热带病学术热点追踪报告

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一、国际热带病热点研究

1. 疟疾相关

（1）*Association of Antibody Responses to the Conserved Plasmodium falciparum Merozoite Surface Protein 5 with Protection against Clinical Malaria.*

Ndiop and Dielmo are two Senegalese villages participating in an on-going long-term observational study of natural immunity to malaria. Blood samples were taken before the transmission season (Ndiop) or before peak transmission (Dielmo) and active clinical surveillance was carried out during the ensuing 5.5-month follow-up. IgG responses to recombinant PfMSP5, PfMSP1p19 and R23 were quantified by ELISA in samples from surveys carried out in Dielmo (186 subjects) and Ndiop (221 subjects) in 2002, and Ndiop in 2000 (204 subjects). The results indicate that MSP5 is recognized by naturally acquired Ab. The large seroprevalence and association with protection against clinical malaria in two settings with differing transmission conditions and stability over time demonstrated in Ndiop argue for further evaluation of baculovirus PfMSP5 as a vaccine candidate[1].

（2）*Maladjusted Host Immune Responses Induce Experimental Cerebral Malaria-Like Pathology in a Murine Borrelia and Plasmodium Co-Infection Model.*

In this study, we investigated the immune responses in BALB/c mice, co-infected with Plasmodium berghei NK65 parasites and the relapsing fever bacterium Borrelia duttonii. In contrast to single infections, we identified in the co-infected mice a reduction of L-Arginine levels in the serum. It indicated diminished bioavailability of NO, which argued for a dysfunctional endothelium. Consistent with this, we observed increased sequestration of CD8+ cells in the brain as well over expression of ICAM-1 and VCAM by brain endothelial cells. Co-infected mice further showed an increased inflammatory response through IL-1β and TNF-α, as well as inability to down regulate the same through IL-10. In addition we found loss of synchronicity of pro- and anti-inflammatory signals seen in dendritic cells and macrophages, as well as increased numbers of regulatory T-cells. Our study shows that a situation mimicking

experimental cerebral malaria (ECM) is induced in co-infected mice due to loss of timing and control over regulatory mechanisms in antigen presenting cells [2].

（**3**）***Malaria in Hadhramout, a southeast province of Yemen: prevalence, risk factors, knowledge, attitude and practices (KAPs).***

Blood specimens were collected from 735 individuals aged 1-66 years. Plasmodium species were detected and identified by microscopic examination of Giemsa-stained thick and thin blood smears. A household-based questionnaire was used to collect demographic, socioeconomic and environmental data. The conclusion is that several environmental, socioeconomic and behavioral issues were discovered to be the contributing factors to the high prevalence of malaria in southeast Yemen. Novel strategies adapted to the local situations need to be established in order to improve the effectiveness of malaria control [3].

（**4**）***Modelling recurrent events: comparison of statistical models with continuous and discontinuous risk intervals on recurrent malaria episodes data.***

This work aimed to compare four different approaches by analysing recurrent malaria episodes from a clinical trial assessing the effectiveness of three malaria treatments, with continuous and discontinuous risk intervals: Andersen-Gill counting process (AG-CP), Prentice-Williams-Peterson counting process (PWP-CP), a shared gamma frailty model, and Generalized Estimating Equations model (GEE) using Poisson distribution. Simulations were also made to analyse the impact of the addition of a confounding factor on malaria recurrent episodes. The conclusion is that repeated event in infectious diseases such as malaria can be analysed with appropriate existing models that account for the correlation between multiple events within subjects with common statistical software packages, after properly setting up the data structures [4].

（5）*Introducing rapid diagnostic tests for malaria into drug shops in Uganda: design and implementation of a cluster randomized trial.*

Three preparatory studies were conducted to explore perceptions on diagnosis and treatment of malaria at drug shops, and affordable prices for mRDTs and ACTs in order to inform the design of the intervention and implementation modalities. Critical components of intervention were: community sensitization and creating awareness, training of drug shop vendors to diagnose malaria with mRDTs, treat and refer customers to formal health facilities, giving pre-referral rectal artesunate and improved record-keeping. The primary outcome was the proportion of patients receiving appropriately-targeted treatment with ACT, evaluated against microscopy on a research blood slide. The main challenges in designing this trial were maintaining a balance between a robust intervention to support effective behaviour change and introducing practices that would be sustainable in a real-life situation in tropical Africa; as well as achieving a detailed evaluation without inadvertently influencing prescribing behaviour [5].

