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第二十九屆生物醫學聯合學術年會　投稿摘要表格（正本）

MiR-145 Strengthens Atherogenic Low-Density Lipoprotein-Induced Platelet Activation

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Background: Human LDL can be chromatically resolved into the most negatively charged subfraction, L5. It is capable of inducing atherogenic responses in vitro and in vivo. microRNAs play a role in atherosclerosis-related disease, such as cardiovascular disease. In addition, platelet activation and aggregation are major events underlying acute thrombosis in myocardial infarction. Thus, we examined whether miR-145 supports L5-induced platelet activation and aggregation. **Material& Methods:** We isolated L5 and L1 (the least negatively charged LDL) from the plasma of patients with STEMI or stroke. Cultivated human platelets were treated with L5 to evaluate the effect of L5 on platelet activation and explore the mechanism of action of L5. Quantitative analysis by stem-loop real-time PCR were used to assess the expression of mature miR-145 after L5-treated platelets. **Results:** L5, but not L1, induced phosphorylation of Iκ B kinase β (IKKβ) and degradation of its inhibitor Iκ Bα , thereby activating NF-κ B. Activated platelets rapidly formed aggregates bridged by the stimulated GPIIb/IIIa receptors. L5-induced degradation of Iκ Bα was inhibited via deubiquitination by USP31, which was in turn inhibited by miR-145. Specific antisense oligodeoxynucleotide (ODN) against miR-145, but not scrambled ODN, prevented USP31 inhibition, thus preventing NF-κ B activation. We injected 5 mg/kg of L5 or L1 into C57/BL6 mice. After 30 min, the tail-bleeding time was 44% shorter in the L5 mice than the L1 mice (n=12; $P<0.05$); this reduction was prevented by coadministering miR-145 antisense ODN, but not scrambled ODN. **Conclusions:** miR-145 plays a role in L5-mediated platelet aggregation. Further investigation is warranted to examine whether silencing miR-145 reduces the risk of myocardial infarction and stroke.

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