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Association of polymorphism within promoter of the interferon-gamma receptor gene and HBV chronicity among Iranian patients

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Background: polymorphism within regulatory regions of immune response genes can affect the level of gene expression. Gamma interferon (INF-g) is a cytokine that plays an important role in immune response to infection of hepatitis B virus (HBV). The aim of this study is to explore the association between the two single nucleotide polymorphisms (SNPs) within promoter (at positions -611G/A,-56T/C) of the gamma interferon receptor1 gene (INFGR1) and susceptibility to chronic HBV infection.

Methods: A total of 400 individuals were included in a case-control study of Iranian populations with chronic HBV infection and healthy control group. Genomic DNA from peripheral blood samples of 200 chronically HBV infected patients and 200 healthy controls were extracted by phenol-chloroform method and genotyping was performed by PCR-RFLP method also p<0.05 considered as significant.

Results: The frequencies of INFGR1 genotypes on -56 position were 36/6% for TT and 43/5% for TC and 20% CC in case group and 20.9% TT and 51/7% TC and 27/4% CC for control group(p value: 0.002) and frequencies of INFGR1 genotypes on -611 position were 41% for AA and 57/5% for AG and 1/5% GG in case group and 37/8% AA and 53/7% AG and 8/5% GG for control group (p value: 0.006) . Significant difference was observed between case and control group.

Conclusion: A number of single- nucleotide mutations have been identified in interferon gamma receptor and its signaling pathway that predispose to chronic HBV infection. There was association between INFGR1 polymorphism (promoter at positions -611G/A,-56T/C) and chronic HBV infection. This study suggested the possibility that INFGR1gene polymorphism beside host genetic factors can be important in determining an individual's susceptibility in the progress to chronic HBV infection.

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A conserved matrix epitope based DNA vaccine protects mice against influenza A virus challenge

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Background: DNA vaccination represents a unique strategy to overcome the limitations of immunization with conventional vaccines which is restricted by the high variability of influenza viruses. The prime objective was to evaluate the protective efficacy of a plasmid DNA (pDNA), encoding an evolutionarily conserved epitope of viral matrix protein, against the influenza A virus infection.

Methods: The vaccine construct was generated by cloning the DNA encoding a nine amino acid long conserved epitope of M1 protein of influenza A virus in pSecTag2B and its expression was checked by SDS PAGE and western blotting. BALB/c mice were used for the ex-vivo study to observe the immune response after injecting the plasmid DNA through intra-muscular route.

Results: It was found that the immunized mice purely elicited cell mediated immune response to the pDNA, with significantly enhanced level of Th1 cytokines (IL-12 and gamma interferon) production in the stimulated splenocyte supernatant. The cytotoxic T lymphocytes in the spleen of immunized mice significantly lysed the virus infected MDCK cells. A significant decrease in virus replication was also observed in the lungs of immunized mice and 83% of the mice were protected against the lethal challenge of influenza A viruses.

Conclusion: Therefore, the vaccine based on minimal DNA constructs encoding the conservedviral epitope seems promising to provide efficient protection against the influenza A virus infection and resulted in broadened immune responses Further engineering of the plasmid DNA to encode more than one epitope of different viral proteins may result in better activation of immune response to provide cross-protection against the emerging viral strains.

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Clinical risk factors of severity and molecular epidemiology of respiratory syncytial virus circulating in Kuala Lumpur, Malaysia: a retrospective study of 21 years

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Background: Respiratory syncytial virus (RSV) is the most common respiratory virus detected in children. RSV disease ranges from

mild flu-like symptoms to bronchiolitis and severe pneumonia, and predisposes to the development of asthma. Preterm birth and pre-existing respiratory tract disorders increase risk of developing severe RSV infection. There is conflicting evidence about whether severe RSV disease is correlated to RSV genotype. Molecular epidemiological data from tropical Asia is relatively lacking. This study aims to identify the potential risk factors of severe RSV infection by analysis of clinical data and RSV genotypes in Malaysia.

