Leptospira interrogans: From Post-Genomics to Vaccine Targets

<u>Nascimento, ALTO</u>^{1,2}, Oliveira, TR¹, Atzingen, MV^{1,2}, Vieira, ML^{1,2}, Oliveira, R^{1,2}, Longhi, MT¹, Andrade, DM¹, Morais, ZM³, Vasconcellos, SA³

¹Centro de Biotecnologia, Instituto Butantan, São Paulo, Brazil; ²Doutorado Interunidades em Biotecnologia, Instituto de Ciências Biomédicas, USP, São Paulo, Brazil; ³Faculdade de Medicina Veterinária e Zootecnia and ⁴Instituto de Medicina Tropical, USP, São Paulo, Brazil <u>tabet@butantan.gov.br</u>.

Leptospirosis is a worldwide zoonosis of human and veterinary concern. The advent of genomics is allowing us to search for conserved antigens and to test their ability to induce protective immune response. Our purpose is to explore the genome sequences of *L. interrogans* and to select new antigen candidates based on cellular localization and lipidation-tag prediction. Using this approach and DNA recombinant techniques we identified novel leptospiral adhesins that are conserved among pathogenic serovars. One of them, named Lsa21, is only expressed in virulent strains, present during human infection and is probably a novel virulence factor of Leptospira. In addition, we identified proteins that are capable to stimulate human umbilical vein endothelial cells (HUVECS) and are expressed during experimental infection in hamsters. Two recombinant proteins MPL17 and MPL21 were recognized by antibodies present in serum samples of individuals diagnosed with leptospirosis as evaluated by ELISA. Most important, the specificity of this assay was 95.5% (MPL17) and 80.6% (MPL21) when serum samples of other febrile illness, such as dengue and malaria were tested. Although preliminary, the immunization/challenge assays in Golden Syrian hamster showed that one protein, rLIC12730, afforded protection against lethal leptospiral inoculation with concomitant raise in antibody titers, suggesting a Th2 response. Our data show that with this strategy we can contribute to the understanding of the leptospiral pathogenesis and to identify immunotargets for vaccine and diagnostic kit development.

Keywords: Leptospira, recombinant protein.

Supported by FAPESP, CNPq, Fundação Butantan