

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) *Structural changes of the follicular cells during developmental stages of the malaria vector mosquitoes Anopheles pharoensis (Diptera: Culicidae) in Egypt.*

The structure modulation of follicular cells and the ovarian changes during fourth larval instar and pupal stage of the malaria vector mosquitoes Anopheles pharoensis Theobald were investigated using the light and electron microscopy.^[1]

(2) *Tracking the mutual shaping of the technical and social dimensions of solar-powered mosquito trapping systems (SMoTS) for malaria control on Rusinga Island, western Kenya.*

This project employed a bottom-up approach that engaged end users from the outset. Bottom-up approaches have the potential to bolster novel interventions and move them towards adaptive and evidence-based strategies. We documented the interlocking of the multiple processes and activities that took place through process observation and document reviews. We analysed the data within the conceptual framework of system innovation by identifying mutual shaping between technical and social factors. Looking at malaria intervention projects employing novel technologies as niches that may evolve towards system innovation, helps to reveal interrelations between the various technical and social aspects. Revealing these interrelations requires a different role for research and different perspective on innovation where innovation is more than the technical aspects. This approach therefore requires that research is designed in a way that enables obtaining feedback from both aspects.^[2]

(3) *P.vivax Malaria and Dengue Fever Co-infection: A Cross-Sectional Study in the Brazilian Amazon.*



Malaria and dengue are the most prevalent vector-borne diseases worldwide and represent major public health problems. A cross-sectional study was conducted (2009 to 2011) in hospitalized patients with acute febrile syndrome in the Brazilian Amazon. All patients were submitted to thick blood smear and PCR for Plasmodium sp. detection, ELISA, PCR and NS1 tests for dengue, viral hepatitis, HIV and leptospirosis. In endemic areas for dengue and malaria, jaundice (in dengue patients) and spontaneous bleeding (in malaria patients) should raise the suspicion of co-infection. Besides, whenever co-infection is confirmed, we recommend careful monitoring for bleeding and hepatic complications, which may result in a higher chance of severity, despite of the fact that no increased fatality rate was seen in this group.^[3]

(4) Spatio-temporal distribution of malaria and its association with climatic factors and vector-control interventions in two high-risk districts of Nepal.

Over the last decade, the incidence of confirmed malaria has declined significantly in Nepal. The aim of this paper is to assess the spatio-temporal distribution of malaria and its association with climatic factors and vector control interventions in two high-risk districts of Nepal. Hotspot analysis was used to visualize the spatio-temporal variation of malaria incidence over the years at village level and generalized additive mixed models were fitted to assess the association of malaria incidence with climatic variables and vector control interventions. The study findings suggest that LLIN coverage should be scaled up to entire districts rather than high-incidence foci only. Climatic factors should be considered for malaria micro-stratification, mosquito repellents should be prescribed for those living in forests, forest fringe and foothills and have regular visits to forests, and imported cases should be controlled by establishing fever check posts at border crossings.^[4]

(5) Epidemiology of malaria in a village in the Rufiji River Delta, Tanzania: declining transmission over 25 years revealed by different parasitological metrics.

Assessments of the epidemiology of malaria over time are needed to understand changes in transmission and guide control and elimination strategies. A longitudinal population study



was established in 1985 in Nyamisati village in the Rufiji River Delta, Tanzania. A physician and research team lived in the village 1984-2000. Parasite prevalence by microscopy and two PCR methods, spleen rates and haemoglobin levels were measured in repeated cross-sectional surveys between 1985 and 2010. Passive surveillance of malaria cases was maintained until end 1999. Bed nets were distributed after the surveys 1993, 1999 and 2010. A marked decline in malaria transmission was observed over 25 years. The decrease was detected after the arrival of the research team and continued gradually both before and after distribution of bed nets. Spleen rates and microscopy identified early changes when transmission was still intense, whereas real-time PCR was a more sensitive metric when transmission was reduced. The study provides historical data on malaria within a closely monitored rural village and contributes to the understanding of changing epidemiology in sub-Saharan Africa.^[5]

2. 血吸虫病相关

(1) The WHO ultrasonography protocol for assessing hepatic morbidity due to *Schistosoma mansoni*. Acceptance and evolution over 12 years.

