



# TRYLEIDIAG PRESS REVIEW

## April 2009

### Content

#### Events Highlights

- *The American Society of Tropical Medicine and Hygiene 58th Annual Meeting*
- *Congress 70th Anniversary of IPK, VII Cuban Congress of Microbiology and Parasitology, IV National Congress of Tropical Medicine*

#### Grants

- *European Foundations launch second call for proposals for African research into neglected tropical diseases*
- *European and Developing Countries Clinical Trials Partnership (EDCTP): Call for applications*

#### Research news

- *Endemic type of animal trypanosomiasis is not associated with lower genotype variability of Trypanosoma congolense isolates circulating in livestock.*
- *Particularities of Mitochondrial Structure in Parasitic Protozoa (Apicomplexa and Kinetoplastida).*
- *The poorest of the poor: a poverty appraisal of households affected by visceral leishmaniasis in Bihar, India.*
- *Epidemiology and diagnostics of visceral leishmaniasis in Serbia.*
- *Multiple relapses of visceral leishmaniasis in a patient treated with liposomal amphotericin.*
- *Update on visceral Mediterranean Leishmaniasis*
- *What determines the success or failure of intracellular cutaneous parasites? Lessons learned from leishmaniasis.*
- *Transmission of Trypanosoma cruzi by Heart Transplantation.*
- *Double trypanosomal chancre revealing West African trypanosomiasis in a Frenchman living in Gabon. [Article in French]*
- *New Bicyclic Amines: Synthesis and SARs of their Action Against the Causative Organisms of Malaria and Sleeping Sickness.*
- *The treatment pathways followed by cases of human African trypanosomiasis in western Kenya and eastern Uganda.*
- *Genetics and visceral leishmaniasis: of mice and man.*

#### Political and regulatory

- *Support Kenyan researchers to innovate more.*

**Perspectives in GENETICS: *Leishmania* Exploit Sex**



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## EVENTS HIGHLIGHTS AND GRANTS

### **The American Society of Tropical Medicine and Hygiene 58<sup>th</sup> Annual Meeting**

November 18-22, 2009 Marriott Wardman Park Washington, DC, USA

Abstract and Young Investigator Awards Submissions Submission deadline: May 6<sup>th</sup>

For more information, please visit

<http://www.astmh.org/AM/Template.cfm?Section=Home&CFID=9110620&CFTOKEN=24615175&jsessionid=ca302602c57f454d1374>

### **Congress 70th Anniversary of IPK, VII Cuban Congress of Microbiology and Parasitology, IV National Congress of Tropical Medicine**

1 - 4 June 2009 Havana, Cuba

For more information, please consult <http://embacuba.cubaminrex.cu/portals/21/ipke.pdf>

The Congresses will deal with several important topics related to infectious and parasitic diseases. All the parasitologists, bacteriologists, mycologists, virologists, infectologists, zoonologists, tropicalists, and those specialists working on other related disciplines who may be interested in these topics are invited in order to present and discuss their experiences and results about this fascinating world of sciences.



## GRANTS

### European Foundations launch second call for proposals for African research into neglected tropical diseases

Organisation: Nuffield Foundation

Closing Date: May 15<sup>th</sup> 2009

The African Fellowship Programme on Neglected Tropical Diseases has launched its second call for proposals from African scientists for its prestigious Fellowships for research in into diseases such as bilharzia, elephantiasis, worms, diarrhoea and sleeping sickness. This unique initiative to support African-led research into neglected tropical diseases stems from a collaboration between five European foundations.

For more information, please visit the African Fellowship Programme on Neglected Tropical Diseases website: <http://www.ntd-africa.net/>

For any questions or queries, please contact email: [slock@nuffieldfoundation.org](mailto:slock@nuffieldfoundation.org)

### European and Developing Countries Clinical Trials Partnership (EDCTP): Call for applications

Organisation: EDCTP

Closing Date: June 1<sup>st</sup> 2009

**Senior Fellowship:** Through this call, EDCTP intends to identify and support senior researchers capable of building and leading research groups at sub-Saharan African institutions that will be internationally competitive and capable of winning grants from international funding bodies. This grant is both available for researchers already working in Africa as well as those looking to return to the continent (re-entry grant). For this grant scheme EDCTP aims to contribute to building sustainable capacity through training and networking with linkage to the EDCTP supported regional Networks of Excellence in sub-Saharan Africa. A maximum of one Senior Fellowship per disease per region will be supported.

