PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Leishmania genes involved in parasitic infection

ArticleInfo		
ArticleID	:	4327
ArticleDOI	:	10.1186/gb-2002-3-3-reports0017
ArticleCitationID	:	reports0017
ArticleSequenceNumber	:	22
ArticleCategory	:	Paper report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2002–1–8 Received : 2002–1–8 OnlineDate : 2002–2–28
ArticleCopyright	:	BioMed Central Ltd2002
ArticleGrants	:	

ArticleContext	:	130593333

Wim D'Haeze

Abstract

Gene-expression studies have identified two new parasite genes potentially involved in the progression of *Leishmania* infection in mammalian hosts

Significance and context

Trypanosomatid parasites of the genus *Leishmania* infect some 12 million people worldwide, with more than 600,000 new clinical cases reported annually. *Leishmania* species go through a complex life cycle: motile promastigotes survive in the gut of the sandfly vector; mammalian hosts are infected when the vector sucks blood; and, finally, host macrophages internalize *Leishmania* parasites that need to differentiate into a nonmotile amastigote form to persist in the macrophage lysosomal compartment. Differentiation is characterized by dramatic morphological, genetic and biochemical changes in the parasite. Understanding promastigote-to-amastigote differentiation is crucial for developing methods of blocking *Leishmania* infection in its mammalian hosts. Duncan *et al*. have identified genes whose expression changes significantly during promastigote-amastigote differentiation, and which might serve as targets for blocking *Leishmania* infection.

Key results

Two full-length genomic clones of *Leishmania donovani*, named *P9* and *A14*, were isolated from a genomic library, based on previously identified mRNAs. The *P9* gene contains 1,448 base pairs (bp) and encodes a putative protein of 482 amino acids; the *A14* gene contains 2,708 bp and encodes a putative protein of 902 amino acids. No homologies with proteins in the database were found. P9 and A14 carry two and four putative membrane-spanning domains, respectively. The expression of *P9* and *A14*, together with that of two known *L. donovani* genes - *c-lpk2*, encoding a homolog of the catalytic subunit of cAMP-dependent protein kinase, and *mkk*, encoding a mitogen-activated protein kinase kinase homolog - was studied during the promastigote- amastigote transition in cells *in vitro*. The highest expression of *P9*, *c-lpk2* and *mkk* was found in the promastigote form, whereas *A14* was preferentially expressed in amastigotes. These expression patterns were confirmed under *in vivo* conditions: northern blots using RNA of amastigotes collected from spleens of hamsters infectedwith *L. donovani* showed that *A14* was abundantly expressed in amastigotes but at very low levels in promastigotes, whereas for *P9*, *c-lpk2* and *mkk* the opposite was observed.

Links

Genomic projects on various *Leishmania* species are currently underway; for information see the *Leishmania* genome network.

Reporter's comments

Duncan *et al*. report the discovery of two new *L. donovani* genes that are differentially expressed during promastigote-amastigote differentiation, a process required for infection of mammalian hosts. Thus, these genes are good candidates to be targeted in therapies aimed at blocking parasite development after infection. An expression analysis does not necessarily prove a function for these two genes in differentiation, however, and it would have been more conclusive if the authors had constructed *L. donovani* knockouts to confirm their involvement. The light-microscopic analysis of morphological changes during promastigote-amastigote differentiation also included in the paper illustrates the complexity of this developmental process, and this complexity implies that many genes and/or gene families are involved. The availability of *Leishmania* genome sequences, large-scale DNA microarray analyses using RNA prepared from promastigote and amastigote forms, and the construction of a comprehensive series of knockouts should eventually provide information for drug discovery and for developing strategies to arrest *Leishmania* infection and cure infected humans.

Table of links

Parasitology Research

Leishmania genome network

References

1. Duncan R, Alvarez R, Jaffe CL, Wiese M, Klutch M, Shakarian A, Dwyer D, Nakhasi HL: Early response gene expression during differentiation of cultured *Leishmania donovani*. Parasitol Res. 2001, 87: 897-906. 0932-0113