热带病学术热点追踪报告

2014年第10期(总第15期) 12月1日-12月30日

录 目

| 一、国际热带病热点研究4 | | | | |
|--|--|--|--|--|
| | | | | |
| 1. 疟疾相关4 | | | | |
| (1) Phenotypic effects of concomitant insensitive acetylcholinesterase (ace-1 ^R) | | | | |
| and knockdown resistance (kdr ^R) in Anopheles gambiae: a hindrance for insecticide | | | | |
| · · · · · | | | | |
| resistance management for malaria vector control 4 | | | | |
| (2) Altitudinal population structure and microevolution of the malaria vector | | | | |
| Anopheles cruzii (Diptera: Culicidae) 4 | | | | |
| (3) Field Evaluation of Picaridin Repellents Reveals Differences in Repellent | | | | |
| Sensitivity between Southeast Asian Vectors of Malaria and Arboviruses | | | | |
| (4) How Effective is Integrated Vector Management Against Malaria and | | | | |
| Lymphatic Filariasis Where the Diseases Are Transmitted by the Same Vector? 5 | | | | |
| (5) Comparing Leishman and Giemsa staining for the assessment of peripheral | | | | |
| blood smear preparations in amalaria-endemic region in India 6 | | | | |
| 2. 血吸虫病相关6 | | | | |
| (1) Compatibility of Schistosoma japonicum from the hilly region and | | | | |
| Oncomelania hupensis hupensis from the marshland region within Anhui, China 6 | | | | |
| (2) The molecular characterization and RNAi silencing of SjZFP1 | | | | |
| in Schistosoma japonicum. | | | | |
| (3) Co-infection with Schistosoma mansoni and Human Immunodeficiency | | | | |
| Virus-1 (HIV-1) among residents of fishing villages of north-western Tanzania | | | | |



| | (4) | The anterior esophageal region of Schistosoma japonicum is a secretory |
|----|------------|---|
| (| organ. | 7 |
| 1. | 其他寄 | 生虫病相关8 |
| | (1) | Universal single-probe rt-PCR assay for diagnosis of dengue virus infections. |
| | (2) | Molecular detection and genotypic characterization of Toxoplasma gondii |
| ' | (3) | Genome Sequence of Afipia felis Strain 76713, Isolated in Hospital Water |
| ι | | Amoeba Co-Culture Procedure. |
| | (4) | Leishmania donovani Infection Enhances Lateral Mobility of Macrophage |
| ſ | Membra | ne Protein Which Is Reversed by Liposomal Cholesterol |
| 二、 | 国内名 | 热带病热点研究9 |
| 1. | 疟疾相 | <i>美</i> 9 |
| | (1) | 红细胞和血小板参数对疟疾流行病学特征的相关性分析10 |
| | (2) | 20092013 年河南省疟疾流行病学特征分析10 |
| | (3) | 用 SYBR green I 法和流式细胞术体外评价 3 种青蒿素类药物的抗疟活性 |
| | | 10 |
| 2. | 血吸虫 | 病相关10 |
| | (1) | Th1 和 Th2 型细胞因子对小鼠感染血吸虫的免疫保护性研究11 |
| | (2) | 流动人口血吸虫病防治知识及行为分析11 |
| | (3) | 日本血吸虫重组质粒 pGEX-Sj32 的构建及其在大肠埃希菌 BL21 中的表达 |
| | | 11 |
| 3. | 其他寄 | 生虫病相关12 |
| | (1) | 西双版纳州重点传染病的疫情分析及防控策略探讨12 |



| (2) | 1978~2014 年我国登革热的流行病学分析 | . 12 |
|-----|-------------------------|------|
| (3) | 埃博拉病毒感染的实验室检测方法 | . 13 |
| (4) | 刚地弓形虫速殖子表面抗原的研究及应用 | . 13 |



一、国际热带病热点研究

1. 疟疾相关

(1) Phenotypic effects of concomitant insensitive acetylcholinesterase (ace-1^R) and knockdown resistance (kdr^R) in Anopheles gambiae: a hindrance for insecticide resistance management for malaria vector control.