**Establishment and Strengthening of African National Ethics Committees (NECs) or Institutional Review Boards (IRBs):** EDCTP wishes to promote the establishment and strengthening of National Ethics Committees (NEC) and Institutional Review Boards (IRB) that are competent and independent. The NECs and the IRBs are encouraged to establish themselves administratively and financially so as to ensure sustained optimal function beyond the EDCTP funding. Strengthening of NEC or IRB aims at making them operational and gives support to their ongoing functions. Networking and training is encouraged and supported. Additional support in the form of online literature access, documents, access to websites on ethics and GCP will be facilitated.

In countries where NECs do not exist, the local institutional review boards are encouraged to contribute to the formation of a NEC. Where neither NECs nor local IRBs exist, the EDCTP will encourage national recognised institutions or scientists affiliated to an established in-country institution to be contracted to initiate the formation of the NEC.

For more information and an application form, please go to: <http://www.edctp.org/>



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Contact: P.O.Box 93015, 2509 AA, The Hague, The Netherlands. Email: [brink@edctp.org](mailto:brink@edctp.org) Tel: +31 (0)70 349 44 22 and Fax: +31 (0)70 344 08 99



## RESEARCH NEWS

### **Endemic type of animal trypanosomiasis is not associated with lower genotype variability of *Trypanosoma congolense* isolates circulating in livestock.**

Masumu J, Geysen D, Bossche PV.

University of Pretoria, Department of Veterinary Tropical Diseases, Onderstepoort, Pretoria, Gauteng 0110, South Africa.

Res Vet Sci. 2009 Apr 6.

In order to verify whether the low impact on livestock production in endemic areas is related to a low number of trypanosome strains circulating in livestock, 37 *Trypanosoma congolense* isolates collected from cattle in 11 sites in an endemic trypanosomiasis area in Eastern Zambia were characterised for genotype variability using a modified amplified fragment length polymorphism technique (AFLP). Isolates were further cloned to evaluate the occurrence of mixed infections in individuals. The results obtained revealed a high genotype diversity (94.6%) among these isolates. Apart from one site, all isolates gave different AFLP profiles in each of the sites. When clones were compared, three (8%) of the 37 isolates had mixed infections. These results indicate the circulation of a high number of strains in this trypanosomiasis endemic area despite the low impact the disease has on livestock production.

### **Particularities of Mitochondrial Structure in Parasitic Protozoa (Apicomplexa and Kinetoplastida).**

de Souza W, Attias M, Rodrigues JC.

Laboratório de Ultraestrutura Celular Hertha Meyer, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, CCS-Bloco G, Ilha do Fundão, 21941-902, Rio de Janeiro-RJ, Brasil; Diretoria de Programas, Instituto Nacional de Metrologia e Qualidade Industrial-INMETRO.

Int J Biochem Cell Biol. 2009 Apr 17.

Without mitochondria, eukaryotic cells would depend entirely on anaerobic glycolysis for ATP generation. This also holds true for Protists, both free-living and parasitic. Parasitic Protists include agents of human and animal diseases that have a huge impact on world populations. In the phylum Apicomplexa, several species of *Plasmodium* cause malaria, whereas *Toxoplasma gondii* is a cosmopolitan parasite found on all continents. Flagellates of the order Kinetoplastida include the genera *Leishmania* and *Trypanosoma* causative agents of human leishmaniasis and (depending on the species) African trypanosomiasis and Chagas disease. Although clearly distinct in many aspects, the members of these two groups bear a single and usually well developed mitochondrion. The single mitochondrion of Apicomplexa has a dense matrix and many cristae with a circular profile. The organelle is even more peculiar in the order kinetoplastida, exhibiting a condensed network of DNA at a specific position, always close to the flagellar basal body. This arrangement is known as Kinetoplast and the name of the Order derived from it. Kinetoplastids also bear glycosomes, peroxisomes that concentrate enzymes of the glycolytic cycle. Mitochondrial volume and activity is maximum when glycosomal is low and vice versa. In both Apicomplexa and Trypanosomatids, mitochondria show



particularities that are absent in other eukaryotic organisms. These peculiar features make them an attractive target for therapeutic drugs for the diseases they cause.

