Exploring a link between mycobacteria structure and virulence

C. Silva[1], J. Perdigao[1], E. Alverca[2], A.P. Matos[3], P.A. Carvalho[4],I. Portugal[1], L. Jordao[5*]

1 CPM, URIA, Faculdade de Farmácia da Universidade de Lisboa
2 Instituto Nacional de Saúde Dr Ricardo Jorge (INSA), DAS
3 Serviço de Anatomia Patológica, Centro Hospitalar de Lisboa Central, Hospital Curry Cabral
4ICEMS, Departamento de Bioengenharia, Instituto Superior Técnico, Universidade Técnica de Lisboa,
5 INSA, DDI
*corresponding author maria.jordao@insa.min-saude.pt

Tuberculosis (TB) is a major health problem. The emergence of multidrug resistant (MDR) Mycobacterium tuberculosis (Mtb) isolates confounds treatment strategies. In Portugal, cases of MDR-TB are reported annually with increased incidence noted in Lisbon. The majority of these MDR-TB cases are due to closely-related mycobacteria known collectively as Lisboa family and Q1 cluster. The genetic determinants linked to drug resistance have been exhaustively studied resulting in the identification of family and cluster specific mutations. Nevertheless little is known about other factors involved in drug resistance development. Here we focused on the study of morphological and structural features of Mtb isolates, collected during 2008-2009 in Lisbon, in order to complement the genetic analysis. For this propose scanning and transmission electron microscopy techniques were used. Particular attention was given to Lisboa family and Q1 cluster isolates since together they account for the majority of reported MDR-TB cases. This analysis allowed the identification of structural differences, such as cell envelope thickness, between Mtb clinical isolates, which are correlated with antibiotic resistance. The infection of human monocyte derived macrophages allowed us to document the relative selective advantage of Lisboa family isolates over other circulating Mtb isolates.