Dimercaptosuccinic acid in combination with carbapenems against strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* producing metallo-ß-lactamase in a murine peritonitis model

Patrice Nordmann[1,2,*] , Sorraya Herrera-Espejo [3] , Maxime Bouvier[1], Laurent Poirel [1,2], and Maria Eugenia Pachon Ibanez [3]

1. Medical and Molecular Microbiology, Faculty of Science and Medicine, University of Fribourg, Fribourg, Switzerland

2. Swiss National Reference Center for Emerging Antibiotic Resistance (NARA), University of Fribourg, Fribourg, Switzerland

3. Division of Infectious Diseases, Microbiology and Parasitology, Instituto de Biomedicina de Sevilla, IBiS/Hospital Universitario Virgen Macarena/CSIC/Universidad de Sevilla,Sevilla, Spain

Background: Carbapenemase-producing *Pseudomonas aeruginosa* and *Acinetobacter baumannii* represent a major therapeutic challenge for present and future of infectious diseases. The activity of metallo-carbapeneamses (MBLs) requiring zinc at their catalytic site, could be inhibited in vitro by meso-dimercaptosuccinic acid (DMSA), a heavy metal chelator already widely used for treating lead intoxication.
Objectives: To evaluate the activity of carbapenems (meropenem) alone or combined with DMSA against MBL-producing in a severe murine peritotinitis model.
Methods: Clinical strains of *P.aeruginosa* producing the MBLs NDM-1, or VIM-2 and of *A. baumannii* producing the MBLs NDM-1 and NDM-5 were used Infected mice were treated intraperitoneally for 24 h with meropenem, (300 mg/kg/q2h , with DMSA (200 mg/kg/q4 h) or their combination. Bacterial counts in spleen and blood were assessed at 24 h.
Results: Those preliminary results indicated that DMSA may have a significant activtiy for recovering susceptibility to meropenem when resistance due carbapenems is due to carbapenemase production is due to MBLs. When resistance to carbapenems is of high levels resulting from assocation of MBL expresssion and outermembrane permeabilty defect (OprD deficiency in the *P .aeruginosa* strain producing NDM-1) the effect of DMSA is evidences.
Conclusions: DMSA may restore the activity of carbapenems against MBL-producing strains in *P.aeruginosa* and *A. baumannii* when MBL expression is the main (or the only) mechanism of resistance to carbapenems.