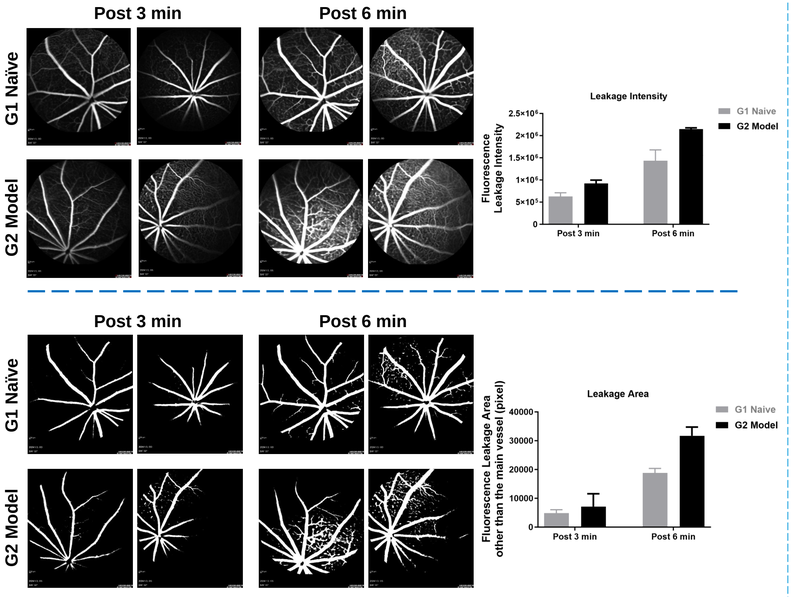

Figure 4. Scanning-laser ophthalmoscopy images of retina fluorescein leakage (left) and quantifications (right) of naïve (G1) and model (G2) mice. Data are presented as Mean±SEM (n=2/group).

Summary

Our study successfully established a model of diabetic retinopathy, demonstrating significant retinal dysfunction and inflammation. Aflibercept effectively alleviated these complications, highlighting its potential therapeutic benefits.

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