热带病学术热点追踪报告

2014 年第 4 期（总第 9 期）

目　录

一、国际热带病热点研究

1. 疟疾相关

（1）*Antibodies to PfSEA-1 block parasite egress from RBCs and protect againstmalaria infection.*

Abstract[*]

Novel vaccines are urgently needed to reduce the burden of severe malaria. Using a differential whole-proteome screening method, we identified Plasmodium falciparum schizont egress antigen-1 (PfSEA-1), a 244-kilodalton parasite antigen expressed in schizont-infected red blood cells (RBCs). Antibodies to PfSEA-1 decreased parasite replication by arresting schizont rupture, and conditional disruption of PfSEA-1 resulted in a profound parasite replication defect. Vaccination of mice with recombinant Plasmodium berghei PbSEA-1 significantly reduced parasitemia and delayed mortality after lethal challenge with the Plasmodium berghei strain ANKA. Tanzanian children with antibodies to recombinant PfSEA-1A (rPfSEA-1A) did not experience severe malaria, and Kenyan adolescents and adults with antibodies to rPfSEA-1A had significantly lower parasite densities than individuals without these antibodies. By blocking schizont egress, PfSEA-1 may synergize with other vaccines targeting hepatocyte and RBC invasion [1].

（2）*Parasite burden and severity of malaria in Tanzanian children.*

Abstract[†]

Severe Plasmodium falciparum malaria is a major cause of death in children. We documented P. falciparum infection and disease in Tanzanian children followed from birth for an average of 2 years and for as long as 4 years. Resistance to severe malaria was not acquired after one or two mild infections. Although the parasite burden was higher on average during episodes of severe malaria, a high

[*] 为了给读者提供更简明扼要的信息，本报告中的英文摘要均经过编辑和精简。

parasite burden was often insufficient to cause severe malaria even in children who later were susceptible. The diverging rates of severe disease and high-density infection after infancy, as well as the similar parasite burdens before and after severe malaria, indicate that naturally acquired resistance to severe malaria is not explained by improved control of parasite density[2].

（3）*Olfactory plays a key role in spatiotemporal pathogenesis of cerebral malaria.*

Abstract

Cerebral malaria is a complication of Plasmodium falciparum infection characterized by sudden coma, death, or neurodisability. Studies using a mouse model of experimental cerebral malaria (ECM) have indicated that blood-brain barrier disruption and CD8 T cell recruitment contribute to disease, but the spatiotemporal mechanisms are poorly understood. We show by ultra-high-field MRI and multiphoton microscopy that the olfactory bulb is physically and functionally damaged (loss of smell) by Plasmodium parasites during ECM. The trabecular small capillaries comprising the olfactory bulb show parasite accumulation and cell occlusion followed by microbleeding, events associated with high fever and cytokine storm. Specifically, the olfactory upregulates chemokine CCL21, and loss or functional blockade of its receptors CCR7 and CXCR3 results in decreased CD8 T cell activation and recruitment, respectively, as well as prolonged survival. Thus, early detection of olfaction loss and blockade of pathological cell recruitment may offer potential therapeutic strategies for ECM [3].

（4）*Evaluation of a novel magneto-optical method for the detection of malaria parasites.*

Abstract

We have recently developed a magneto-optical (MO) method which allows high-sensitivity detection of malaria pigment (hemozoin crystals) in blood via the magnetically induced rotational motion of the hemozoin crystals. Here, we evaluate this MO technique for the detection of Plasmodium falciparum in infected

erythrocytes using in-vitro parasite cultures covering the entire intraerythrocytic life cycle. Our novel method detected parasite densities as low as ~40 parasites per microliter of blood at the ring stage and less than 10 parasites/μL in the case of the later stages. We also applied the MO technique to investigate the change in hemozoin concentration during parasite maturation. Our preliminary data indicate that this method may offer an efficient tool to determine the amount of hemozoin produced by the different parasite stages in synchronized cultures. Hence, it could eventually be used for testing the susceptibility of parasites to antimalarial drugs [4].

（5）*Asymptomatic Plasmodium falciparum Malaria in Pregnant Women in the Chittagong Hill Districts of Bangladesh.*

Abstract

The nature and impact of malaria, however, is not well understood in pregnant women residing in areas of low, unstable malaria transmission where P. falciparum and P. vivax co-exist. A large longitudinal active surveillance study of malaria was conducted in the Chittagong Hill Districts of Bangladesh. Over 32 months in 2010-2013, the period prevalence of asymptomatic P. falciparum infections was assessed by rapid diagnostic test and blood smear and compared among men, non-pregnant women and pregnant women. A subset of samples was tested for infection by PCR. Hemoglobin was assessed. Independent risk factors for malaria infection were determined using a multivariate logistic regression model. The conclusion is that pregnancy is a risk factor for asymptomatic P. falciparum infection in the Chittagong Hill Districts of Bangladesh, and pregnancy and malaria interact to heighten the effect of each on hemoglobin. The even distribution of asymptomatic malaria, without temporal and spatial clustering, may have critical implications for malaria elimination strategies [5].

