Introduction

Diabetes profoundly impacts the microvasculature in nearly every tissue. Diabetic retinopathy is a dramatic example of this, resulting in retinal capillary dropout, vessel leakage, and pathological neovascularization, leading to severe loss of vision which current treatments are incapable of reversing.\(^1,2\) We have recently shown that intra-vitreal injection of adipose-derived stem cell (ASCs) stabilize retinal microvasculature and encourage regeneration of damaged capillary beds in several mouse models of retinal vasculopathy.\(^3\) ASCs are desirable because of their relative ease of harvest from accessible fat depots, as well as their potential for autologous or allogeneic treatment. However, it is unknown if ASCs obtained from diabetic patients are negatively impacted by the disease. Thus we seek to evaluate whether or not diabetic ASCs affect the retinal microvasculature to the same extent as healthy ASCs in a murine model of retinal vasculopathy.

Materials and Methods

Using the hyperglycemic Akimba mouse model of diabetic retinopathy, which exhibits hallmarks of the human disease, including capillary drop-out and edema, we have probed the differences in treatment efficacy and function of mASCs derived from healthy vs. diabetic mice. mASCs were obtained from the epididymal fat pad of adult wild-type (healthy) or Akimba (diabetic) mice using the SVF isolation method in (4). Five-week old, immuno-competent male Akimba mice received intra-vitreal injections of DiI-labeled, passage-4 mASCs (healthy or diabetic) in one eye and PBS vehicle in the contralateral eye. Four weeks later, mice were euthanized and retinae were harvested and stained with fluorescently-labeled lectin to visualize microvessels. Confocal images (10x, 20x, and 60x) were obtained and cell location and morphology, as well as vascular density were quantified.

Results

mASCs from healthy, non-diabetic mice were more effective than diabetic mASCs in revascularizing the diabetic retina and protecting against vascular regression, showing a 69% increase vs. 7% decrease in capillary density, respectively. Furthermore, a greater number of healthy mASCs (68%) assumed perivascular positions along microvessels than diabetic mASCs (47%), which is indicative of a pericyte-like support role, as has been previously shown by our group and others.

Conclusion

Our findings suggest that injected ASCs derived from diabetic mice have a decreased ability to affect the retinal vasculature as compared to healthy ASCs, supporting the utility of an allogeneic approach in the clinical arena. Furthermore, this might indicate that endogenous populations of stem cells differ in diabetes and thus contribute to progression of the disease.

References


Disclosures

The authors have nothing to disclose.