The aim of this study is to review the worldwide acceptance of the World Health Organization (WHO) ultrasound protocol for assessing hepatosplenic morbidity due to *Schistosoma mansoni* since its publication in 2000. A PubMed literature research using the keywords "schistosomiasis and ultrasound," "schistosomiasis and ultrasonography," and "S. mansoni and ultrasound" from 2001 to 2012 was performed. Results obtained using the pictorial image pattern approach of the protocol are reported in 38/41 studies, whereas measurements of portal branch walls were applied in 19/41 and results reported in 2/41 studies only. The ability of this protocol to predict complications in severe cases should be further evaluated in a higher number of patients.^[6]

(2) Effect of water temperature and population density on the population dynamics of *Schistosoma mansoni* intermediate host snails.



Mathematical models can be used to identify areas at risk of increased or new schistosomiasis transmission as a result of climate change. Laboratory experiments were conducted to estimate *Biomphalaria sudanica* mortality, fecundity and growth rates at ten different constant water temperatures, ranging from 13-32°C. Snail cages were used to determine the effects of snail densities on *B. sudanica* and *B. stanleyi* mortality and fecundity rates in semi-natural conditions in Lake Albert. **Conclusions:** snail populations may experience large fluctuations in numbers, even in the absence of any external factors such as seasonal temperature changes. Survival also decreased with increasing density for *B. stanleyi*, in contrast to *B. sudanica* and other studied *Biomphalaria* species where only fecundity has been shown to decrease.^[7]

(3) Field-derived *Schistosoma mansoni* and *Biomphalaria pfeifferi* in Kenya: a compatible association characterized by lack of strong local adaptation, and presence of some snails able to persistently produce cercariae for over a year.

We investigated compatibility of two isolates of *S. mansoni* from school children from Asao and Mwea with *B. pfeifferi* collected directly from Asao stream or the Mwea rice fields. We exposed snails from both regions to four different doses of miracidia (1, 5, 10 and 25) from sympatric or allopatric *S. mansoni*, and maintained them in a shaded, screened out-of-doors rearing facility in Kisian, in western Kenya. Both snail survival and the number of snails that became infected were monitored weekly. This was done for 25 weeks post-exposure (PE). Those infected snails which survived beyond this period were monitored until they all died. There were no significant local adaptation effects for either schistosomes or snails. Long-term shedders could provide an ongoing source of cercariae to initiate human infections for many months, suggesting care is required in considering how human MDA treatments are timed. Future control programs should incorporate means to eliminate infected snails to complement chemotherapy interventions in controlling schistosomiasis.^[8]

(4) A *Fasciola hepatica*-derived fatty acid binding protein induces protection against schistosomiasis caused by *Schistosoma bovis* using the adjuvant adaptation (ADAD) vaccination system.



Several efforts have been made to identify anti-schistosomiasis vaccine candidates and new vaccination systems. The fatty acid binding protein (FAPB) has been shown to induce a high level of protection in trematode infection. The adjuvant adaptation (ADAD) vaccination system was used in this study, including recombinant FAPB, a natural immunomodulator and saponins. Mice immunised with the ADAD system were able to up-regulate proinflammatory cytokines (IL-1 and IL-6) and induce high IgG2a levels. Moreover, there was a significant reduction in worm burden, egg liver and hepatic lesion in vaccinated mice in two independent experiments involving *Schistosoma bovis* infected mice. The foregoing data shows that ADAD system using FAPB provide a good alternative for triggering an effective immune response against animal schistosomiasis.^[9]

3. 其他寄生虫病相关

(1) Approaches to refining estimates of global burden and economics of dengue.

This systematic review aims to identify and examine estimates of dengue disease burden and costs, discuss major sources of uncertainty, and suggest next steps to improve estimates. Economic analysis of dengue is mainly concerned with costs of illness, particularly in estimating total episodes of symptomatic dengue. However, national dengue disease reporting systems show a great diversity in design and implementation, hindering accurate global estimates of dengue episodes and country comparisons. A combination of immediate, short-, and long-term strategies could substantially improve estimates of disease and, consequently, of economic burden of dengue. Short-term recommendations include merging multiple data sources, such as cohort and surveillance data to evaluate the accuracy of reporting rates (by health sector, treatment, severity, etc.), and using covariates to extrapolate dengue incidence to locations with no or limited reporting. Long-term efforts aim at strengthening capacity to document dengue transmission using serological methods to systematically analyze and relate to epidemiologic data.^[10]



(2) Identification of host proteins interacting with the integrin-like A domain of *Toxoplasma gondii* micronemal protein MIC2 by yeast-two-hybrid screening.

