peptides (AMPs) have the ability to target microbial pathogens within eukaryotic cells. In the present study, we aimed to investigate the activity of a series of structurally related AMPs, D-LAK peptides, against Mycobacterium tuberculosis (Mtb) including the drug-resistant strains.

Methods: The antituberculosis activities of six D-LAK peptides (with different hydrophobicity and structural conformation) were examined against clinical isolates of drug susceptible and MDR-Mtb using broth micro-dilution assay in 96 well plates. The cytotoxicity of the D-LAK peptides on human macrophage-like cells (THP-1) was examined by lactate dehydrogenase (LDH) and 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide) (MTT) assays. Furthermore, the effect of the combination of isoniazid and D-LAK peptides was also evaluated against MDR-TB.

Results: All the D-LAK peptides tested could successfully inhibit the growth of Mtb in vitro to a certain extent against MDR-TB. D-LAK peptides effectively dispersed the clumping of mycobacteria, consistent with the 'detergent-like effect' that could reduce the hydrophobic interactions between the highly lipidic surface of the mycobacteria, preventing bacteria cell aggregation. Although D-LAK peptides could not eradicate Mtb at non-toxic concentrations, they were effective as adjunct agent at low concentrations to potentiate the efficacy of isoniazid against drug-resistant Mtb without inducing cytotoxicity to mammalian cells, possibly by improving the uptake of the hydrophilic isoniazid into the mycobacteria by enhancing the surface permeability of the pathogen.

Conclusions: Out of the six tested D-LAK peptides, D-LAK120-A was identified as the optimal peptide within the peptide series based on the balance between the anti-TB activity against MDR-TB and the low cytotoxicity towards mammalian cells. Although D-LAK peptides alone may not be sufficiently potent at their non-toxic concentrations as the sole anti-TB agent, they could be used in combination with other anti-TB agents to improve their efficacy against drug-resistant TB. This combination approach could potentially improve the treatment against MDR-TB and reduce the adverse effects caused by the anti-TB drugs by lower their effective concentrations, leading to the improvement of patient compliance and treatment outcome.

Ref. No.: 11100682

P73-Ab0032
Characterization of Novel Anti-HIV/TB Natural Product Analogues

Xiaofan Lu, Zhiwei Chen
AIDS Institute, Department of Microbiology Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong

Nonnucleoside reverse transcriptase inhibitors (NNRTIs) are one of the key components of antiretroviral therapy drug regimen against human immunodeficiency virus type 1 (HIV-1) replication. We previously described a newly synthesized small molecule, 10-chloromethyl-11-demethyl-12-oxo-calanolide A (F18), a (+)-calanolide A analog, as a novel anti-HIV-1 NNRTI (H. Xue et al., J. Med. Chem. 53:1397-1401, 2010). Here, we further investigated its antiviral range, drug resistance profile, and underlying mechanism of action. F18 consistently displayed potent activity against primary HIV-1 isolates, including various subtypes of group M, circulating recombinant form (CRF) 01_AE, and laboratory-adapted drug-resistant viruses. Moreover, F18 displayed distinct profiles against 17 NNRTI-resistant pseudoviruses, with an excellent potency especially against one of the most prevalent strains with the Y181C mutation (50% effective concentration, 1.0 nM), which was in stark contrast to the extensively used NNRTIs nevirapine and efavirenz. Moreover, we induced F18-resistant viruses by in vitro serial passages and found that the mutation L100I appeared to be the dominant contributor to F18 resistance, further suggesting a binding motif different from that of nevirapine and efavirenz. F18 was nonantagonistic when used in combination with other antiretrovirals against both wild-type and drug-resistant viruses in infected peripheral blood mononuclear cells. Interestingly, F18 displayed a highly synergistic antiviral effect with nevirapine against nevirapine-resistant virus (Y181C). Furthermore, in silico docking analysis suggested that F18 may bind to the HIV-1 reverse transcriptase differently from other NNRTIs. This study presents F18 as a new potential drug for clinical use and also presents a new mechanism-based design for future NNRTI.

