An APJ agonist suppresses the loss of retinal neuronal cells in diabetes model mouse fed a high-fat diet

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Diabetic retinopathy is a leading cause of blindness and leads to retinal neuronal cell death at the early stage. We have previously shown that an apelin receptor (APJ) agonist suppresses the reduction of the retinal neuronal function observed in a mouse model of diabetes fed a high-fat diet (HFD). In the present study, we investigated the protective effect of endogenous apelin and ML233, an APJ agonist, against retinal neuronal cell death in the diabetes model mice fed the HFD by immunohistochemistry. We used Ins2 mutant ($Ins2^{+/-}$) mouse (Akita mouse), which is a mouse model of type 1 diabetes. Akita mouse was fed the HFD from 5 to 9 weeks after birth. ML233 (5 mg/kg) was administered intraperitoneally on every other day for 4 weeks. Immunohistochemical staining showed that intraperitoneal injection of ML233 prevented the loss of retinal ganglion cells, bipolar cells, and cone cells in Akita mice fed the HFD for 4 weeks. The loss of these retinal neuronal cells was accelerated by deletion of apelin. These results suggest that systemic administration of APJ agonists could protect against retinal neuronal cell death in diabetic retinopathy.