### **The poorest of the poor: a poverty appraisal of households affected by visceral leishmaniasis in Bihar, India.**

Boelaert M, Meheus F, Sanchez A, Singh SP, Vanlerberghe V, Picado A, Meessen B, Sundar S.

Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium.

Trop Med Int Health. 2009 Apr 17.

To provide data about wealth distribution in visceral leishmaniasis (VL)-affected communities compared to that of the general population of Bihar State, India. Methods After extensive disease risk mapping, 16 clusters with high VL transmission were selected in Bihar. An exhaustive census of all households in the clusters was conducted and socio-economic household characteristics were documented by questionnaire. Data on the general Bihar population taken from the National Family Health Survey of India were used for comparison. An asset index was developed based on Principal Components Analysis and the distribution of this asset index for the VL communities was compared with that of the general population of Bihar. Results 83% of households in communities with high VL attack rates belonged to the two lowest quintiles of the Bihar wealth distribution. All socio-economic indicators showed significantly lower wealth for those households. Conclusion Visceral leishmaniasis clearly affects the poorest of the poor in India. They are most vulnerable, as this vector-borne disease is linked to poor housing and unhealthy habitats. The disease leads the affected households to more destitution because of its impact on household income and wealth. Support for the present VL elimination initiative is important in the fight against poverty.

### **Epidemiology and diagnostics of visceral leishmaniasis in Serbia.**

Dacic ZD, Pelemis MR, Stevanovic GD, Poluga JL, Lavadinovic LS, Milosevic IS, Indjic NK, Ofori-Belic IV, Pavlovic MD.

Clin Microbiol Infect. 2009 Apr 18.

Parasitological Laboratory, Institute for Infectious and Tropical Diseases, Bulevar oslobođenja, Belgrade, Serbia.

A retrospective epidemiological and diagnostic study of visceral leishmaniasis (VL) was carried out during the period 2001-2007 and included patients suspected of VL who had been diagnosed at the Parasitological Laboratory at the Institute for Infectious and Tropical Diseases, Belgrade. Diagnosis of VL was confirmed by microscopic examination of Giemsa-stained bone marrow (BM) smears. BM smears from 134 patients were examined; 22 cases of VL were diagnosed, the majority of which involved individuals who had been on holiday at the Montenegrin sea coast. The sensitivity of the initial BM smears was inadequate; this required the application of a serological test, adapted for routine use, for the diagnosis of VL.

### **Multiple relapses of visceral leishmaniasis in a patient treated with liposomal amphotericin.**

Akin M, Polat A, Balci YI, Kaya B, Karaca A, Turk M.



Department of Pediatric Haematology, Pamukkale University, Postal Code-20100, Denizli, Turkey, drmakin80@hotmail.com.

Indian J Pediatr. 2009 Apr 23.

### **Update on visceral Mediterranean Leishmaniasis**

[Article in French]

Rosenthal E, Marty P.

Service de médecine interne, hôpital de l'Archet, centre hospitalier universitaire de Nice, 151, route de Saint-Antoine de Ginestière, 06202 Nice cedex 3, France.

Rev Med Interne\_ 2009 Apr 24. [Epub ahead of print]

### **What determines the success or failure of intracellular cutaneous parasites? Lessons learned from leishmaniasis.**

Maurer M, Dondji B, von Stebut E.

Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Berlin, Germany.

Med Microbiol Immunol\_ 2009 Apr 25.

Most parasitic skin infections are averted by very efficient strategies of preventing pathogen invasion. Innate immune cells such as mast cells, macrophages and dendritic cells are responsible for detecting parasites and for recruiting proinflammatory cells that help to contain and control the pathogen at sites of infection. This induces efficient adaptive immunity, which is crucially important for parasite control. Using the example of cutaneous leishmaniasis, we highlight how the skin utilizes different strategies to prevent skin infection and how containment of the infection to the skin site may reduce the harm that otherwise may result for the entire organism.