Ref. No.: 09080772

P74-Ab0132
Clostridium difficile Diarrhea: Risk Factors for Development and Recurrence

Nelson Lee, Sunny Wong, Margaret Ip, Joseph Sung
The Chinese University of Hong Kong, Hong Kong

Introduction: Clostridium difficile infection is a major cause of antibiotic-associated diarrhoea. Epidemiological studies in Western countries have shown a rapidly increasing incidence; nevertheless, limited epidemiological data are available in Asia.

Methods: We conducted a prospective case-control study comprising more than 140 cases and 110 controls in an acute-care hospital in Hong Kong. Clinical variables including patient characteristics, antibiotics history, concomittant medications and severity of the C. difficile infection, as well as microbiological variables including the ribotypes, antimicrobial susceptibility and toxin levels were studied.

Results: Compared to control subjects, patients with C. difficile infections had a longer hospital stay (20.4 vs 14.0 days, $p<0.01$) and a higher 60-day mortality (25.7% vs 12.0%, $p<0.01$). They were also more likely to have received proton-pump inhibitors (OR=2.21, 95%CI=1.28-3.86, $P<0.01$) or fluoroquinolones (OR=2.64, 95%CI=1.07-6.96, $P=0.024$) compared with the controls. The major ribotypes found were 002 (23%), 012 (14%) and 014 (14%). The ribotype 002 carried a mortality of 50%, and was shown to have a significantly higher toxin titre.

Conclusions: C. difficile infection in Hong Kong is associated with high morbidity and mortality. Risk factors include recent antibiotics exposure and use of acid suppressant. Our findings have major implications on disease prevention and control.

Ref. No.: CU-09-03-04

P75-Ab0034
Prevalence and Predictors of Maternal Seasonal Influenza Vaccination in Hong Kong

Marie TARRANT[1], Carol, Y. S. YUEN[1], Daniel, Y. T. FONG[1], Irene, L. Y. LEE[2], Chu SING[3], Esther, S. M. SIU[4]
[1]School of Nursing, The University of Hong Kong, Hong Kong, [2]Queen Mary Hospital, Hong Kong, [3]Kwong Wah Hospital, Hong Kong, [4]Tuen Mun Hospital, Hong Kong

Background: Pregnant women infected with influenza virus are

more likely to experience severe complications when compared with their non-pregnant peers. Yet influenza vaccine uptake is low among pregnant women. The purpose of this study was to assess the prevalence of seasonal influenza vaccine uptake among pregnant women in Hong Kong and to identify predictors of vaccine uptake.

Methods: Using a multi-center cross-sectional design, we recruited 2822 new mothers during their immediate postpartum stay from all eight public obstetric hospitals in Hong Kong. We assessed antenatal maternal influenza vaccination status as well as health beliefs and perceptions toward influenza and influenza vaccination. Bivariable and multivariable logistic regression was used to identify the predictors of vaccination uptake.

Results: Only 49 (1.7%; 95% CI 1.3-2.3%) participants were vaccinated during their pregnancy. Fear that the vaccine would cause harm to the fetus or themselves were the most common reasons for not being vaccinated. Being aware of the vaccination recommendations (OR = 2.69; 95% CI 1.06-6.82), being advised by a health-care provider (OR = 6.30; 95% CI 3.19-12.46), history of vaccination (OR = 2.47; 95% CI 1.25-4.91), perceived susceptibility to influenza infection (OR = 3.67; 95% CI 1.64-8.22), and perceived benefits of influenza vaccination (OR = 9.98; 95% CI 3.79-26.24) were all independently associated with vaccination. Perceived barriers to vaccination (OR = 0.17; 95% CI 0.07-0.40) were strongly associated with failure to vaccinate.

Conclusions: Low seasonal influenza vaccination uptake among Hong Kong pregnant women was related to a number of factors, all of which are amenable to interventions. Vaccination promotion strategies need to focus on encouraging health-care providers to discuss vaccination with their pregnant clients and in providing pregnant women with accurate and unbiased information about the risks of influenza infection and the benefits of vaccination.

