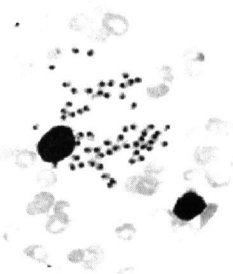
CYTED-RIMLEV



WORKSHOP ON CANINE VISCERAL LEISHMANIASIS

CPqGM-FIOCRUZ (SALVADOR, BA, BRAZIL)

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Proteomic analysis as a tool to identify macrophage targets for anti-*Leishmania* chemotherapy.

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The experimental murine model of leishmaniasis has been widely used to characterize the immune response against *Leishmania*. CBA mice develop severe lesions, while C57BL/6 present small chronic lesions under *L. amazonensis* infection. Employing a transcriptomic approach combined with biological network analysis, the gene expression profiles of C57BL/6 and CBA macrophages, before and after *L. amazonensis* infection in vitro, were compared. These strains were selected due to their different degrees of susceptibility to this parasite. In addition, CBA mice are known to be resistant to infection by *L. major*, yet susceptible to *L. amazonensis*. Moreover, CBA macrophages control *L. major* infection while are permissive to *L. amazonensis*. These findings open the possibility to use these infection models to identify markers, as well as chemotherapeutic targets for the control of the *Leishmania* infection. Using transcriptomic approach combined with biological network analysis, we found that macrophages from resistant mice were shown to be involved in the macrophage pathway of activation. Microarray analysis does not provide comprehensive information with respect to several modulations that occur during infection, observable only at the proteomic level. Employing a proteomic approach, we compared the levels of differential protein expression by CBA macrophages infected with *L. major* or *L. amazonensis* after six and 24 hours of infection. Protein extracts were obtained to characterize peptides using multi-dimensional liquid chromatography in conjunction with tandem mass spectrometry (LC-MS/MS) analysis. A total of 162 proteins were found to be modulated by macrophages infected with *L. amazonensis* in comparison to those infected by *L. major*. Using biological network analysis, differentially expressed proteins were organized in networks and those with greater degrees of differential expression in infected macrophages were found to be mainly involved in cellular metabolism and grouped into a cellular development biological network. This is the first report that used a proteomic approach that describe parasite species modulating proteins involved in cell metabolism during the initial events of *Leishmania*–macrophage interaction. These findings suggest that the differentially expressed proteins likely play a pivotal role in determining the course of infection, as well as can be used as novel targets in *Leishmania* infection for chemotherapeutic intervention.