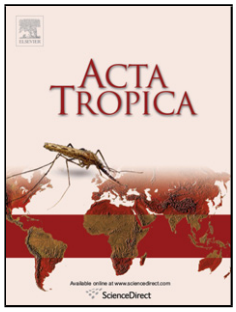

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PII: S0001-706X(16)30108-5
DOI: http://dx.doi.org/doi:10.1016/j.actatropica.2016.03.018
Reference: ACTROP 3890

To appear in: *Acta Tropica*

Received date: 3-2-2016
Revised date: 9-3-2016
Accepted date: 14-3-2016

Please cite this article as: Rhaiem, Rafik Ben, Houimel, Mehdi, Targeting Leishmania major parasite with peptides derived from a combinatorial phage display library.Acta Tropica http://dx.doi.org/10.1016/j.actatropica.2016.03.018

Targeting *Leishmania major* parasite with peptides derived from a combinatorial phage display library

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ABSTRACT

Cutaneous leishmaniasis (CL) is a global problem caused by intracellular protozoan pathogens of the genus *Leishmania* for which there are no suitable vaccine or chemotherapy options. Thus, *de novo* identification of small molecules binding to the *Leishmania* parasites by direct screening is a promising and appropriate alternative strategy for the development of new drugs. In this study, we used a random linear hexapeptide library fused to the gene III protein of M13 filamentous bacteriophage to select binding peptides to metacyclic promastigotes from a highly virulent strain of *Leishmania major* (Zymodeme MON-25; MHOM/TN/94/GLC94). After four rounds of stringent selection and amplification, polyclonal and monoclonal phage-peptides directed against *L. major* metacyclic promastigotes were assessed by ELISA, and the optimal phage-peptides were grown individually and characterized for binding to *L. major* by monoclonal phage ELISA. The DNA of 42 phage-peptides clones was amplified by PCR, sequenced, and their amino acid sequences deduced. Six different peptide sequences were obtained with frequencies of occurrence ranging from 2.3% to 85.7%. The biological effect of the peptides was assessed *in vitro* on human monocytes infected with *L. major* metacyclic promastigotes, and *in vivo* on susceptible parasite-infected BALB/c mice. The development of cutaneous lesions in the right hind footpads of infected mice after 13 weeks post-infection showed a protection rate of 81.94