*In this study, we used a yeast-two-hybrid system to search for host proteins that interact with MIC2. Different adhesive domains of MIC2 were cloned into the pGBKT7 vector and expressed in fusion with the GAL4 DNA-binding domain as baits. Expression of bait proteins in yeast cells was analyzed by immuno-blotting and their autoactivation was tested via comparison with the pGBKT7 empty vector, which expressed the GAL4 DNA binding-domain only. To identify host proteins interacting with MIC2, a mouse cDNA library cloned into a GAL4 activation-domain expressing vector was screened by yeast-two-hybrid using the integrin-like A domain of MIC2 as bait. After initial screening and exclusion of false positive hits, positive preys were sequenced and analyzed using BLAST analysis and Gene Ontology Classifications. This study is the first one to report interactions between *Toxoplasma gondii* MIC2 and two host proteins, LAMTOR1 and RNaseH2B. The data will help us to gain a better understanding of the function of MIC2 and suggest that MIC2 may play roles in modulating host signal transduction and other biological processes in addition to binding host cells.*^[11]

(3) Draft Genome Sequences of Amoeba-Resistant *Aeromonas* spp. Isolated from Aquatic Environments.

*Amoeba-resistant *Aeromonas veronii* ARB3 and *Aeromonas media* ARB13 and ARB20, which may be important intracellular pathogens of eukaryotic hosts, were isolated from pond and river waters. The draft genome sequences indicate that the strains harbor multiple protein secretion systems and toxins that induce disruption of the actin cytoskeleton.*^[12]

(4) CD8+ T cells Are Preferentially Activated during Primary Low Dose *Leishmania major* Infection but Are Completely Dispensable during Secondary Anti-*Leishmania* Immunity

*Here we compared primary and secondary immunity to low and high dose *L. major* infections and assessed the influence of infectious dose on the quality and magnitude of*



secondary anti-Leishmania immunity. In addition, we investigated the contribution of CD8+ T cells in secondary anti-Leishmania immunity following recovery from low and high dose infections. We found that the early immune response to low and high dose infections were strikingly different: while low dose infection preferentially induced proliferation and effector cytokine production by CD8+ T cells, high dose infection predominantly induced proliferation and cytokine production by CD4+ T cells. This differential activation of CD4+ and CD8+ T cells by high and low dose infections respectively, was imprinted during in vitro and in vivo recall responses in healed mice. Collectively, our results show that although CD8+ T cells are preferentially activated and may contribute to optimal primary anti-Leishmania immunity following low dose infection, they are completely dispensable during secondary immunity.^[13]

二、国内热带病热点研究

1. 疟疾相关

(1) 恶性疟原虫信号肽酶-绿色荧光蛋白突变株的建立及其在疟原虫体内的表达分析

构建恶性疟原虫信号肽酶基因转染载体,筛选可在体内表达疟原虫信号肽酶-绿色荧光蛋白(PfSPP-GFP)的疟原虫。方法是提取 Trager-Jensen 法培养的恶性疟原虫 3D7 株基因组 DNA, PCR 扩增 PfSPP C 端不含终止密码子的 883 bp 基因片段,克隆构建重组转染载体 pSPPcGT。重组载体经 PCR 和双酶切鉴定后送测序。电转化法将重组载体转染入恶性疟原虫体内,采用 5 nmol/L 恶性疟原虫二氢叶酸还原酶抑制剂 WR99210 筛选转染后,恶性疟原虫经无水乙醇固定、4',6-二脒基-2-苯基吲哚(DAPI)染色后,荧光显微镜下观察 PfSPP-GFP 在其体内的表达分布情况。提取筛选后恶性疟原虫全蛋白,Western blotting 分析虫体内