### **Transmission of Trypanosoma cruzi by Heart Transplantation.**

Kun H, Moore A, Mascola L, Steurer F, Lawrence G, Kubak B, Radhakrishna S, Leiby D, Herron R, Mone T, Hunter R, Kuehnert M; Chagas Disease in Transplant Recipients Investigation Team.

Epidemic Intelligence Service, Career Development Division, Office of Workforce and Career Development, 2Division of Parasitic Diseases, and 3Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; 4Los Angeles Department of Health Services, Acute Communicable Disease Control Program, 5Department of Medicine, University of California, 6Department of Medicine, University of Southern California, 7American Red Cross, Southern California Region, 8OneLegacy, and 9California Department of Health, Laboratory Field Services, Biologics, Los Angeles, California; and 10American Red Cross Holland Laboratory, Rockville, Maryland.

Clin Infect Dis. 2009 Apr 28.



**Background.** *Trypanosoma cruzi* infection (i.e., Chagas disease) is an unusual complication that can occur after solid-organ transplantation and that can result in severe illness or death. In 2006, there were 2 heart transplant recipients in Los Angeles, California, reported to have acute trypanosomiasis during the same month. We conducted an investigation to determine the source of these infections. **Methods.** We reviewed the medical, organ procurement, and donor transfusion and transplantation records of these 2 heart transplant recipients. The 2 heart transplant recipients were interviewed regarding any kind of natural exposure and were screened for parasites by obtaining blood and other tissue samples for buffy coat, culture, and polymerase chain reaction. Serum samples from the heart transplant recipients, organ donors, and blood donors were tested for *T. cruzi* antibodies by use of immunofluorescence assay and radioimmunoassay. Tissue samples from the organ donors were examined by use of polymerase chain reaction and immunohistochemical staining. Other recipients of organs from the same donors were monitored for *T. cruzi* infection by use of polymerase chain reaction and immunofluorescence assay. **Results.** Both heart transplant recipients had no apparent risk factors for preexisting *T. cruzi* infection. Both were seronegative but tested positive for the parasite, indicating recent infection. Both recipients died despite medical treatment. The organ donors tested positive for *T. cruzi* antibodies by use of radioimmunoassay; the blood donors were seronegative. Six other patients had received a liver or kidney from these organ donors. None showed evidence of *T. cruzi* infection. **Conclusions.** To our knowledge, this is the first report of *T. cruzi* transmission associated with heart transplantation. Clinicians and public health authorities should be aware that manifestations of Chagas disease can occur after transplantation, requiring rapid evaluation, diagnosis, and treatment.

### **Double trypanosomal chancre revealing West African trypanosomiasis in a Frenchman living in Gabon.** [Article in French]

Hope-Rapp E, Moussa Coulibaly O, Klement E, Danis M, Bricaire F, Caumes E.

Service de maladies infectieuses et tropicales, hôpital Pitié-Salpêtrière, 47-83, boulevard de l'Hôpital, 75651 Paris cedex 13, France.

Ann Dermatol Venereol. 2009 Apr;136(4):341-5.

**BACKGROUND:** Human African trypanosomiasis (sleeping sickness), an endemic disease, is currently reemerging in Africa with an estimated incidence of 45,000 new cases per year. It is caused by *Trypanosoma brucei* subspecies and transmitted by day-biting tsetse flies. **PATIENTS AND METHODS:** We report a case of West African trypanosomiasis due to *Trypanosoma brucei gambiense* involving a Frenchman living in Libreville, Gabon. The patient presented with fever and polyadenopathies as well as two skin ulcerations highly suggestive of trypanosomiasis. Microscopic examination of cutaneous and peripheral blood smears confirmed the diagnosis of haemolympathic infection with *T. b. gambiense* with trypanosomal chancres. Examination of the cerebrospinal fluid was normal. The patient was successfully treated with pentamidine isethionate. **CONCLUSIONS:** Recognition of cutaneous manifestations may allow a rapid diagnosis of African trypanosomiasis that is essential for timely and efficient treatment and survival.