Malaria is endemic in sub-Saharan Africa with considerable burden for human health. Methods: Larval and adult bioassays were performed with different insecticide classes used in public health following WHO standard guidelines on four laboratory Anopheles gambiae strains, sharing the same genetic background but harboring distinct resistance status: KISUMU with no resistance allele; ACERKIS with ace-1^R allele; KISKDR with kdr^R allele and ACERKDRKIS with both resistance alleles ace-1^R and kdr^R. Conclusion: The presence of both kdr^R and ace-1^R alleles seems to increase the resistance levels to both carbamate and organophosphate insecticides and at operational level, may represent an important threat to malaria vector control programs in West Africa. [1]

(2) Altitudinal population structure and microevolution of the malaria vector Anopheles cruzii (Diptera: Culicidae).

We explored the homogeneity of the An. cruzii population across its altitudinal range of distribution using wing shape and mtDNA gene analysis. We also assessed the stability of wing geometry over time. Larvae were sampled from lowland and hilltop areas in a primary Atlantic Forest region, in the municipality of Cananéia. The right wings of males and females were analysed by standard geometric morphometrics. Eighteen landmarks were digitised for each individual and a discriminant analysis was used to compare samples from the hilltop and lowland. A 400-bp DNA fragment of the mitochondrial cytochrome oxidase gene subunit I (CO-I) was PCR-amplified and sequenced. Conclusions: Wing geometry and CO-I gene analysis indicated that An. cruzii is vertically structured. Wing shape varied rapidly, but altitude



structure was maintained. Future investigations should identify the biotic/abiotic causes of these patterns and their implications in the local epidemiology of malaria. [2]

(3) Field Evaluation of Picaridin Repellents Reveals Differences in Repellent Sensitivity between Southeast Asian Vectors of Malaria and Arboviruses.

The protective efficacy of two formulated picaridin repellents against mosquito bites, including arbovirus and malaria vectors, was evaluated in a field study in Cambodia. Based on a total of 4996 mosquitoes collected on negative control persons, the overall five hour protection rate was 97.4% [95%CI: 97.1-97.8%], not decreasing over time. Picaridin 20% performed equally well as DEET 20% and better than picaridin 10%. Field evaluation shows that repellents can provide additional personal protection against early and outdoor biting malaria and arbovirus vectors, with excellent protection up to five hours after application. The heterogeneity in repellent sensitivity between mosquito genera and vector species could however impact the efficacy of repellents in public health programs. Considering its excellent performance and potential to protect against early and outdoor biting vectors, as well as its higher acceptability as compared to DEET, picaridin is an appropriate product to evaluate the epidemiological impact of large scale use of topical repellents on arthropod borne diseases. [3]

(4) How Effective is Integrated Vector Management Against Malaria and Lymphatic Filariasis Where the Diseases Are Transmitted by the Same Vector?

We developed a general model of malaria and LF transmission and derived expressions for the basic reproductive number (R0) for each disease. Transmission of both diseases was most sensitive to vector mortality and biting rate. Simulating different levels of coverage of long lasting-insecticidal nets (LLINs) and larval control confirms the effectiveness of these interventions for the control of both diseases. Conclusions: despite the low level of vector control required to eliminate LF, simulations suggest that prevalence of LF will decrease at a slower rate than malaria, even at high levels of coverage. If representative of field situations, integrated management should take into account not only how malaria control can facilitate filariasis elimination, but strike a balance between the high levels of coverage of (multiple)



interventions required for malaria with the long duration predicted to be required for filariasis elimination. [4]

(5) Comparing Leishman and Giemsa staining for the assessment of peripheral blood smear preparations in amalaria-endemic region in India.

Microscopy of peripheral blood thin and thick films remains the reference for malaria diagnosis. Peripheral blood thin and thick smears from consecutive febrile patients admitted to Ispat General hospital, Rourkela, Odhisa, India, were stained with Giemsa and Leishman stain. Methods were compared for species identification, parasite quantification, and ability for identification of alternative diagnoses. Conclusion: Leishman's staining method for thin and thick smears is a good alternative to Giemsa's stain for identifying Plasmodium parasites. The Leishman method is superior for visualization of red and white blood cell morphology. [5]

2. 血吸虫病相关

(1) Compatibility of Schistosoma japonicum from the hilly region and Oncomelania hupensis hupensis from the marshland region within Anhui, China.

