PLB46D
Paper Poster Session
Late breaker session: Other

Additive beneficial effects of soluble CD6 forms and bactericidal antibiotics in experimental polymicrobial sepsis

Mario Martínez Florens*[1]

[1]*Institut D´investigacions Biomediques August Pi I Sunyer, Immune Receptors of the Innate and Adaptive System, Barcelona, Spain*

Background:

The soluble form of the scavenger-like human CD6 lymphocyte surface receptor (shCD6) has been shown to bind to pathogen-associated molecular patterns present in Gram-positive or -negative bacteria, and to be time- and dose-dependent effective when infused in mouse models of monobacterial-induced sepsis of intraabdominal origin. The aim of the present work was to demonstrate the efficacy of shCD6 in the prevention and treatment of polymicrobial sepsis caused by cecal ligation and puncture (CLP).

Material/methods:

- Sepsis was induced in pathogen free male C57BL/6 mice 8-10 weeks old (20-25g). Mice were anesthetized with ketamine and xylazine cocktail. Afterwards the cecum was movilizzed, ligated below the ileocecal valve, and puncture twice with a 21 gauge needle to induce polymicrobial peritonitis with a 90-100% of letality on the first 48h. The abdominal wall was closed in two layers. After surgery, mice were administrated with 1 mL physiologic saline solution.
- Chemokine serum levels were analyzed following the manufacturers indications by ELISA method.
- Infection with hepatotropic recombinant adeno-associated virus (AAV) expressing a recombinant soluble murine CD6 form or Luciferase.

Results:

- The intraperitoneal prophylactic or therapeutic of 1,25 mg/kg rshCD6 administration improves survival rate on 40% and 25% respectively and it acts in a dose and time dependent way on CLP septic shock model. Likewise either prophylactic or therapeutic treatments decreases significantly the proinlflamatory-chemokine serum levels on the first 24h, and dicreases also the bacteremia levels.
- The intraperitoneal antibiotic administration has similar effects like single treatment than the rshCD6 administration. On the other hand, there is and additive effect when they are administered like combinated compounds.
- The intravenous therapeutic of 1,25 mg/kg rshCD6 treatment improves survival rate delaying its administration improving its therapeutical potential.
- Mice transduced with AAV expressing soluble murine CD6 (smCD6) two weeks before CLP-induction showed significant higher survival rates than those transduced with control empty AAV

Conclusions:

Soluble CD6 has been shown to display *in vitro* and *in vivo* beneficial effects on survival rate, decrease of pro-inflammatory cytokine release and bacteremia levels. The administration of rshCD6 and broad spectrum antibiotic (Imipenem) like combined compounds has additive effects on survival rate in a polimicrobial septic shock model. Mice transduced with AAV expressing smCD6 two weeks before CLP-induction showed significant higher survival rates than those transduced with control empty AAV