### **New Bicyclic Amines: Synthesis and SARs of their Action Against the Causative Organisms of Malaria and Sleeping Sickness.**

Weis R, Seebacher W.

Institute of Pharmaceutical Sciences, Pharmaceutical Chemistry, Karl-Franzens-University, Universitätsplatz 1, A-8010 Graz, Austria. [we.seebacher@uni-graz.at](mailto:we.seebacher@uni-graz.at).



Curr Med Chem. 2009;16(11):1426-41.

Diaryl-substituted bicyclic amines are a scarcely investigated class of compounds. Only few of them are described and their biological activities are reported poorly. During our work in the field of heterocyclic chemistry, we found that 4-dialkylaminobicyclo[2.2.2]octan-2-ones and -ols show antiprotozoal properties against *Plasmodium falciparum* K(1) and *Trypanosoma brucei rhodesiense*, the causative organisms of Malaria tropica and of Human African Trypanosomiasis. Therefore, we synthesized over 200 derivatives in order to investigate their antitrypanosomal and antiplasmodial activities as well as their cytotoxicity using in vitro microplate assays. Even if the target and the mechanism of action of these compounds are still unknown, we can at least provide several structure-activity relationships for this interesting class of compounds. Moreover, we achieved a distinct improvement of their antiplasmodial and antitrypanosomal properties.

### **The treatment pathways followed by cases of human African trypanosomiasis in western Kenya and eastern Uganda.**

Bukachi SA, Wandibba S, Nyamongo IK.

Institute of Anthropology, Gender and African Studies, University of Nairobi, P.O. Box, 30197-00100, Nairobi, Kenya.

Ann Trop Med Parasitol. 2009 Apr;103(3):211-20.

Although early diagnosis and treatment are key factors in the effective control of human African trypanosomiasis (HAT), many cases of the disease delay taking appropriate action, leading to untold suffering. As a better understanding of treatment-seeking behaviour should help in identifying the obstacles to early diagnosis and effective treatment, the treatment pathways followed by 203 former HAT cases in western Kenya and eastern Uganda have recently been explored. About 86% of the HAT cases had utilized more than two different healthcare options before being correctly diagnosed for HAT, with about 70% each using more than three different health facilities. Only about 8% of the cases reported that they had been correctly diagnosed the first time they sought treatment. Just over half (51%) of the HAT cases had been symptomatic for >2 months before being correctly diagnosed for HAT, and such time lags in diagnosis contributed to 72% of the cases receiving their first appropriate treatment only in the late stage of the disease. The likelihood of a correct diagnosis increased with the time the case had been symptomatic. These observations indicate an urgent need to build the diagnostic capacity of the primary healthcare facilities in the study area, so that all HAT cases can be identified and treated in the early stage of the disease.

### **Genetics and visceral leishmaniasis: of mice and man.**

Blackwell JM, Fakiola M, Ibrahim ME, Jamieson SE, Jeronimo SB, Miller EN, Mishra A, Mohamed HS, Peacock CS, Raju M, Sundar S, Wilson ME.

Telethon Institute for Child Health Research, Centre for Child Health Research, The University of Western Australia, Western Australia, Australia. [jblackwell@ichr.uwa.edu.au](mailto:jblackwell@ichr.uwa.edu.au)

Parasite Immunol. 2009 May;31(5):254-66.

Ninety per cent of the 500,000 annual new cases of visceral leishmaniasis (VL) occur in India/Bangladesh/Nepal, Sudan and Brazil. Importantly, 80-90% of human infections are sub-clinical



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or asymptomatic, usually associated with strong cell-mediated immunity. Understanding the environmental and genetic risk factors that determine why two people with the same exposure to infection differ in susceptibility could provide important leads for improved therapies. Recent research using candidate gene association analysis and genome-wide linkage studies (GWLS) in collections of families from Sudan, Brazil and India have identified a number of genes/regions related both to environmental risk factors (e.g. iron), as well as genes that determine type 1 vs. type 2 cellular immune responses. However, until now all of the allelic association studies carried out have been underpowered to find genes of small effect sizes (odds ratios or OR < 2), and GWLS using multigene pedigrees have only been powered to find single major genes, or at best oligogenic control. The accumulation of large DNA banks from India and Brazil now makes it possible to undertake genome-wide association studies (GWAS), which are ongoing as part of phase 2 of the Wellcome Trust Case Control Consortium. Data from this analysis should seed research into novel genes and mechanisms that influence susceptibility to VL.



