OMICS Group Conferences
Accelerating Scientific Discovery
3rd International Conference on
Clinical & Experimental Ophthalmology
April 15-17, 2013 Hilton Chicago/Northbrook, USA

(Pro) renin receptor is associated with angiogenic activity in proliferative diabetic retinopathy

Susumu Ishida

Hokkaido University Graduate School of Medicine, Japan

Abstract

The renin-angiotensin system (RAS) plays a potential role in the development of end-organ damage, and tissue RAS activation has been suggested as a risk factor for diabetic retinopathy. We have recently shown the significant involvement of (pro)renin receptor [(P)RR] with retinal inflammation in a rodent model of early diabetes. We herein aim to elucidate (P)RR-associated pathogenesis of fibrovascular proliferation, the late-stage angiogenic complication in human diabetic retinopathy. Vitreous fluids from 23 eyes with proliferative diabetic retinopathy (PDR) and 16 controls with non-diabetic, idiopathic macular diseases (macular hole and epiretinal membrane) were collected and protein levels of soluble (P)RR were measured by ELISA, and immunofluorescence was performed to assess localization of (P)RR and related molecules in fibrovascular tissues from PDR eyes. (P)RR immunoreactivity was detected in neovascular endothelial cells, co-localized with prorenin, phosphorylated extracellular signal-regulated kinase (ERK) and vascular endothelial growth factor (VEGF). Prorenin application to human retinal microvascular endothelial cells significantly up regulated mRNA expression of VEGF, especially the VEGF165 isoform, which was abolished by (P)RR or ERK signaling blockade. Proteases known for the cleavage of (P)RR including furin were positive in endothelial cells in fibrovascular tissues. Protein levels of soluble (P)RR in the vitreous fluids were higher in PDR eyes than in non-diabetic control eyes, and were significantly correlated with vitreous prorenin and VEGF levels and the vascular density of fibrovascular tissues. Our data using human samples provide the first evidence that (P)RR is associated with angiogenic activity in PDR.

Biography

Ishida undertook his residency in ophthalmology at Keio University Hospital after completing his medical degree at the age of 24 years. He completed fellowships in the Department of Ophthalmology at Keio University School of Medicine, and the Massachusetts Eye and Ear Infirmary at Harvard Medical School, and received a PhD from Keio University on the subject of vascular endothelial growth factor in diabetic retinopathy. Prof. Ishida is an author on over 150 scientific publications (impact factor: over 450) and currently Professor and Chairman of Ophthalmology at Hokkaido University Graduate School of Medicine in Sapporo, Japan.