Schistosome japonicum remains one main public concern in China. This is exemplified in the hilly region in Anhui Province, where rodents have served as reservoirs for the parasite and no effective intervention could target such wild animals. The closer relationship between the hilly region and the near marshland induces the worry of spread of the hill parasite to the marshland region. Therefore, the level of snail-parasite compatibility between the hill parasite and snail populations from the Yangtze River valley was investigated. The results suggested a high compatibility between the marshland strains of snail and both the hill and the marshland strains of parasite. This would have practical implications. Moreover, the fact of the lower compatible relationship between the hill parasite and its local intermediate hosts warranted more studies. [6]



(2) The molecular characterization and RNAi silencing of SjZFP1 in Schistosoma japonicum.

In our current study, we cloned the open reading frame (ORF) of SjZFP1 of S. japonicum, which encodes a zinc finger protein. We analyzed the complementary DNA (cDNA) sequence of SjZFP1 and examined the expression of SjZFP1 messenger RNA (mRNA) at various developmental stages. We also tested the effects of RNA interference (RNAi) silencing on worm burden, spawning, and egg hatching. Our results suggest that the SjZFP1 gene might be important for parasite development, spawning in the vertebrate host, and egg hatching. [7]

(3) Co-infection with Schistosoma mansoni and Human Immunodeficiency Virus-1 (HIV-1) among residents of fishing villages of north-western Tanzania.

A cross-sectional study was conducted among 1,785 randomly selected adults in fishing villages of north-western Tanzania. Single stool samples were obtained and examined for S. mansoni eggs using the Kato Katz technique. Finger prick and venous blood samples were collected for HIV-1 screening and CD4+ cell quantification. Demographic information was collected by questionnaire. Conclusion: Our findings suggest that HIV-1 infection may not have a major effect on S. mansoni infection or on the excretion of eggs from the co-infected individuals. However, further studies are needed to understand the biological interaction between HIV-1 and S. mansoni in a large cohort of co-infected individuals. [8]

(4) The anterior esophageal region of Schistosoma japonicum is a secretory organ.

The heads of adult Schistosoma japonicum were detached and prepared for both transmission and scanning electron microscopy to define the detailed ultrastructure of the anterior esophagus. Cryosections of heads were also prepared for immunocytochemistry and confocal microscopy to define the pattern of intrinsic host antibody binding in the anterior esophageal lining. Conclusions: We suggest that the anterior esophageal region is an independent secretory organ. The contents of light vesicles are released into the esophageal



lumen via the tips of corrugation to interact with incoming blood. Our immediate task is to establish their composition and role in blood processing. [9]

1. 其他寄生虫病相关

(1) Universal single-probe rt-PCR assay for diagnosis of dengue virus infections.

The assay did not cross-react with human RNA, nor did it produce false-positive results for other human pathogenic flaviviruses or clinically important etiological agents of febrile illnesses. We used clinical serum samples obtained from returning travelers with dengue-compatible symptomatology (n=163) to evaluate the diagnostic relevance of our assay, and laboratory diagnosis performed by the RT-PCR assay had 100% positive agreement with diagnosis performed by NS1 antigen detection. In a retrospective evaluation including 60 archived serum samples collected from confirmed dengue cases 1-9 days after disease onset, the RT-PCR assay detected viral RNA up to 9 days after appearance of symptoms. The validation of the RT-PCR assay presented here indicates that this technique can be a reliable diagnostic tool, and hence we suggest that it be introduced as the method of choice during the first 5 days of dengue symptoms. [10]

(2) Molecular detection and genotypic characterization of Toxoplasma gondii infection in bats in four provinces of China.

During May 2005 to August 2013, bats were sampled from Jilin, Liaoning, Jiangxi, and Guangdong provinces, China, and liver tissues were collected for the detection of T. gondii by a nested PCR targeting the B1 gene. The positive samples were genotyped at 11 genetic markers (SAG1, 5-and 3-SAG2, alternative SAG2, SAG3, BTUB, GRA6, L358, PK1, c22-8, c29-2, and Apico) using multilocus polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Conclusions: The present study revealed an overall T. gondii prevalence of 6.1% in bats from Jilin, Liaoning, Jiangxi and Guangdong provinces in China, and reported two T. gondii genotypes (ToxoDB#9 and #10) having a wide geographical distribution in China. These results provide new genetic information about T. gondii infection in



bats, and have implications for better understanding of the genetic diversity of T. gondii in China and elsewhere. [11]

(3) Genome Sequence of Afipia felis Strain 76713, Isolated in Hospital Water Using an Amoeba Co-Culture Procedure.