## Political and regulatory

**Support Kenyan researchers to innovate more.** Kenyan innovators and researchers need more support to patent their work, says an editorial in *Business Daily Africa*. Since 2001, only ten products have been registered with the Kenyan patent office and none of them are from institutions of higher learning. But these very institutions should be spearheading innovation in Kenya, says the editorial. It argues that a key issue is building awareness of the need — and benefit — of innovators and researchers patenting their work to protect it from foreign interests. A sound industrial base relies on manufacturing locally-invented products and marketing them for export, says the editorial. Authorities should be offering academics incentives to pursue projects that promise practical solutions to local problems. But university laboratories also have a role to play, says the editorial, by collaborating with manufacturers to identify gaps in production processes. Engaging people from outside established research centres could also help protect innovation, argues the editorial. Recognising traditional knowledge and incorporating breakthroughs in fields such as traditional medicine into organised research processes would help speed up discoveries. *Business Daily Africa*, April 7<sup>th</sup> 2009



**Perspectives in GENETICS:  
*Leishmania* Exploit Sex**

**Deadly Parasite's Rare Sexual Dalliances May Help Scientists Neutralize It** For years, microbiologist Stephen Beverley, Ph.D., has tried to get the disease-causing parasite *Leishmania* in the mood for love. In this week's *Science*, he and colleagues at the National Institutes of Health report that they may have finally found the answer: Cram enough *Leishmania* into the gut of an insect known as the sand fly, and the parasite will have sex. ScienceDaily Apr. 13<sup>th</sup>, 2009

***Leishmania* Exploit Sex**

Michael A. Miles, Matthew Yeo, Isabel L. Mauricio

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*Science* 10 April 2009: Vol. 324. no. 5924, pp. 187 - 189

*Leishmania* are the last of the three major groups of trypanosomatid parasites to give up their secret-- a healthy capacity for genetic exchange. Protozoan parasites of the genus *Leishmania* (*Kinetoplastida:Trypanosomatidae*) cause widespread and devastating human diseases. Visceral leishmaniasis is responsible for overwhelming fatal epidemics, and cutaneous leishmaniasis can lead to destructive and life-threatening mucocutaneous lesions. Since the discovery of these disease agents more than a century ago, there has been debate as to whether they reproduce entirely clonally or undergo genetic exchange, although naturally occurring putative hybrids have been described. That debate is now over. [...]

**Reports: Demonstration of Genetic Exchange During Cyclical Development of *Leishmania* in the Sand Fly Vector**

Natalia S. Akopyants,<sup>1\*</sup> Nicola Kimblin,<sup>2\*</sup> Nagila Secundino,<sup>2</sup> Rachel Patrick,<sup>2</sup> Nathan Peters,<sup>2</sup> Phillip Lawyer,<sup>2</sup> Deborah E. Dobson,<sup>1</sup> Stephen M. Beverley,<sup>1</sup> David L. Sacks<sup>2</sup>

1 Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110, USA. 2 Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD 20892, USA. ‡To whom correspondence should be addressed. E-mail: [dsacks@nih.gov](mailto:dsacks@nih.gov)

*Science* 10 April 2009: Vol. 324. no. 5924, pp. 265 - 268

Genetic exchange has not been shown to be a mechanism underlying the extensive diversity of *Leishmania* parasites. We report here evidence that the invertebrate stages of *Leishmania* are capable of having a sexual cycle consistent with a meiotic process like that described for African



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trypanosomes. Hybrid progeny were generated that bore full genomic complements from both parents, but kinetoplast DNA maxicircles from one parent. Mating occurred only in the sand fly vector, and hybrids were transmitted to the mammalian host by sand fly bite. Genetic exchange likely contributes to phenotypic diversity in natural populations, and analysis of hybrid progeny will be useful for positional cloning of the genes controlling traits such as virulence, tissue tropism, and drug resistance.