2. 血吸虫相关

（1）*Efficient linkage mapping using exome capture and extreme QTL inschistosome parasites.*

Identification of parasite genes that underlie traits such as drug resistance and host specificity is challenging using classical linkage mapping approaches. Extreme QTL (X-QTL) methods, originally developed by rodent malaria and yeast researchers, promise to increase the power and simplify logistics of linkage mapping in experimental crosses of schistosomes (or other helminth parasites), because many 1000s of progeny can be analysed, phenotyping is not required, and progeny pools rather than individuals are genotyped. We explored the utility of this method for mapping a drug resistance gene in the human parasitic fluke Schistosoma mansoni. The results (a) demonstrate the utility of exome capture for generating reduced representation libraries in Schistosoma mansoni, and (b) provide proof-of-principle that X-QTL methods can be successfully applied to an important human helminth. The combination of these methods will simplify linkage analysis of biomedically or biologically important traits in this parasite [6].

（2）*Ly6Chigh monocytes become alternatively activated macrophages in schistosome granulomas with help from CD4+ cells.*

We characterized monocyte and macrophage dynamics in the livers of infected CX3CR1GFP/+ mice. CX3CR1-GFP+ monocytes and macrophages accumulated around eggs and in granulomas during infection and upregulated PD-L2 expression, indicating differentiation into AAM. Intravital imaging of CX3CR1-GFP+ Ly6Clow monocytes revealed alterations in patrolling behavior including arrest around eggs that were not encased in granulomas. Differential labeling of CX3CR1-GFP+ cells in the blood and the tissue showed CD4+ T cell dependent accumulation of PD-L2+ CX3CR1-GFP+ AAM in the tissues as granulomas form. By adoptive transfer of Ly6Chigh and Ly6Clow monocytes into infected mice, we found that AAM originate primarily from transferred Ly6Chigh monocytes, but that these cells may transition through a Ly6Clow state and adopt patrolling behavior in the vasculature. Thus, during chronic helminth infection AAM can arise from recruited Ly6Chigh monocytes via help from CD4+ T cells[7].

3. 其他寄生虫相关

（1）*Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan.*

Dengue virus infection (DVI) is very common infection. There is scarcity of data on factor associated with increased hospital stay and mortality in dengue virus infection (DVI). This study was done to know about factors associated with increased hospital stay and mortality in patients admitted with DVI. Conclusions: Increasing age, coagulopathy and acute kidney injury in patients with DVI is associated with increased hospital stay. Morality was more in patients with AKI, DHF and DSS, respiratory failure, coagulopathy and these patients had more prolonged hospitalization[8].

（2）*Discovery and design of cyclic peptides as dengue virus inhibitors through structure-based molecular docking.*

To find potential peptide inhibitors against the NS2B/NS3 protease of DENV which in turn, can inhibit the viral replication inside host cell. Cyclic peptides were designed having combination of positively charged amino acids using ChemSketch software and were converted to 3D structures. DENV NS3 protein structure was retrieved from Protein Data Bank (PDB) using PDB Id: 2FOM. DENV NS3 and cylic peptides were docked using MOE software after structural optimization. The conclusion is that it can be concluded from the study that these peptides could serve as important inhibitors to inhibit the viral replication and need further in-vitro investigations to confirm their efficacy[9].

（3）*Tissue tropism and parasite burden of Toxoplasma gondii RH strain in experimentally infected mice.*

To evaluate parasite distribution and tissue tropism of Toxoplasma gondii tachyzoites in experimentally infected mice using real time QPCR. In this survey 16 Balb/c mice were inoculated with 1×10(4) alive tachyzoites of Toxoplasma gondii RH strain. After 1, 2, 3 days post infection and the last day (before death), different tissues of mice including blood, brain, eye, liver, spleen, kidney, heart and muscle were harvested. Following tissues DNA extraction, the parasite burden was quantified using real time QPCR targeting the B1 gene (451 bp). The data provide significant baseline information about Toxoplasma pathogenesis, vaccine monitoring and drug efficiency[10].

（4）*Ebola Outbreak Response; Experience and Development of Screening Tools for Viral Haemorrhagic Fever (VHF) in a HIV Center of Excellence Near to VHF Epicentres.*

There have been 3 outbreaks of viral hemorrhagic fever (VHF) in Uganda in the last 2 years. VHF often starts with non-specific symptoms prior to the onset of haemorrhagic signs. We designed tools to help with communication to staff, infection control and screening of HIV patients with non-specific symptoms in a large HIV clinic during the outbreaks in Uganda. We describe our experiences in using these tools in 2 Ebola Virus Disease outbreaks in Uganda. Use of simple screening tools can be helpful in managing large numbers of symptomatic patients attending for routine and non-routine medical care (including HIV care)

within a country experiencing a VHF outbreak, and can raise medical staff awareness of VHF outside of the epidemics[11].