PfSPP-GFP 蛋白的表达情况。结论：构建了恶性疟原虫 PfSPP-GFP 重组转染载体,筛选获得了能在疟原虫体内表达 PfSPP-GFP 的突变株。^[14]

(2) 2009--2013 年上海金山区疟疾疫情监测及流行特征分析

分析上海市金山区2009--2013年疟疾疫情流行特征,为科学防治疟疾和消除疟疾目标提供依据。方法为通过中国疾病预防控制中心网络直报系统收集金山区2009--2013年疟疾监测数据、流行病学调查资料数据,运用Microsoft Excel 2003软件进行统计学分析。结论:2009—2013年,金山区未发现本地感染疟疾病例,全部为输入性疟疾,应重点加强对输入性疟疾的监测和防控。^[15]

(3) 成都市中华按蚊在疟疾传播中的阈值

研究成都市中华按蚊传播疟疾的阈值和潜势,为当地疟疾监测、预警与防治提供科学评价指标。方法是选取蚊密度较高的4个村为调查点,其中坝区2个、浅丘1个、深丘1个。于2011-07/09现场调查媒介按蚊的叮人率、经产蚊比例、人血指数,收集观察期间的平均气温数据。根据基本繁殖率概念计算以媒介按蚊临界叮人率为指标的传播疟疾阈值。结论:成都市按蚊的实际叮人率低于其传播疟疾的临界叮人率,由中华按蚊引起的疟疾传播已被阻断。^[16]

(4) 基于序贯分析模型的疟疾计量诊断方法

建立序贯分析诊断模型的疟疾计量判断方法。方法是设立疟疾病例和非疟疾病例的假设检验,选择对疟疾诊断价值大的征候作为鉴别依据,拟定序贯试验类型,确定误诊概率和诊断阈值,根据疟疾病例和非疟疾病例各征候表现的条件概率比建立序贯分析模型诊断指数,通过序贯分析逐一判断和分析,达到诊断阈值,



得出结论。结论：序贯分析诊断模型具有一定的判别价值，而且方便、快捷。^[17]

2. 血吸虫病相关

(1) 三峡建坝后四川省血吸虫病流行变化及其对三峡库区的影响

分析三峡建坝后库区上游的四川省血吸虫病流行区的疫情变化及其对三峡库区血吸虫病的传播影响。方法为收集分析2000-2012年四川省血吸虫病疫情年报、2001-2012年血吸虫病监测点资料、2001年四川省血吸虫病流行病学抽样调查数据及三峡相关课题研究数据等文献资料，调查人群、家畜和钉螺的情况。选择距离库区最近的简阳市五指乡前进村开展钉螺现场调查。结论：三峡建坝后，四川省血吸虫病流行区范围和有螺面积已明显缩小，上游流行区疫情向库区扩散的可能性极小。^[18]

(2) 日本血吸虫感染对 C57BL/6J 小鼠脂肪肝及胰岛素抵抗的影响

观察血吸虫感染对高脂饮食诱导的脂肪肝小鼠肝组织结构与功能、肿瘤坏死因子- α (TNF- α)、核因子- κ B(NF- κ B)及Ym-1 mRNA 表达的影响，探讨巨噬细胞选择性活化对肥胖鼠肝脏及胰岛素抵抗的影响及可能机制。方法是建立日本血吸虫感染复合高脂饲养C57BL/6J 小鼠模型，测定空腹血糖、血浆胰岛素水平，计算胰岛素抵抗指数；测定肝匀浆液谷丙转氨酶、三酰甘油及胆固醇水平；HE 染色观察肝组织病理改变，RT-PCR 检测肝组织TNF- α 、NF- κ B 及Ym-1 转录水平等。结论：肥胖鼠脂肪肝组织中炎症因子TNF- α 及调控因子NF- κ B 的表达水平与胰岛素抵抗的形成有一定关系，日本血吸虫感染通过诱导肥胖鼠巨噬细胞选择性活化Ym-1 转录水平增高及TNF- α 和NF- κ B 转录水平的降低，改善胰岛素抵



抗，为糖尿病防治研究提供新思路。^[19]

