Executive Summary

Project Title:

Pharmacogenomic and molecular epidemiological study of HIV/AIDS patients co-infected with Hepatitis C virus (HCV) (MSS-245R)

Objectives:

This project has 4 major objectives:

1. Develop laboratory expertise in host genetic polymorphism for *interferon-lambda-4* (*IFNL4*) among HIV/HCV co-infected patients
2. Evaluate the relationship between IFNL4 TT/△G and peg-IFN/RBV or direct acting antivirals responsiveness among HIV/HCV co-infected patients
3. Estimate the correlation between IFNL4 TT/△G and IL-28B rs12979860 T/C and rs8099917 G/T polymorphisms
4. Study the epidemiological and phylogenetic linkage of HIV/HCV co-infections for better illustration of transmission patterns

Design and Setting:

In this 1-year project, the protocol for IFNL4 genetic polymorphism was optimized and evaluated using archived samples from project MSS-220R. In brief, *IFNL4* genetic polymorphisms were detected by an in-house HybProble real-time assay with melting curve analysis and validated by Sanger sequencing. The remaining 40 archived samples from project MSS-220R and fresh samples collected from Oct 2015 to Sept 2016 were used to determine the genetic polymorphisms in IFNL4 & IL-28B and genotypes in HIV & HCV.

Participants:

Thirty HIV/HCV co-infected patient samples were prospectively collected from Integrated Treatment Centre (Department of Health) and 80 archived samples were retrieved from project MSS-220R. The patient background and treatment history was blinded which patient privacy will not be disturbed.

Interventions:

This project provided the first comprehensive set of surveillance data in Hong Kong regarding the prevalence of *IFNL4* polymorphisms in association with therapeutic prognosis among HIV/HCV co-infected patients in our locality.

Main Outcome Measures:

The protocol development of *IFNL4* polymorphisms by real-time assay and the prevalence of *IFNL4* in our locality are determined as the major outcome measure.

Results:

Among 110 HIV/HCV co-infected patients, the frequency of *IFNL4* ss469415590 wild-type (TT/TT) was 84.5%, while the frequency for TT/△G and △G/△G mutants was 14.5% and 1%, respectively. The prevalence of *IL-28B* polymorphism in rs12979860 was identical to *IFNL4* polymorphism in ss469415590. In contrast, the prevalence of *IL-28B* polymorphism in rs8099917 was slightly differed, which had 87.3% wild-type (T/T), 11.8% G/T and 0.9% G/G mutants.

HCV genotypes were detected in 107 patients, including genotype 1/1a/1b (29.9%), 2a (1.9%), 3/3a/3b (48.6%) and 6a/6d/6e (19.6%). An in-house HIV-1 genotyping resistance test revealed that the recruited patients were infected by subtype B (35.4%), CRF01_AE (45.6%), subtype C (1.3%), CRF07_BC (8.9%), CRF08_BC (1.3%) and other recombinants (7.6%).

The transmission routes of HIV and HCV are slightly differed. Of 110 co-infected patients, 107 of them got HIV and HCV infections via identical routes, including 46 injecting-drug use (IDU), 10 heterosexuals, 46 men-have-sex-with-men (MSM) and 5 through blood products. The remaining 3 patients contracted HIV from heterosexual activity but HCV from IDU. Both IDU and MSM population are of high risk concern on HIV and HCV co-infection. No significant association was observed between HIV-1 genotypes, HCV genotypes, *IFNL4* and *IL-28B* polymorphisms.

Conclusions:

Throughout this project, a simple and efficient duplex real-time HybProbe® assay with excellent performance on detecting *IFNL4* polymorphisms on ss469415590 was developed successfully.

The prevalence of *IFNL4* polymorphisms was identical to the prevalence of *IL-28B* rs12979860 but slightly differed from rs8099917. Over 80% of HIV/HCV co-infected patients were transmitted either through injecting-drug use and men-have-sex-with-men.