二、国内热带病热点研究

1. 疟疾相关

（1）2000—2012年贵州省榕江县疟疾流行病学特征

通过分析榕江县 2000—2012 年疟疾流行病学特征，为该县消除疟疾行动计划提供依据。方法为收集该县 2000—2012 年疟疾防治资料，包括疟疾疫情报告、各乡镇卫生院疟疾诊断和治疗等资料，采用 Excel 软件进行统计和分析。结论为该县近几年疟疾防治效果明显，但仍需加强当地居民及流动人口的疟疾病例监测[12]。

（2）陕西省消除疟疾全球基金项目实施效果评价

评价陕西省消除疟疾全球基金项目的实施效果，为科学实施消除疟疾行动计划及考核评估工作提供参考依据。方法为收集整理 2010-2012 年陕西省 27 个全球基金疟疾项目县疟疾防治工作资料并进行统计学分析，评价陕西省消除疟疾全球基金项目的实施效果。结论是全球基金疟疾项目的实施加速了陕西省消除疟疾工作的进程，项目实施地区的疟疾防治工作能力得到显著提升[13]。

2. 血吸虫相关

（1）589 例血吸虫病患者病变部位分析

探讨血吸虫病流行地区血吸虫病患者病变部位分布的特点。方法为选择 2009～2013 年到该院就诊的血吸虫病患者，对其进行病理检查，并收集临床资料。结果为阑尾为最常见病变部位，共 287 例，其次为结、直肠 235 例，肝脏 33 例。此外尚有 34 例病变分布于其他较少见的部位，其中归属门静脉系统的胆囊 19 例，胃 9 例，十二指肠 2 例，小肠 1 例，门静脉系统外的异位损害 3 例。阑

尾炎和结、直肠癌是最常见的疾病类型。结论是血吸虫病患者病变部位的分布特点能在一定程度上反映临床病理过程，有助于对血吸虫病的治疗[14]。

（2）血吸虫核受体的研究进展

核受体在后生动物中作为一类重要的转录调控因子，在一系列重要的生化过程中发挥重要的作用，包括细胞分化和增殖。核受体包含共有的蛋白结构，包含一个 N 端-A/B 区，一个高度保守的 DBD，一个铰链区(D 区)和一个 C-端 LBD区。到目前为止，寄生扁形动物中的核受体，只在曼氏血吸虫和日本血吸虫中有报道。本文对近年来血吸虫的核受体的研究成果做简要综述，为今后更进一步的研究提供参考[15]。

3.其他寄生虫相关

（1）咸阳市学龄前儿童蛲虫感染综合防治效果观察

对咸阳市 8 所幼儿园 886 名儿童进行蛲虫感染情况调查。选择城区、农村各 2 所幼儿园（干预点）学龄前儿童 480 名为综合防治措施实施对象，另选 4 所幼儿园（对照点）学龄前儿童 406 名为对照。对干预点实施的综合防治措施，主要包括药物治疗、健康教育，同时改善基础设施、环境卫生；对照点除对阳性儿童给予药物治疗外，不进行任何干预。结论为实施综合防治措施对控制蛲虫感染效果显著[16]。

（2）西双版纳州登革热暴发现场 BGS-trap 媒介蚊虫监测研究

评价 BG-Sentinel mosquito trap (BGS-trap)对登革热媒介成蚊的监测效果，为我国登革热暴发现场伊蚊成蚊监测、风险评估及预测预警提供基础数据。在西双版纳州所辖景洪市、勐腊及勐海县，利用 BGS-Trap 进行伊蚊成蚊监测，捕获蚊种进行形态学鉴定。利用描述流行病学方法对日捕获所有蚊虫进行分析。结论为 BGS-trap 在此次云南省西双版纳州登革热暴发现场伊蚊成蚊监测中效果不理想，需在现场和实验室对该装置进行进一步媒介伊蚊成蚊监测效果评价工作[17]。

（3）广西壮族自治区肝吸虫病的高发流行特点及其超声诊断价值探讨

　　探讨广西壮族自治区肝吸虫病的高发流行特点及其超声诊断价值。选择 2010 年 1 月～2013 年 1 月携带疑似肝吸虫感染的 B 超单来广西壮族自治区疾病预防控制中心门诊就诊的患者共 455 人作为调查对象，根据他们来自的家乡分为有食生鱼片风俗习惯的地区(横县、武鸣和南宁吴圩镇，A 组)，无生鱼片风俗习惯的地区(宾阳、贵港、桂平，B 组)。记录调查对象的基本情况，确定当地与肝吸虫病感染有关的危险因素。结论为年龄大、缺乏相关医学背景、文化程度低都将增加感染的风险。超声检测可及时发现门脉及肝动脉血流情况的异常，对早期诊断肝吸虫病并发肝硬化有积极意义[18]。

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（如需参考文献中论文全文，请发送论文标题至 yaoyaoyu1987@163.com）

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