Results. Echos from 29 KD, 30 iKD, 28 febrile, and 27 healthy patients were reviewed. The initial echo of 41% of KD and 43% of iKD groups met echo criteria for diagnosis of iKD and 55% and 57%, respectively, had CA dilation or aneurysm. Among febrile patients, 7 (25%) had an abnormal CA size of which 4 (14%) met echo criteria for iKD. In the healthy patients, four (15%) had abnormal CA of which two (7.4%) met echo criteria for iKD. Among patients with a positive echo read, the median number of readers who read a CA as dilated was similar for each group. Furthermore, of all patients meeting echo criteria for iKD, 90% had aneurysmal CA dilatation.

Conclusion. Although CA abnormalities diagnostic of KD were commonly present at time of diagnosis in patients with KD or iKD, these findings were also present in some healthy and some febrile patients. Diagnosis of iKD in febrile children using echo criteria may result in an over-diagnosis of KD.

Disclosures. **All authors:** No reported disclosures.

644. How Antibody Isotype Affects Anti-Capsular Antibody Protection Against Carbapenem-Resistant *Klebsiella pneumoniae* Infection

Michael Motley, BS; Elizabeth Diago-Navarro, PhD and Bettina C. Fries, MD, FIDSA[1]; [1]Department of Medicine (Division of Infectious Disease), Stony Brook University Hospital, Stony Brook, New York

Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. New monoclonal antibodies (mAb) are being developed against infectious disease. However, antibody isotype is an important consideration, as different IgG variants interact with different Fc receptors and differ in avidity due to Fc structural differences. Our recent anti-capsular murine IgG_3 mAb 17H12 was shown to mediate protection against clade 2 ST258 carbapenem-resistant *Klebsiella pneumoniae* (CR-*Kp*). However, our previous studies showed an IgG_1 mAb to perform better than an IgG_3 mAb in mediating infection against a carbapenem-sensitive *Kp* isolate. Therefore, we sought to determine whether differences in antibody isotype contribute to differences in protection against CR-*Kp* infections.

Methods. We treated IgG_3-producing 17H12 parent hybridomas with LPS and IL-4 to generate isotype variants which were subcloned by sib selection. This yielded an IgG_1-producing clone which was sequenced and compared with the complementary-determining region (CDR) sequence of the parent. We then compared binding kinetics of the two mAbs to CR-*Kp* capsular polysaccharide by ELISA. Opsonophagocytosis by macrophages was compared between CR-*Kp* strains pre-opsonized with the IgG_1 or IgG_3 mAb. Finally, mice were infected intratracheally with CR-*Kp* pre-opsonized with either IgG_1 or IgG_3 mAbs and organ burdens were compared after 24 hours.

Results. Sequence analysis showed the IgG_1 antibody sequence to be identical to the 17H12 IgG_3 parent. Interestingly, the IgG_1 antibody bound at nanomolar affinity, but 10-fold less than the parent, suggesting loss of affinity or avidity. IgG_1-opsonized CR-*Kp* were phagocytized by macrophages 40–60% less than IgG_3-opsonized CR-*Kp*. However, both antibodies performed comparatively *in vivo*, reducing bacterial burden in the lung, liver and spleen of intratracheally infected mice by an average of 3 log.

Conclusion. The IgG_1 isotype variant of mAb 17H12 appears to have inferior binding and *in vitro* efficacy when compared with its IgG_3 parent, despite having the same CDR region. However, *in vivo* efficacy is unaffected in our model. Future studies plan to further analyze the differences in binding kinetics between these two antibodies, as well as their ability to bind pro and anti-inflammatory Fc Receptors and mediate the host response to CR-*Kp* infection.

Disclosures. **All authors:** No reported disclosures.