2. 血吸虫相关

（1）*Brain schistosomiasis in mice experimentally infected with Schistosoma mansoni.*

Abstract

Introduction Human neuroschistosomiasis has been reported in the literature, but the possibility of modeling neuroschistosomiasis in mice is controversial. Methods In two research laboratories in Brazil that maintain the Schistosoma mansoni life cycle in rodents, two mice developed signs of brain disease (hemiplegia and spinning), and both were autopsied. Results S. mansoni eggs, both with and without granuloma formation, were observed in the brain and meninges of both mice by optical microscopy. Conclusions This is the first description of eggs in the brains of symptomatic mice that were experimentally infected with S. mansoni. An investigation of experimental neuroschistosomiasis is now feasible [6].

（2）*Induction of protective immune responses against schistosomiasis using functionally active cysteine peptidases.*

Abstract

For schistosomiasis, there is no vaccine available but one is urgently needed especially since praziquantel-resistant parasites are likely to emerge at some time in the future. The disease is caused by several worm species of the genus Schistosoma. These express several classes of papain-like cysteine peptidases, cathepsins B and L, in various tissues but particularly in their gastrodermis where they employ them as digestive enzymes. We have shown that sub-cutaneous injection of recombinant and functionally active Schistosoma mansoni cathepsin B1 (SmCB1), or a cathepsin L from a related parasite Fasciola hepatica (FhCL1), elicits highly significant protection (up to 73%) against an experimental challenge worm infection in murine models of schistosomiasis. The immune modulating properties of this subcutaneous injection can boost protection levels (up to 83%) when combined with other S. mansoni vaccine candidates, glyceraldehyde 3-phosphate dehydrogenase (SG3PDH) and peroxiredoxin (PRX-MAP). Here, we discuss these data in the context of the parasite's biology and development, and provide putative mechanism by which the native-like cysteine peptidase induce protective immune responses [7].

（3）*Effectiveness of a Pre-treatment Snack on the Uptake of Mass Treatment for Schistosomiasis in Uganda: A Cluster Randomized Trial.*

Abstract

School-based mass treatment with praziquantel is the cornerstone for schistosomiasis control in school-aged children. However, uptake of treatment among school-age children in Uganda is low in some areas. The objective of the study was to examine the effectiveness of a pre-treatment snack on uptake of mass treatment. In a cluster randomized trial carried out in Jinja district, Uganda, 12 primary schools were randomized into two groups; one received education messages forschistosomiasis prevention for two months prior to mass treatment, while the other, in addition to the education messages, received a pre-treatment snack shortly before mass treatment. The results suggest that provision of a pre-treatment snack combined with education messages achieves a higher uptake compared to the education messages alone. The use a pre-treatment snack was associated with reduced side effects as well as decreased prevalence and intensity of S. mansoni infection [8].

3. 其他寄生虫相关

（1）*Recombinant Leishmania infantum Heat Shock Protein 83 for the Serodiagnosis of Cutaneous, Mucosal, and Visceral Leishmaniases.*

Abstract

Routine serological diagnoses for leishmaniases, except in visceral cases, are performed using whole-parasite antigens. We used enzyme-linked immunosorbent assay (ELISA) to evaluate the performance of Leishmania infantum rHsp83 compared with L. major-like total promastigote antigen in the diagnosis of cutaneous (CL), mucosal (ML), and visceral leishmaniases (VL). ELISA-rHsp83 was significantly more

sensitive than ELISA-L. major-like when considering either CL/ML (P = 0.041) or all leishmaniasis patients (P = 0.013). When samples from other infectious disease patients were evaluated for cross-reactivity, ELISA-rHsp83 was more specific than ELISA-L. major-like, specifically for Chagas disease samples (P < 0.001). We also evaluated the anti-rHsp83 antibody titers months after treatment and observed no significant difference in ML (P = 0.607) or CL (P = 0.205). We recommend ELISA-L. infantum-rHsp83 as a routine confirmatory serological assay for the diagnosis of Leishmania infection because of the high sensitivity, the specificity, and the insignificant cross-reactivity with other infectious diseases [9].

