Introduction

Group B streptococcus (GBS) is one of the leading agents of invasive infection in adults ≥ 65 years old and responsible for more than 50% of all deaths in the elderly [1]. The world population is rapidly aging along with the burden of GBS disease [2]. The increased predisposition of infection in the elderly has age as a common dominator, that comprises several associated factors such as pre-existing comorbidities, immunosenescence, and decline of physical barriers to pathogens. With a clinical presentation divergent from young adults and frequently muted, their clinical status quickly deteriorates from sepsis to septic shock [2, 4]. Despite intensive research on sepsis, clinical translation has been considerably unsuccessful due to the use of young animal models rendering mismatch information that does not translate the pathophysioloogy of sepsis among the older population [2].

Aim

In elderly population pneumonia is a preferential infection route to cause sepsis. In this context, we intend to established an animal model reproducing the clinical and cardinal features of sepsis acquired by pneumonia in elderly population and to determine the time window for pharmacological intervention that resembles to the clinics in humans.

Methodology

Figure 1. Experimental design and score system. a) C57BL/6 mice (22 months of age) were randomly distributed into control (n=1) and inoculated (n=8) groups. (a) C57BL/6 mice from the infected group were intranasally inoculated with GBS (10⁵ CFU) and euthanized when reaching human endpoints or in a time course interval from 24h to 72h post-inoculation. In vivo measurements of lactate (Lac) levels and b) sepsis clinical score were assessed before inoculation and in a time course interval from 24h to 96h post-inoculation. (c) Organs from C57BL/6 mice were harvested to confirm GBS dissemination, to evaluate MPO activity, levels and histopathological evidence of tissue damage.

Results

- Intranasal inoculation with GBS decreases survival rate and increases blood lactate levels in elderly C57BL/6 animals

Figure 2. Effect of GBS BM110 WT intranasal inoculum of C57BL/6 22 months old males on (a) survival rate (b) clinical score and (c) blood lactate. Each C57BL/6 male (n=5) was intranasally inoculated with 10⁵ CFU of GBS BM110. (a) Kaplan-Meir survival curve monitored for 96h post-inoculation. Numbers in parentheses represent males that reached human endpoints versus total inoculated. (b) The clinical score*Panel (c) In vivo measurements of lactate levels were assessed 48h prior to inoculation (baseline) and in a time course interval from 24h to 96h post-inoculation. Data represent the mean±SEM. Each symbol represents data from individual males. The horizontal line indicates the mean. Comparisons between control and inoculated groups with unpaired t-test with Welch’s correction. Significance when p<0.05.

Conclusion

- In conclusion, our preliminary results suggest that GBS BM110 intranasal inoculation can induce an elderly murine pneumonia model of sepsis with a time point of sepsis onset in the interval between 24h to 48h post-inoculation.

References


Figure 3. Time course of (a) GBS colonization and (b) IL-1β levels at lungs, liver, brain and kidney were assessed from 24h to 96h post-inoculation. Data represent the mean±SEM. Each symbol represents data from individual males. The horizontal line indicates the mean.

Figure 4. Organ histopathology of 22 months old male C57BL/6 control (left panel) and intranasally inoculated with GBS BM110 at the time interval 48h (middle panel and right panel) mice developed by Hematoxylin-eosin staining. Enlarged areas of the figures are shown on the limited squares within each figure (160x magnification; panel Lung B 40x magnification). 40x magnification.

- Intranasal inoculation with GBS leads to a systemic bacterium spread from the nasopharynx to the major organs and to an increase of pro-inflammatory cytokine, IL-1β, levels in the time point 48h post-inoculation.