Essential Role of IL-12 in Angiogenesis in Type 2 Diabetes.


Abstract:

Recently, IL-12 emerged as a critical player in type 2 diabetes complications. We previously reported that ischemia-induced angiogenesis is compromised in type 2 diabetic mice. In this study, we determined that IL-12 disruption rescued angiogenesis and arteriogenesis in type 2 diabetic mice. To induce type 2 diabetes, wild-type (WT), p40IL-12-/- (p40-/-), and p35IL-12-/- (p35-/-) mice were fed a high-fat diet (HFD) for 12 weeks. Body weight, glucose test tolerance, and insulin test tolerance were assessed. After 12 weeks of an HFD, the femoral artery was ligated and blood flow recovery was measured every week for 4 weeks. WT, p40-/-, and p35-/- mice fed an HFD become obese after 12 weeks and exhibit glucose intolerance and insulin resistance. Blood flow recovery was fully restored in 2 to 3 weeks after femoral artery ligation in all groups of mice fed a normal diet. However, after 12 weeks of an HFD, blood flow recovery was compromised in WT mice, whereas it was fully recovered in p40-/- and p35-/- mice. The mechanism of blood flow recovery involves an increase in capillary/arteriole density, endothelial nitric oxide synthase/Akt/vascular endothelial growth factor receptor 2 signaling, and a reduction in oxidative stress and inflammation. The disruption of IL-12 promotes angiogenesis and increases blood flow recovery in obese type 2 diabetic mice by an endothelial nitric oxide synthase/Akt/vascular endothelial growth factor receptor 2/oxidative stress-inflammation-dependent mechanism.

Published In:

Am J Pathol. , Vol. 187 - No. 11 , pp. 2590-2601