of Gram-negative bacterial species and the infection sites. The PK/PD analysis for 3-dimensional preparations of differentiated normal cardiomyocytes at concentrations up to 100 µM prodrug. After 8 hours, medium was replaced with fresh medium without drug. The triphosphates (TPs) of selected prodrugs were measured in phytohaemagglutinin stimulated human lymphocyte cultures up to 100 µM prodrug. The formation and half-lives (t1/2) of TPs were determined in phytohaemagglutinin stimulated human lymphocyte cultures. The EC90% at concentrations (EC90) were observed at the latest sampling time point (up to 10 to 50%) using the MIC in CAMHB.

Conclusion. The PK/PD analysis using murine thigh/leg infection models showed that ID-CAMHB is the appropriate media for MIC determination for the prediction of in vivo efficacy irrespective of infection sites and bacterial species.

Methods. Human and murine lung levels of TPs were determined at single dose plasma PK parameter ranges include: Cmax 2.6–77 mg/L, AUC0–T 93–4046 ng·h/mL. Single dose plasma PK was determined in groups of three mice after IP injection. Treatment dose range was 0.016 – 64 mg/kg, given once by IP injection 2 hours after infection. The Table below shows survival, CFU gram of lung, and change in CFUs (Standard Error of the Mean (S.E.M.) from baseline by treatment or vehicle group.

Results. Four different mAb-producing hybridoma clones were generated IgM that bound to AB and KPC. 40–800 µg/mL of mAb reduced susceptibility to AB or KPC in vitro. Two of mAb (25 µg/mL each) resulted in protecting A549 cells from AB- or KPC-induced damage by ~80% vs. cells incubated with isotype-matching Ab (P < 0.05). Finally, one of the mAb resulted in 70% or 100% long-term survival of mice infected with lethal doses of KPC or AB, respectively (P < 0.05).

Conclusion. We used Candida Hyr1p to generate cross-protective mAb against MDR AB and KPC. Our results warrant the further development of these mAb as novel immunotherapeutics against MDR GNB.

Disclosures. All authors: No reported disclosures.

1527. Novel Immunization Strategies Against Multi-drug-resistant Gram-negative Bacteria

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Session: 167. Preclinical Study with New Antibiotics and Antifungals

Friday, October 6, 2017: 12:30 PM

Background. Healthcare-related infections due to multi-drug-resistant (MDR) Gram-negative bacteria (GNB) such as Acinetobacter baumannii (AB) and carbapenemase producing Klebsiella pneumoniae (KPC) are associated with high mortality rates. New methods to prevent or treat these infections are needed. Cándidahantigen Hyr1p is predicted to share structural and sequence homology with the hemagglutinin/hemolysin protein (FhA) and siderophore-binding protein of GNB including AB and KPC, respectively. Indeed, active and passive immunization using Hyr1p as a target protect against AB infections in mice. Thus, we attempted to develop protective monoclonal antibodies (mAb) and test efficacy against AB and KPC in vitro and in vivo.

Methods. Murine hybridomas were generated from Balb/c mice after vaccination with recombinant Hyr1p. The concentration and identification of the collected mAbs were determined using Bradford and SDS-PAGE. Binding ability of mAb was tested against AB and KPC in vitro using studies on the ability of these mAbs to kill KPC and AB were tested by quantitative culturing. The ability of these mAbs to protect from AB- or KPC-mediated alveolar epithelial cell (A549) damage was studied with 3H-release assay. The efficacy of mAb in protecting against AB- or KPC-induced pneumonia was studied in neutrophilic or immunocompetent CD1 mice by administering 30 µg of mAb (i.p.), on Day 1 + 4 and 7, relative to infection, respectively. Survival of mice served as an endpoint.

Results. Four different mAb-producing hybridoma clones were generated IgM that bound to AB and KPC. 40–800 µg/mL of mAb reduced susceptibility to AB or KPC in vitro. Two of mAb (25 µg/mL each) resulted in protecting A549 cells from AB- or KPC-induced damage by ~80% vs. cells incubated with isotype-matching Ab (P < 0.05). Finally, one of the mAb resulted in 70% or 100% long-term survival of mice infected with lethal doses of KPC or AB, respectively (P < 0.05).

Conclusion. We used Candida Hyr1p to generate cross-protective mAb against MDR AB and KPC. Our results warrant the further development of these mAb as novel immunotherapeutics against MDR GNB.

Disclosures. All authors: No reported disclosures.

1526. Discovery of a Series of Potent and Selective Nucleotide Prodrug Inhibitors of Respiratory Syncytial Virus (RSV) Replication

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Background. The objective of this study was to demonstrate the effect of iclaprim, a new generation diaminopyrimidine, in a neutrophilic rat lung infection model with methicillin resistant Staphylococcus aureus (MRSA).

Methods. S. aureus strain AH1252, a thymidine knockout of the MRSA wild type ATCC strain, was utilized for this study. The bacterial strain was diluted in a 2% alginate buffer, which was added dropwise in a ratio of 1:5 to 100 mM MgCl2 to form alginic beads. The alginic beads reduce the efficacy of bacterial clearance similar to that seen in the cystic fibrosis population. A 5.25 x 10^7 bacterial inoculum was administered intracellularly to 3 rats per group. In vitro studies on the ability of these mAbs to kill KPC and AB were tested by quantitative culturing. The ability of these mAbs to protect from AB- or KPC-mediated alveolar epithelial cell (A549) damage was studied with 3H-release assay. The efficacy of mAb in protecting against AB- or KPC-induced pneumonia was studied in neutrophilic or immunocompetent CD1 mice by administering 30 µg of mAb (i.p.), on Day 1 + 4 and 7, relative to infection, respectively. Survival of mice served as an endpoint.

Results. Four different mAb-producing hybridoma clones were generated IgM that bound to AB and KPC. 40–800 µg/mL of mAb reduced susceptibility to AB or KPC in vitro. Two of mAb (25 µg/mL each) resulted in protecting A549 cells from AB- or KPC-induced damage by ~80% vs. cells incubated with isotype-matching Ab (P < 0.05). Finally, one of the mAb resulted in 70% or 100% long-term survival of mice infected with lethal doses of KPC or AB, respectively (P < 0.05).

Conclusion. We used Candida Hyr1p to generate cross-protective mAb against MDR AB and KPC. Our results warrant the further development of these mAb as novel immunotherapeutics against MDR GNB.

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