Methods: The medical records of 138 RSV cases were analysed for demographic and clinical data, including age, gender, ethnicity, prematurity, co-morbidity, and source of infection. Severe RSV infection was defined in patients who died, or required ventilation, intensive care, or inotropes. The hypervariable region of the G gene was sequenced for 91 RSV samples from 1989-2009, for genotype identification and phylogenetic analysis. Demographic factors, clinical factors and genotype were entered into logistic regression analysis as predictors of severe RSV disease. A p-value of <0.05 was considered significant.

Results: The mean age of the study population was 1.4 years, with a majority (62.3%) aged <1 year. Multivariate analysis showed three independent predictors of severe RSV: male gender (odds ratio 4.25; 95% confidence intervals 1.14–15.85), underlying co-morbidity or prematurity (OR 7.11; CI 2.11–23.94), and nosocomial infection (OR 4.71; CI 1.27–17.41). Genotype was not associated with severity. Of the 91 RSV samples sequenced, 66 (72.5%) were in subgroup A and 25 (27.5%) were in subgroup B. The most commonly detected genotypes were GA2 (52.8%, n=48), GB13 (20.9%, n=19), and GA5 (13.2%, n=12). Nucleotide and amino acid similarity between subgroups were 49.9% and 27.0%. RSV A was detected every year, but RSV B only circulated for 2-3 years before being undetected for 1-2 years.

Conclusion: Male gender, underlying co-morbidity or prematurity, and nosocomial infection increases the risk of developing severe RSV infection. RSV A was seen every year, while RSV B circulated in 4-5 year cycles.

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Unsolved epidemiological questions on dengue/dengue hemorrhagic fever– From Taiwan's experiences to global control

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Background: The numbers of dengue hemorrhagic fever (DHF) have been increasing globally in recent three decades. The mechanisms that can explain these epidemiological changes have remained enigma. Through epidemiological field observations, two past major hypotheses for DHF are: (1) primary infection due to viral virulence proposed by Dr. L Rosen and (2) secondary infection of heterologous serotypes of dengue viruses (DENV) with antibody-dependent enhancement (ADE) advocated by Dr. S Halstead. However, not all secondary infection of DENV resulted in DHF cases whereas primary infection of DENV has frequently identified in Taiwan and other areas without dengue endemicity. Most interestingly, these two hypotheses have not yet fully explained the mechanisms in increasing epidemic severity caused by DENV with high sequence identities over time in the same epidemics (Taiwan's 1998, 2001-2002, 2006 and 2009-2010 epidemics of dengue/DHF) or over years during cross-country spread.

Methods: Viral load, DENV quasispecies and cytokines/chemokines were measured from DF and DHF patients.

Results: We found that Taiwan's DHF cases in later period of epidemics of dengue/DHF in 1998, 2002 and 2006 showed more severe DHF cases. Additionally, DENV obtained from later cases of the same family member showed more virus diversity based on quasispecies analysis and thus leading to higher viral load in DHF than DF patients. Recently, our research team identified key epidemiologic conditions for increasing DHF cases, including longer duration per epidemic wave and higher transmission intensity of dengue cases in areas regardless high or low population density that would be very helpful in global control to minimize numbers of DHF cases. At present, we are investigating viral factors, immuno-attributes and entomologic transmission features with clear epidemiological characteristics and clinical findings in Kaohsiung's DENV-2 epidemic in Taiwan that might explain the increasing clinical and epidemiological severity of DHF over time periods not only in Taiwan but also in Cuba in 1981, 1997 and other South American countries. The preliminary results showed that both innate immunity and adaptive immunity contribute to immune-pathogenesis of DHF cases.

Conclusion: In conclusion, evolution of dengue viruses might happen through epidemics with more influence of immunity at both individual and population levels.

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Frequent in-migration and highly focal transmission of dengue viruses among children in Kamphaeng Phet, Thailand

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Background: Dengue is the leading cause of mosquito-borne viral disease in the world, and dengue fever (DF) and dengue hemorrhagic fever (DHF) continue to increase and geographic range.