中文題目: 微小核糖核酸 200a/200b 透過對 O-連接的 N-乙酰葡糖胺轉移酶的調控來影響高糖刺激下的內皮細胞發炎反應

英文題目：MicroRNA-200a/200b Modulate High Glucose-Induced Endothelial Inflammation via Targeting O-linked N-acetylglucosamine Transferase Expression

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**ABSTRACT**

**Aims:** Enhanced O-linked N-acetylglucosamine (O-GlcNAc) modification by O-GlcNAc transferase (OGT) is associated with diabetic complications. Enhanced oxidative stress causes endothelial inflammation in diabetes. Previous studies documented that members of microRNA-200 family are oxidative stress-sensitive. Here, we examined whether microRNA-200a/200b (miR-200a/200b) regulate high glucose (HG)-induced OGT expression in human aortic endothelial cells (HAECs), and whether microRNA-200a/b target OGT to regulate HG-induced endothelial inflammation.

**Methods:** HAECs were treated with HG (25 mmol/L) for 12 and 24 h. Q-PCR, Western blotting, monocyte adhesion assay, bioinformatics prediction, microRNA-200a/200b mimic and siRNA OGT transfection were performed *in vitro*. *In vivo*, the aortic tissues of db/db diabetic mice were examined by fluorescent immunohistochemistry.

**Results:** HG increased OGT mRNA, OGT protein, protein O-GlcNAcylation levels in HAECs, and was associated with increased ICAM-1/VCAM-1/E-selectin gene expression and monocyte adhesion. Bioinformatics predicated the homology between members of miR-200 family and the 3'-UTR of OGT mRNA and Q-PCR confirmed that miR-200a, miR-141, miR-200b, miR-200c, and miR-429 were significantly decreased in HG-stimulated HAECs, suggesting impaired feedback restraints on HG-induced endothelial O-GlcNAcylation via OGT upregulation. Both miR-200a/200b mimics transfection significantly inhibited HG-induced OGT expression, protein O-GlcNAcylation levels, ICAM-1/VCAM-1/E-selectin gene expression and monocyte adhesion. Additionally, OGT depletion via siRNA reduced HG-induced protein O-GlcNAcylation, ICAM-1/VCAM-1/E-selectin gene expression and monocyte adhesion; indicating HG-induced

inflammation were mediated partially through OGT-induced O-GlcNAcylation. *In vivo*, intravenous injections of miR-200a/200b mimic prevented endothelial OGT and ICAM-1 expression in db/db mice.

**Conclusion:** miR-200a/200b are involved in the regulation of HG-induced endothelial inflammation via modulation of OGT-mediated O-GlcNAcylation, indicating that miR-200a/200b may be a novel target for the treatment of diabetic vascular complications.