（2）*Lanthanide complexes containing 5-methyl-1,2,4-triazolo[1,5-a] pyrimidin-7(4H)-one and their therapeutic potential to fight leishmaniasis and Chagas disease.*

Abstract

Research on therapeutic potential of lanthanide complexes and the understanding of their mechanism of action is still taking its first steps, and there is a distinct lack of research in the parasitology field. In the present work, we describe the synthesis and physical properties of seven new lanthanide complexes with the anionic form of the bioactive ligand 5-methyl-1,2,4-triazolo[1,5-a]pyrimidin-7(4H)-one (HmtpO), namely [Ln(mtpO)3(H2O)6]·9H2O (Ln=La(III), Nd(III), Eu(III), Gd(III), Tb(III), Dy(III) and Er(III)). In addition, results on the in vitro antiproliferative activity against Leishmania spp. and Trypanosoma cruzi are described. The high activity of the new compounds against parasite proliferation and their low cytotoxicity against reference host cell lines show a great potential of this type of compounds to become a new generation of highly effective and non-toxic antiparasitic agents to fight the so considered neglected diseases leishmaniasis and Chagas disease [10].

（3）*Current Status of Taeniasis and Cysticercosis in Vietnam.*

Abstract

Several reports on taeniasis and cysticercosis in Vietnam show that they are distributed in over 50 of 63 provinces. In some endemic areas, the prevalence of

taeniasis was 0.2-12.0% and that of cysticercosiswas 1.0-7.2%. Clinical manifestations of cysticercosis in humans included subcutaneous nodules, epileptic seizures, severe headach, impaired vision, and memory loss. The species identification of Taenia in Vietnam included Taenia asiatica, Taenia saginata, and Taenia solium based on combined morphology and molecular methods. Only T. solium caused cysticercosis in humans. Praziquantel was chosen for treatment of taeniasis and albendazole for treatment ofcysticercosis. Risk factors investigated with regard to transmission of Taenia suggested that consumption of raw meat (eating raw meat 4.5-74.3%), inadequate or absent meat inspection and control, poor sanitation in some endemic areas, and use of untreated human waste as a fertilizer for crops may play important roles in Vietnam, although this remains to be validated [11].

（4）*Structural Basis for the Immunomodulatory Function of Cysteine Protease Inhibitor from Human Roundworm Ascaris lumbricoides.*

Abstract

Immunosuppression associated with infections of nematode parasites has been documented. Cysteine protease inhibitor (CPI) released by the nematode parasites is identified as one of the major modulators of host immune response. In this report, we demonstrated that the recombinant CPI protein of Ascaris lumbricoides (Al-CPI) strongly inhibited the activities of cathepsin L, C, S, and showed weaker effect to cathepsin B. Crystal structure of Al-CPI was determined to 2.1 Å resolution. Two segments of Al-CPI, loop 1 and loop 2, were proposed as the key structure motifs responsible for Al-CPI binding with proteases and its inhibitory activity. Mutations at loop 1 and loop 2 abrogated the protease inhibition activity to various extents. These results provide the molecular insight into the interaction between the nematode parasite and its host and will facilitate the development of anthelmintic agents or design of anti-autoimmune disease drugs[12].

二、国内热带病热点研究

1. 疟疾相关

（1）2006－2012 年眉山市疟疾病例流行病学分析

【摘要】*

分析眉山市 2006－2012 年的 100 例疟疾病例发病及分布特点，为做好后期监测及制定防治对策提供依据。方法是收集眉山市 2006－2012 年疫情报告和疟疾防治工作年报表及个案调查材料，按常规流行病学统计方法进行分析和描述。结论为应进一步加强外出回归人员防治监测工作，以流动人口管理和输入性疟疾防控作为今后疟防工作的重点[13]。

（2）广西基本消灭恶性疟后的疟疾监测

【摘要】

分析评价基本消灭恶性疟后的疟疾监测效果，为消除恶性疟提供依据。方法为开展疟疾病例侦查，治疗病人，疫点处理；加强临床医生疟疾诊疗知识培训，提高疟疾诊治能力；开展健康教育，增强农民工防治疟疾意识。结论是广西消除恶性疟后，控制输入性疟疾传播是巩固成果的关键[14]。

（3）广西省二类县区居民和学生疟疾防治知识知晓现况调查分析

【摘要】

目的是了解广西省二类县区居民和学生疟疾防治基本知识知晓和行为情况，为制定有效的疟疾健康教育宣传策略提供依据。方法为采取随机抽样的方法确定调查人群，用统一的问卷进行疟疾防治知识知晓情况调查。结论是广西省二类县区居民和学生对疟疾防治知识的认知水平较低，针对性的疟疾健康促进教育有待进一步加强[15]。

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*为了给读者提供更简明扼要的信息，本报告中的中文摘要均经过编辑和精简。

（4）疟疾疫苗研究进展

【摘要】

疟疾是一种世界范围内的传染病，严重影响人类的身体健康和生命安全。疫苗作为控制乃至消灭传染病的有效手段，在疟疾研究中受到广泛关注。目前针对疟原虫生活史各期的期特异性疫苗、传播阻断型疫苗、多阶段/多抗原疫苗以及减毒活疫苗都处于研究中。尽管尚无成熟疫苗推入市场，但一些候选疫苗已进入临床实验，并产生了非常有希望的结果。该文就疟疾疫苗的研究进展做一综述[16]。