Afipia felis is a Gram-negative alphaproteobacterium originally described as the agent of cat-scratch disease (CSD). We sequenced the genome from a strain of A. felis, which was recovered from a hospital water sample using an amoebal co-culture procedure. It is composed of 3,989,646 bp, with a G+C content of 61.27% and encodes 4,068 protein-coding genes and 53 RNA genes. [12]

(4) Leishmania donovani Infection Enhances Lateral Mobility of Macrophage Membrane Protein Which Is Reversed by Liposomal Cholesterol.

We determined the lateral mobility of a membrane protein in normal, LD infected and liposome treated LD infected cells using GFP-tagged PLCδ1 as a probe. The mobility of PLCδ1 was computationally analyzed from the time lapse experiment using boundary distance plot and radial profile movement. Our results showed that the lateral mobility of the membrane protein, which is increased in infection, is restored to normal upon liposomal cholesterol treatment. We found that F-actin is decreased in infection but is restored to normal upon liposomal cholesterol treatment as evident from phalloidin staining and also from biochemical analysis by immunoblotting. To our knowledge this is the first direct demonstration that LD parasites during their intracellular life cycle increases lateral mobility of membrane proteins and decreases F-actin level in infected macrophages. Such defects may contribute to ineffective intracellular signaling and other cellular functions. [13]

二、国内热带病热点研究

1. 疟疾相关



(1) 红细胞和血小板参数对疟疾流行病学特征的相关性分析

疟疾是我国常见的严重威胁人们健康的传染性疾病之一,其中恶性疟疾发病迅猛,容易引起脑型疟而危害患者生命。本次研究对疟疾患者的红细胞和血小板的水平与疟疾流行病学的特征的相关性进行了探讨。结论为:红细胞及血小板相关参数对疟疾的诊断具有一定的意义,可以通过观察红细胞及血小板的变化及相关临床表现为临床早期诊断、治疗提供依据。[14]

(2) 2009--2013 年河南省疟疾流行病学特征分析

分析2011~2013 年河南省的疟疾疫情,为今后制定防治措施提供科学依据。 收集河南省2011-2013 年疟疾疫情数据并进行统计分析。结论是河南省近3 年输入性疟疾大幅增加,应加强疟疾监测,对高疟区回归人员加强疟疾筛检和健康教育,尽快遏制输入性疟疾疫情上升势头,确保消除疟疾工作顺利实施。[15]

(3) 用 SYBR green I 法和流式细胞术体外评价 3 种青蒿素类药物的 抗疟活性

用SYBR green I法和流式细胞术评价3种青蒿素类药物对体外培养恶性疟原虫的抗疟活性。采用SYBR green I法观察不同浓度的青蒿素、蒿甲醚及双氢青蒿素对体外培养的恶性疟原虫增殖的抑制作用。结论为SYBR green I法的灵敏性与流式细胞术的直观性可以满足体外测定抗疟药对疟原虫抑制作用的需要,均可适于抗疟药物体外活性评价;ART、AM与DHA的体外抗疟活性由高到低的次序为DHA>AM>ART。[16]

2. 血吸虫病相关



(1) Th1 和 Th2 型细胞因子对小鼠感染血吸虫的免疫保护性研究

探讨Thl和Th2类细胞因子对小鼠感染血吸虫的免疫保护作用。方法是小鼠48 只,抽签法随机均分为4组,白细胞介素-4组、IL-12组、胸腺基质淋巴生成素组、生理盐水组。4组均为腹腔注射,每周3次,持续注射8周。给药后2周,各组小鼠经皮攻击感染日本血吸虫尾蚴,感染后第3、6周剖杀,计算各组小鼠虫荷数、肝脏卵荷数。芯片检测各组小鼠感染前和感染后不同时间点血清中IL-5、IL-10、干扰素及肿瘤坏死因子的动态变化。观察小鼠肝、脾的病理变化。结论为Th1或Th2类细胞因子单独注射对减虫或减卵没有显著作用,但对于肝脏病理变化均有一定的保护作用,并以Th1类细胞因子作用最为显著。[17]

