投稿學會：	收件編號：	分類編號：

第二十八屆生物醫學聯合學術年會 **ABSTRACT FORM** （正本）

新穎基因 ARHGAP22 在第二型糖尿病視網膜病變致病機轉之研究

Novel Role of ARHGAP22 in the Development of Type 2 Diabetic Retinopathy

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Backgrounds:

We previously identified *ARHGAP22*, which is implicated in endothelial cell angiogenesis and increased capillary permeability, as a novel diabetic retinopathy (DR) gene. Here, we would like to investigate if the expression of ARHGAP22 and its related mechanism proteins increases or decreases *in vitro* and *in vivo* in response to exposure to different glucose concentrations.

Materials and Methods:

To determine the expression level of ARHGAP22 and its mechanism of action, including Rac1, VEZF1 and EDN1, we used a Western blot assay in human retinal endothelial cells (HRECs) under different glucose concentrations (5 mM or 30 mM D-glucose). In addition, we used intraperitoneal injection of streptozotocin (STZ)-induced diabetic mouse model to examine the expression of ARHGAP22 and Rac1. Total protein and RNA from mouse retina were subjected to Western blot analyses and real-time PCR.

Results:

The results showed that high levels of D-glucose (30 mM) decreased the expression of the ARHGAP22 protein in HRECs for 24 h compared with normal glucose (5 mM). However, the expression of VEZF1 and EDN1 at high levels of D-glucose was increased for 24 h compared with normal glucose. The total protein expression of Rac1 increased under high glucose levels for 5 min compared with low glucose levels. In contrast, the protein expression of active Rac1-GTP protein increased at high glucose levels. At an mRNA level, the mRNA expression of ARHGAP22 at high glucose levels increased for 24 h and 48 h, whereas the mRNA expression of Rac1 at high glucose levels was similar to that observed at low glucose levels. Furthermore, the results of STZ-induced diabetic mouse model have shown that the protein expression either in ARHGAP22 or in VEZF1 was decreased in STZ-induced diabetic mouse compared with saline control mouse. The mRNA expression level of ARHGAP22 was decreased in STZ-induced diabetic mouse compared with saline control mouse, but the mRNA expression level of Rac1 was increased in STZ-induced diabetic mouse.

Conclusion:

In summary, the protein expression of ARHGAP22 was decreased and the expression of VEZF1 and EDN1 was increased under high levels of glucose condition. ARHGAP22 is the only reported regulatory cell signal for VEZF1, which participates in a direct protein-protein interaction with VEZF1. VEZF1 specifically bound to the EDN1 promoter and suggested that the VEZF1 binding site was responsible for endothelial cell dependent EDN1 expression. Therefore, it is suggested that ARHGAP22 inhibits VEZF1 transcriptional activation of the EDN1 expression in high glucose condition may increase to DR development.

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