GS01-3 **GLP-1 is a new therapeutic target for the diabetic endothelial dysfunction via suppressing GRK2 activity**

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Diabetes mellitus is an important risk factor for hypertension and other cardiovascular diseases, and impaired endothelial function. Abnormal G-protein-coupled receptor kinase 2 (GRK2) accumulation has a crucial role in the development of insulin resistance and diabetes. We previously reported that GRK2 levels and these activations increase in diabetic aortas and livers, and that suppressing them is improved the vascular endothelial dysfunction. Glucagon-like peptide-1 (GLP-1) is a gut hormone that promote insulin secretion and improve blood glucose level. However, it is unknown whether GLP-1 directly affects diabetic endothelial dysfunction, especially GRK2 signaling. In this study, we investigated the relationship between GLP-1 and GRK2 under insulin stimulation for endothelial dysfunction. GLP-1 increased the impaired insulin-induced vascular relaxation responses via Akt/endothelial nitric oxide synthase (eNOS) signaling pathway in diabetes. However, these responses were disappeared by treatment of a GLP-1 receptor antagonist. Furthermore, GLP-1/insulin stimulation upregulated the phosphorylation levels of Akt and eNOS in diabetes compared with non-stimulation. Additionally, in diabetes GRK2 activity was inhibited under GLP-1/insulin stimulation, although GRK2 levels were not altered between the two groups. Those results suggest that in diabetes GLP-1 improves the endothelial dysfunction by increasing insulin-induced nitric oxide (NO) production via the suppression of GRK2 activity and the upregulation of Akt/eNOS signaling.