(2) 流动人口血吸虫病防治知识及行为分析

了解流动人口血吸虫病防治知识知晓及行为情况,为开展流动人口血吸虫病防治提供科学依据。方法是采用意图抽样法在上海市选取来自血吸虫病流行省份的流动人口,采用整群抽样法在湖南、湖北、江西、安徽、江苏、四川和云南省的血吸虫病流行村及上海市选取常住居民。运用个人问卷调查法调查个人基本情况,血吸虫病基本知识知晓情况和预防行为。对流动人口、流出地和流入地常住人口的血吸虫病防治知识知晓情况进行比较。结论为流动人口的血吸虫病基本知识知晓程度和预防行为均差于流入地和流出地常住人口的情况,应将干预措施前移,在流出地加强外出人口防治血吸虫病健康教育和查治措施。[18]

(3) 日本血吸虫重组质粒 pGEX-Sj32 的构建及其在大肠埃希菌 BL21 中的表达



构建日本血吸虫(Sj)重组质粒pGEX-Sj32并研究其在大肠埃希菌BL21中的表达效率。方法为从该实验室保存的BL21(pET28α—Sj32)重组菌中抽提质粒pET28α—Sj32,PCR扩增Sj32抗原编码基因,定向克隆入穿梭载体pGEX—1λT,构建重组质粒pGEX—Sj32。将重组质粒转化大肠埃希菌BL21(DE3),经异丙基硫代—β—D—半乳糖苷(IPTG)诱导表达;表达产物用SDS—PAGE和Western blot进行鉴定。结论为成功构建日本血吸虫重组质粒pGEX—Sj32,该重组质粒在大肠埃希菌BL21中得到了高效表达,且表达蛋白具有特异的抗原性。[19]

3. 其他寄生虫病相关

(1) 西双版纳州重点传染病的疫情分析及防控策略探讨

分析西双版纳州近10 年重点传染病发病情况及流行规律,为调整防控策略和防控措施提供依据。方法是采用描述性流行病学方法对《国家疾病监测信息报告管理系统》管理的西双版纳州2004-2013 年重点传染病监测数据进行分析,并在疫情分析的基础上对现行防控策略和措施进行评价。结论为西双版纳州重点传染病的疾病谱因受防控投入差异、境外传染源输入的影响正发生改变,防控效果较好的是鼠疫、霍乱、疟疾、麻风病,流行水平仍然较高的是结核、艾滋病、肠道寄生虫病,新增传染病疫情频发,进一步加强传染源监测、实时调整防控策略及其落实必不可少。[20]

(2) 1978~2014 年我国登革热的流行病学分析

自1978年以来,我国几乎每年都有登革热病例报告,表现为间断性流行,有 每隔4~7年发生1次流行的趋势。高发年龄段为20~60岁,男女发病比例接近;4 个血清型均有流行,但以1型为主。1997年以后,登革热疫情得到一定的控制,但2013年开始,登革热发病率明显上升,尤其是2014年,流行规模更是达到1986年以来的新高。截至11月23日广东省登革发病人数已经达到44894人,疫情的严重性已经引起高度关注。本文对1978年以来我国登革热的流行状况、地区和人群分布以及今年登革热疫情大爆发的影响因素等进行了分析。[21]

(3) 埃博拉病毒感染的实验室检测方法

2014年初,西非埃博拉病毒感染暴发,且流行呈播散趋势,引起全球高度重视。由埃博拉病毒引起的埃博拉病毒病具有潜伏时间短、发病急、传染性强和致死率高的特点,目前尚无预防疫苗和特异治疗药物。早诊断并隔离治疗可降低病毒的传播风险,这对准确、快速和敏感的实验室检测方法的需求增加。本文将有关埃博拉病毒感染实验室检测方法作简要综述。[22]

(4) 刚地弓形虫速殖子表面抗原的研究及应用

弓形虫是一种专性细胞内寄生原虫,能感染包括人在内的所有温血动物。近年来弓形虫速殖子表面抗原已成为候选的诊断和疫苗抗原。弓形虫速殖子表面蛋白可增强免疫动物抗攻击感染的能力,具有免疫保护作用。P35、P30、P22和P23蛋自均有可能成为疫苗候选分子。通过寻找表达产物抗原性更强的候选基因和适宜的表达载体,构建多价、高效的复合蛋白疫苗或含有佐剂的混合疫苗,可能会提高弓形虫疫苗的免疫保护效果。[23]

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编辑:中国疾病预防控制中心寄生虫病预防控制所

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