

Project Title:

A study of pharmacogenomics for therapeutic and prognostic guidance towards HIV/AIDS patients co-infected with Hepatitis C virus (HCV) (Project Code: MSS-220R)

Executive Summary:**Objectives:**

This project has 3 major objectives:

1. Develop laboratory expertise in HCV genotyping, viral load monitoring, and host genetic polymorphisms in *IL-28B* among HIV/HCV co-infected patients
2. Monitor HCV genotypes and prevalence of host polymorphisms of CC genotypes of *IL-28B* in association with therapeutic prognosis among HIV/HCV co-infected patients
3. Build up a database on host and viral genomics as guidance for personalized regimen of HAARY and anti-HCV therapy for HIV/HCV co-infections in Hong Kong

Design and Setting:

In Year 1, the protocols for *IL-28B* genetic polymorphism, HCV viral load and genotyping were optimized and evaluated using archived samples. In brief, *IL-28B* genetic polymorphisms were detected by an in-house duplex HybProbe real-time assay with melting curve analysis and validated by Sanger sequencing. HCV viral load was detected by Abbott *m2000* RealTime HCV PCR assay. HCV genotypes were determined by sequencing the highly conserved 5'UTR region and analyzed through the Basic Local Alignment Search Tool (BLAST) at the National Centre for Biotechnology Information (NCBI) website. Subsequent experiments and follow-up on prospective patient samples were completed in Year 2.

Participants:

In this 2-year study (1st April 2013 ó 31st March 2015), a total of 100 HIV/HCV co-infected patient samples were collected from Integrated Treatment Centre (Department of Health). 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 HCV genotypes and host polymorphisms of *IL-28B* in association with therapeutic prognosis among HIV/HCV co-infected patients in our locality.

Main Outcome Measures:

The protocol development of *IL-28B* polymorphisms by real-time assay and the prevalence of *IL-28B* in our locality are determined as the major outcome measure.

Results:

Among the 100 HIV/HCV co-infected patients recruited in this project, the frequency of rs12979860 wild-type (C/C) was 89%, while the frequency for C/T and T/T mutants was 9% and 2%, respectively. The prevalence of *IL-28B* polymorphisms in rs8099917 was slightly differed, which had 91% wild-type (T/T), 7% G/T and 2% G/G mutants.

HCV genotypes were detected in 82 patients, including genotype 1/1a/1b (35.4%), 2a (1.2%), 3a/3b (36.6%) and 6a/6d/6e (26.8%). An in-house HIV-1 genotyping resistance test revealed that the recruited patients were infected by subtype B (24.7%), CRF01_AE (54.3%), subtype C (3.7%), CRF07_BC (11.1%), CRF08_BC (2.5%) and other recombinants (3.7%). Due to low HIV-1 or HCV viral load at sample collection, about 15 ó 20% of the co-infected patients were unable to have either or both viral genotyping results.

No significant association was observed between *IL-28B* polymorphisms, HCV genotypes and HIV-1 genotypes.

Conclusions:

Throughout this project, a simple and efficient duplex real-time HybProbe assay with excellent performance on detecting *IL-28B* polymorphisms on rs12979860 and rs8099917 was developed successfully. Together with the HCV genotypes and viral load assay, the rapid detection on *IL-28B* polymorphisms enables clinicians to make decision on treatment option and duration as early as possible.

Publications:

1. Utilization of a duplex hybprobe real-time PCR to detect and estimate *IL-28B* polymorphisms prevalence among HIV/HCV co-infected patients in Hong Kong. To SWC, Siu GKH, Wong KH, Chan KC, Yuen KT, Ng HM & Yam WC. *J Med Microb Diagn* (In Press).
2. Poster presentation at International Conference on Advanced Molecular Technologies 2014, 7th ó 9th March 2014, Hong Kong. Determination of *IL-28B* genotyping using rs12979860 and rs8099917 SNPs among HIV/HCV co-infected patients in Hong Kong. Ng HM, To SW and Yam WC.