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C-PEPTIDE PREVENTS VASCULAR ENDOTHELIAL GROWTH FACTOR-MEDIATED MICROVASCULAR LEAKAGE IN DIABETIC RETINA


Diabetic retinopathy is predominantly caused by vascular endothelial growth factor (VEGF)-induced microvascular leakage; however, the underlying mechanism is unclear. Here, we demonstrated that hyperglycemia induced microvascular leakage by activating TGase2 and this vascular leakage was inhibited by C-peptide in diabetic retina. VEGF elevated TGase2 activity through sequential elevation of intracellular Ca²⁺ and reactive oxygen species (ROS) levels in endothelial cells. TGase inhibitors or TGase2 siRNA prevented VEGF-induced stress fiber formation and VE-cadherin disruption, which play a critical role in modulating endothelial permeability. C-peptide inhibited the VEGF-induced ROS generation, stress

fiber formation, and disassembly of vascular endothelial cadherin in endothelial cells. Intravitreal injection of C-peptide, TGase inhibitors, or TGase2 siRNA successfully inhibited hyperglycemia-induced TGase activation and microvascular leakage in the retinas of diabetic mice. Thus, our findings suggest that C-peptide prevents VEGF-induced microvascular permeability by inhibiting ROS-mediated activation of TG2 in diabetic mice.

Biography

Kwon-Soo Ha has completed his PhD in 1991 from the University of Texas at Austin and continued his Postdoctoral study at the Vanderbilt University School of Medicine. He has served as the President of two academic societies, Korean Society for Cell Biology and Korean Biochip Society, in 2012 and 2013, respectively. He has published over 220 papers in peer reviewed international journals, including Journal of Cell Biology, Diabetes, and Biosensors & Bioelectronics. His research interests include prevention of diabetic complications and applications of protein chips to serodiagnosis and proteomic analysis of protein activity and interactions.

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