中文題目：微核醣核酸(microRNA) let-7g 調節 C 型肝炎病毒複製之研究

英文題目：The study of microRNA let-7g on the modulation of the replication of hepatitis C virus

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Background: The microRNAs (miRNA) have been implicated in hepatitis C virus (HCV) infection. The present study aimed to investigate the effects of let-7g miRNA on the HCV replication.

Methods: The replicon cells Huh7/Ava.5 (genotype 1b), Huh7/J6/JFH (genotype 2a) and Huh7.5/Con1 (genotype 1b) were obtained and the mirVana™ let-7g mimic/inhibitor, miR-122 inhibitor and miRNA mimic/inhibitor negative control were purchased. The 1.0-kb and 0.5-kb fragments of the let-7g promoter were amplified by PCR. Site-directed mutagenesis of the AP-1 binding-site presented in the let-7g promoter region was carried out. WST-1 assay and Renilla Luciferase Assay were used. Expression levels of let-7g in each sample were normalized to the corresponding level of snU6B. Expression levels of let-7g were determined by using the Quantitative real-time PCR. Anti-phospho-ERK, p38, JNK, and total-ERK, p38, JNK antibodies, Anti-GAPDH and α-tubulin antibodies were used for Immunoblot analysis.

Results: Our results demonstrated that overexpression of let-7g reduces HCV expression in the cell line. The HCV loads were more decreased by let-7g mimic than miR-122 inhibitor transfected cell. High levels of lin28 correlate with low levels of let-7g in HCV-infected cells and the knockdown of lin28 via siRNA reduces HCV replication. The treatment with a let-7g mimic alone was shown to induce IFN-induced genes inclusion MxA and OAS1. Interferon (IFN)/RBV induces let-7g expression, and let-7g and IFN/ribavirin also elicited an addictive inhibitory effect on HCV expression. The anti-viral effects of let-7g mediated IFN/RBV signalling and the regulation of let-7g by IFN/RBV occurs through p38/AP1 signalling.

Conclusion: We have indicated an important role of let-7g on the replication of HCV and on the response of HCV to anti-HCV treatment. The IFN/ribavirin induces let-7g expression through p38/AP-1 signalling and the let-7g and IFN/RBV have additively inhibitory effect on HCV replication.