Ref. No.: 10090982

P76-Ab0037
Influenza-like Illness and Viral Aetiology in Hong Kong Children

Lan Wei, Dennis Ip, Kwok-Hung Chan, Malik Peiris, Benjamin Cowling
The University of Hong Kong, Hong Kong

Background: Respiratory viruses are responsible for thousands of hospitalizations and deaths every year in Hong Kong. However, there are few studies on the patterns in incidence of specific respiratory viruses in the community. The objectives of our study were to characterise the incidence rates of common respiratory viruses in children that lead to clinical presentation with ILI at primary care providers in the local community setting, and to compare our findings from primary care settings with inpatient data.

Methods: We recruited patients with acute respiratory illness from outpatient clinics across Hong Kong between 2007 and 2010. A nose and throat swab specimen was collected from each participant and stored at -70°C. In the present study, we tested those stored specimens for 18 respiratory viruses using the xTAG RVP FAST multiplex assay.

Results: We tested specimens from 2,090 specimens collected from eligible pediatric outpatients during the four-year study period, among which 1,343 (64%) were positive for any respiratory virus, and 81 (6%) specimens were found with more than one virus. The most frequently detected viruses were entero/rhinovirus (23.4%) and influenza A (19.6%). Compared to outpatients, detection of RSV, parainfluenza, adenovirus and bocavirus was more common in inpatients in some age groups.

Conclusions: Respiratory viruses are frequently detected in pediatric outpatients in Hong Kong and the non-influenza viruses together appear to be associated with a much greater burden on ambulatory care than influenza A and B viruses. The increased detections of RSV, parainfluenza, adenovirus and bocavirus among inpatients suggest that these viruses may be associated with more severe illnesses than influenza and rhinovirus particularly.

Ref. No.: 10091272

P77-Ab0038
Effectiveness of Vaccinating Children in Reducing Influenza Among Household Contacts: A Community-based, Randomized Controlled Trial

Benjamin Cowling, Kwok-Hung Chan, Dennis Ip, Susan Chiu, Malik Peiris, Gabriel Leung
The University of Hong Kong, Hong Kong

Background: Seasonal influenza vaccination is effective in preventing influenza infection and disease in healthy school-age children. Vaccinating a substantial proportion of children in a community can lead to indirect benefits via herd immunity, but less is known about the household-level indirect benefits of influenza vaccination of children. Moreover, the effectiveness of seasonal vaccine is unclear against a pandemic virus that was not included in the vaccine. The aim of this study was to estimate the direct effectiveness of 2009-10 seasonal trivalent inactivated influenza vaccine (TIV) in preventing influenza infection and illness in children aged 6-17, and the indirect effectiveness in preventing infection and disease in their household contacts.

Methods: A cluster-randomized trial in 796 households recruited between August 2009 and February 2010. One child in each household was randomized to receive 2009-10 seasonal TIV or saline placebo. Households were followed up for approximately 1 year. Sera were collected from all household members at the beginning and end of the study, and also collected from vaccine recipients one month after vaccination, and from 25% of all participants in April 2010. Households reported acute respiratory illness episodes in daily symptom diaries and biweekly telephone follow-up, and home visits were arranged to collect respiratory specimens during illness episodes. The primary outcomes were influenza infection confirmed by reverse transcription polymerase chain reaction (RT-PCR) or serologic testing by hemagglutination inhibition assay.

Results: Children who received TIV had reduced risk of seasonal influenza B confirmed by RT-PCR with vaccine effectiveness estimate of 66% (95% confidence interval, CI: 31%, 83%). Children who received TIV also had reduced risk of influenza B and pandemic influenza A(H1N1) confirmed by serology, with vaccine effectiveness estimates of 83% (95% CI: 46%, 95%) and 47% (95% CI: 15%, 67%) respectively. There was no significant difference in risk of influenza A and B virus infections among household contacts of children who received TIV or placebo. No serious adverse events were reported following vaccination, and most reported reactions to TIV were mild and local to the injection site.

Conclusions: Seasonal TIV had moderate effectiveness in preventing pandemic influenza A(H1N1) and influenza B infection. Indirect benefits were not observed in household