

Diseases Control and Prevention. The annual number of cases and the annual incidence were mapped by matching them to corresponding province- and county-level administrative units in a geographic information system. The distribution of falciparum malaria by age, gender and origin of infection was analysed. Time-series analysis was conducted to investigate the relationship between the falciparum malaria in the endemic provinces and the imported falciparum malaria in non-endemic provinces.

Results: Falciparum malaria was endemic in two provinces of China during 2004-05. Imported malaria was reported in 26 non-endemic provinces. Annual incidence of falciparum malaria was mapped at county level in the two endemic provinces of China: Yunnan and Hainan. The sex ratio (male vs. female) for the number of cases in Yunnan was 1.6 in the children of 0-15 years and it reached 5.7 in the adults over 15 years of age. The number of malaria cases in Yunnan was positively correlated with the imported malaria of concurrent months in the non-endemic provinces.

Conclusion: The endemic area of falciparum malaria in China has remained restricted to two provinces, Yunnan and Hainan. Stable transmission occurs in the bordering region of Yunnan and the hilly-forested south of Hainan. The age and gender distribution in the endemic area is characterized by the predominance of adult men cases. Imported falciparum malaria in the non-endemic area of China, affected mainly by the malaria transmission in Yunnan, has increased both spatially and temporally. Specific intervention measures targeted at the mobile population groups are warranted.

CS6-03 Malaria Programmed Cell Death: Pathways and Perspectives

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Aims: Several recent discoveries of the hallmark features of programmed cell death (PCD) in *Plasmodium falciparum* have presented the possibility of revealing novel targets for anti-malarial therapy. In this study, we aim to identify drug-induced PCD pathways and molecular mediators in *P. falciparum*.

Methods & Results: Using a combination of cell-based assays, flow cytometry and fluorescence microscopy, we detected features including mitochondrial dysregulation, activation of caspase-like proteases and *in situ* DNA fragmentation in parasites induced with the antimalarial chloroquine (CQ) and apoptosis inducer staurosporine (ST). The use of the pan-caspase inhibitor, z-Val-Ala-Asp-fmk (zVAD), and the mitochondria outer membrane permeabilization (MOMP) inhibitor, 4-hydroxy-tamoxifen, enabled the characterization of a novel chloroquine-induced pathway linking caspase-like protease activation to downstream mitochondrial dysregulation, amplified protease activity and DNA fragmentation. The PCD features were observed only at high (μ M) concentrations of CQ. The use of a new synthetic fluorophore-labeled chloroquine (FP-CQ) showed that these features may be due to concentration-dependent differences in drug localization. By further using cysteine protease inhibitors z-Asp-Glu-Val-Asp-fmk (zDEVd), z-Phe-Ala-fmk (zFA), z-Phe-Phe-fmk (zFF), z-Leu-Leu-Leu-fmk (zLLL), E64d and CA-074, we were able to implicate clan CA cysteine proteases in CQ-mediated PCD.

Conclusions: PCD pathways exist in *P. falciparum* and are broadly similar to classical apoptosis pathways of mammalian cells, but with some distinct differences. Malaria PCD pathways are mediated by cysteine proteases belonging to clan CA instead of clan CD, suggesting that PCD pathways converged in evolution and that novel parasite-specific PCD mediators may be exploited in antimalarial strategies.

Acknowledgements: This work was generously funded by a grant from the Life Science Institute, National University of Singapore.

CS6-04 Identification of a 16 kDa Specific Protein from Cyst Fluid of Cysticercus and its N-Terminal Amino Acid Sequencing

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In order to search a molecular biomarker with low molecular weight for the diagnosis of cysticercosis, cysticercuses from the muscle of a naturally infected pig were isolated and collected. Rough antigen was prepared from the cyst fluid of the cysticercus and used to immunize rabbits. General protein of the cyst fluid was analyzed by SDS-PAGE. Specific protein was identified with Western Blot method by antiserum obtained from the immunized rabbits. N-terminal amino acids of the identified protein were detected and sequenced with Edman degradation. The results demonstrated that a 16kDa protein with high specificity was identified from the cyst fluid of cysticercus and 10 amino acids were detected in its N-terminal and sequenced as DLKSGEWQLV. It is shown that the 16kDa protein has 80% identity to myoglobin. It will be useful in the further study on the immunodiagnosis of cysticercosis.

Concurrent Session 7 – Management of Hepatitis C Patients

CS7-01 Management of Hepatitis C Patients and Prevention of HCC

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Natural course of HCV infection: Previous studies including ours indicate the progression of fibrosis is steady but slow, and was estimated from 0.5 stages per year (normal-ALT) to 1.3. The efforts to establish non-invasive measures including Fibroscan helped us to relate the importance of liver fibrosis or rather “stiffness” of the liver to the development of HCC in a prospective fashion. To the end, the slow down of fibrosis progression or even reversal could obviously anticipated to reduce the incidence of HCC.

Chronic hepatitis: In 1994, we set up a national surveillance program for HCC development among chronic hepatitis C patients and enrolled about 2,900 biopsy-proven cases. 2,400 of them received interferon treatment, showing a sustained virologic response rate of 33% on average. The risk of HCC was reduced by half among the interferon-treated patients as a whole, and down to one-fifth among sustained virologic responders. Even among the cirrhotic, the incidence of HCC was decreased by long term follow-up. We also confirmed histologically the resolution of cirrhosis following sustained virologic response and the calculated rate of fibrosis regression rate was 0.28 fibrosis stage per year. It was also shown that, not only the reduction of HCC incidence, but also overall mortality including non-liver related death, was decreased.

Anti-viral for HCC: It could be assumed that the anti-viral could be only for prevention. However, our data clearly indicated that the eradication of HCV in patients who already developed HCC were also beneficial to prolong the patients' life. Now, we are able to expect 80% 5-year survival rate in the combination of RFA and the eradication of HCV.