(3) 江苏省血吸虫病疫情监测与风险评估系统的研究 I 疫情监测点布局与应用效果

构建江苏省血吸虫病疫情监测与风险评估系统,为及时掌握血吸虫病传播风险并采取针对性防控措施提供技术支撑。方法为按照血吸虫病流行程度、流行类型、流域水系特点在全省设立血吸虫病疫情监测点,开展人、畜病情和螺情现场调查,并对血检查病进行质量控制,分析、比较不同监测点人畜血吸虫感染率、螺情分布及血检漏检情况。结论:江苏省血吸虫病疫情监测点布局合理,全省血吸虫病疫情呈低度流行态势。^[20]

(4) 日本血吸虫硫氧还蛋白谷胱甘肽还原酶同源建模及功能分析

对日本血吸虫硫氧还蛋白谷胱甘肽还原酶(TGR)进行结构及功能分析。方法是基于结构序列比较利用 Swiss-Pdbviewer 构建了日本血吸虫的 TGR 同源结构模型,并对模型进行结构评估;分析日本血吸虫 TGR 与底物结合时可能的位点,比较这些位点在不同来源 TGR 中的异同。结论:作用于 GDS、NADPH 结合区的其它来源的 TGR 抑制剂可能对日本血吸虫 TGR 也有作用;GSH 结合区是设计寄生虫 TGR 特异性抑制剂的潜在靶点之一;TGR 的 C 末端对电子传递起着重要作用并可能参与底物的结合,因而阻断日本血吸虫 TGR 的 C 末端摆动的抑制剂将可能有效地抑制日本血吸虫 TGR 活性。^[21]



3. 其他寄生虫病相关

(1) 基于 CLINPROT 技术鉴定弓形虫感染的血清分子标志物

旨在通过液体蛋白芯片-MS/MS 技术 (即 CLINPROT 技术) 发现并鉴定弓形虫感染的血清分子标记物, 并分析其应用于临床检测的敏感性和特异性。方法为运用 CLINPROT 技术对弓形虫感染患者的血清样本进行分析, 并进一步采用蛋白电泳、质谱鉴定等方法对筛选的蛋白分子进行鉴定, 最后通过 ELISA 方法对其在健康正常人和弓形虫感染患者的血清样品中的表达情况进行了检测, 并采用 ROC 曲线评价了其临床应用价值。结论: 可将 CLINPROT 技术应用于弓形虫感染血清分子标记物的寻找和鉴定; 可将 SAA 蛋白用作为弓形虫感染的血清分子标志物。^[22]

(2) 2007—2011 年江苏省土源性线虫病省级监测点监测结果分析

目的是了解江苏省土源性线虫感染情况, 为制定防治策略和措施提供依据。方法为采用改良加藤厚涂片法检查土源性线虫卵; 3~12 周岁儿童加做透明胶纸肛拭法检查蛲虫卵; 用土壤蛔虫卵分离培养法检查土壤蛔虫卵污染情况。结论: 江苏省土源性线虫感染率逐年下降, 需调整防治策略和措施, 并继续做好监测工作。^[23]

(3) 利用细胞色素氧化酶亚单位 I 分析青海藏区细粒棘球绦虫系统发育学

本文旨在分析流行于青南地区细粒棘球绦虫系统发育学及基因多态性。本文利用线粒体 DNA 细胞色素氧化酶亚单位 I (COXI) 分子对收集到的流行于青



海省的 59 例包虫病样本进行测序。总计 71 条序列（其中 12 条来自 GenBank）碱基通过 Clustal X 软件比对，构建贝叶斯进化树。结论：流行于青海省细粒棘球绦虫系统发育学比我们想象复杂。^[24]

（4）我国包虫病的诊断和治疗进展

本文就我国包虫病的流行现状，以及诊断和治疗的进展做一综述。我国目前包虫病诊断仍以影像学检查和免疫学检查为主要手段，并逐渐发展分子生物学技术诊断方法。包虫病治疗以手术治疗为首选方式，以药物治疗作为辅助手段。用放射疗法等新方法治疗包虫病的研究也在进行中。我国包虫病防治尚处于起始阶段，偏远贫困的牧区和半农半牧区是防治重点。随着我国对这项工作的重视和资金支持力度的加大，包虫病防治工作一定会见成效。^[25]

【参考文献】

（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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