2. 血吸虫相关

（1）初探日本血吸虫ＳＷＡ及ＳＥＡ对Ｉ型糖尿病小鼠血糖的抑制作用

【摘要】

探讨日本血吸虫ＳＷＡ及ＳＥＡ对实验性Ｉ型糖尿病小鼠血糖的抑制作用。方法:制备日本血吸虫可溶性成虫抗原ＳＷＡ与可溶性虫卵抗原ＳＥＡ并构造实验性Ｉ型糖尿病小鼠模型。把２４只糖尿病实验小鼠随机平分为Ａ、Ｂ、Ｃ组(每组８只)。Ａ组实验小鼠从腹部皮下多点免疫注射日本血吸虫ＳＷＡ；Ｂ组实验小鼠从腹部皮下多点免疫注射日本血吸虫ＳＥＡ;Ｃ组实验小鼠用ＰＢＳ进行腹部皮下多点免疫，３组小鼠每周免疫１次，连续免疫４周后，采小鼠尾静脉血，检测实验小鼠的血糖变化。结论：日本血吸虫ＳＥＡ 对实验性Ｉ型糖尿病小鼠的血糖具有一定的抑制作用,其机制可能是日本血吸虫ＳＥＡ刺激了机体的免疫应答，导致Ｔｈ１反应向Ｔｈ２反应偏移[17]。

（2）湖北省 2008－2012 年血吸虫病防治效果评估

【摘要】

评估 2008－2012 年湖北省血吸虫病流行状况，为下阶段全省血吸虫病防治工作提供理论指导和科学依据。方法是开展人畜查治病、钉螺控制等传染控制为

主的综合防治措施，评价 2008－2012 年湖北省血吸虫病防治效果。结论为湖北省实施传染源控制为主的综合防治策略效果显著，但防治任务仍然十分艰巨，要根据疫区实际情况采取有针对性的血吸虫病防治措施，最终实现消除血吸虫病的目标[18]。

（3）荆门市 10 年血吸虫病监测结果分析

【摘要】

分析荆门市血吸虫病疫情变化趋势，指导防治工作。方法为收集 2003-2012 年荆门市血吸虫病疫情监测资料，分析人群、耕牛血吸虫感染率和钉螺面积、感染率变化情况。结论是荆门市血吸虫病呈低度流行状态，且疫情极不稳定。要加强其他动物传染源控制和钉螺控制，注重交界地区流动人畜管理和健康教育等措施[19]。

3. 其他寄生虫相关

（1）Th17 细胞在弓形虫感染小鼠中的免疫病理作用研究

【摘要】

分析弓形虫感染小鼠后 Th17 细胞及相关细胞因子变化，探讨 Th17 细胞及相关细胞因子可能的免疫病理作用。方法为 Giemsa 染色、常规病理学检查、免疫荧光法及 PCR 扩增弓形虫核酸，确定弓形虫速殖子感染 BALB/c 小鼠模型的建立；流式细胞术动态检测感染小鼠脾脏中 CD3 + CD4 + IL-17 + Th17 细胞变化；ELISA 法动态检测血清中 IL-17、IL-6 以及抗弓形虫特异性 IgM 抗体的变化。结论为弓形虫感染小鼠后诱导的 Th17 细胞及其相关细胞因子可能参与小鼠的免疫病理过程[20]。

（2）广西省 2008 －2012 年阿米巴痢疾的流行病学分析

【摘要】

目的是了解近年来广西阿米巴痢疾的流行特征，为制定相应防治对策提供依据。方法为采用描述流行病学方法对国家疾病监测信息报告管理系统网络直报的2008 — 2012 年广西阿米巴痢疾疫情报告进行流行病学分析。结论是阿米巴痢疾防治应重点做好幼儿监护人的卫生宣教，加强食品卫生监督和疾病的监测[21]。

（3）青海省大通县 2012 年包虫病流行病学调查报告

【摘要】

目的是掌握青海省大通县人群和家犬的包虫病感染等流行现状。方法是按农业区、城镇 2 个层次采取分层整群随机抽样的方法，选取朔北、逊让、新城、宝库、桥头 5 个乡 16 个村作为调查点，研究对象为 7 岁以上的常住居民。结论为大通县包虫病人间和畜间的感染率处于低流行状态，仍需根据其流行病学特征开展具体工作[22]。

（4）西双版纳州登革热暴发现场 BGS-trap 媒介蚊虫监测研究

【摘要】

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。方法为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，捕获蚊种经形态学鉴定。利用描述流行病学方法对日捕获所有蚊虫进行分析。结论是 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[23]。

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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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