645. Mucosal-Associated Invariant T cells in Renal Tissue From Patients With Recurrent Urinary Tract Infections

Matty Terpstra, MD[1,2]; Marjan Sinnige, Bsc[2]; Ester Remmerswaal, Dr. Ing.[2]; Michiel V. Aalderen, MD PhD[2]; Jesper Kers, MD PhD[3,4]; Frederike Bemelman, MD, PhD[1] and Suzanne E. Geerlings, MD, PhD[5]; [1]Renal Transplant Unit, Academic Medical Center, Amsterdam, Netherlands, [2]Department of Experimental Immunology, Academic Medical Center, Amsterdam, Netherlands, [3]Department of Pathology, Academic Medical Center, Amsterdam, Netherlands, [4]Van 't Hoff Institute for Molecular Sciences (HIMS), University of Amsterdam, Amsterdam, Netherlands, [5]Department of Infectious Diseases, Academic Medical Centre, Amsterdam, Netherlands

Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. Mucosal associated invariant T (MAIT) cells are innate-like T-cells involved in the antibacterial and fungal response by recognizing riboflavin metabolites produced by these organisms. MAIT cells are present in blood and are highly abundant in the mucosa of the liver, lungs and intestines. In murine models of urinary tract infection (UTI), MAIT cells appear to migrate to the bladder and decrease the bacterial load. It is however unknown whether MAIT cells reside in the human urogenital tract and renal tissue and whether they play a role in the first-line defense against (recurrent) UTI (RUTI).

Methods. We used a fluorescently labelled MR1-tetramer in conjunction with 14-color flowcytometry to identify and characterize MAIT cells in renal allografts after allograft failure caused by RUTI ($n = 6$) or rejection ($n = 6$) and in healthy kidney tissue surgically removed because of renal cell carcinoma (adjacent nontumorous tissue) ($n = 5$).

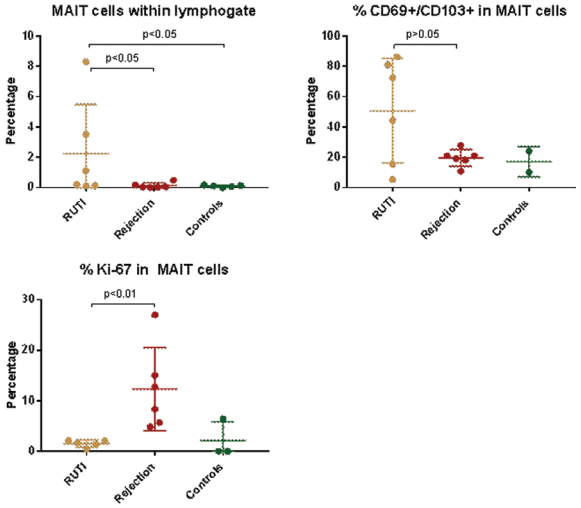
Results. The mean percentage of MAIT cells within the lymphogate was higher in the RUTI kidneys (2.24%) compared with the rejection kidneys (0.14%) and the control kidneys (0.11%) ($P < 0.05$).

Characterization of MAIT cells was impossible in some control samples due to MAIT cells counts <25 (predefined cutoff value), therefore the control group was excluded from further statistical analysis.

MAIT cells in RUTI kidneys appear to have a less activated profile compared with the rejection kidneys, with a lower expression of Ki67 ($P < 0.01$). Though the expression of the tissue resident marker CD69/CD103 was higher in 4/6 RUTI kidneys, this difference was not significant.

Conclusion. MAIT cells are present in renal tissue that is or has been subjected to an immunologic response. MAIT cells in RUTI kidneys display a more quiescent and in some samples more tissue resident phenotype than MAIT cells in rejection kidneys. These findings may suggest that (I) MAIT cells play a role in the first-line defense in the kidney and (II) that after RUTI, MAIT cells remain in renal tissue in a quiescent state. We postulate that this might be favorable in case of a second hit from an uropathogen.

Figure 1. Presence and characterization of MAIT cells in renal tissue.



Disclosures. **F. Bemelman**, Astellas: We received an unrestricted grant from Astellas to establish a Biobank for patients with renal diseases. The samples described in this abstract are obtained from this Biobank., Grant recipient.

646. Activated Macrophages as Pathogenesis Factors in Ebola Virus Disease in Humans

Anita McElroy, MD, PhD[1,2,3]; Punya Shrivastava-Ranjan, PhD[2]; Jessica Harmon, MS[2]; Roosecelis Martines, MD, PhD[2]; Luciana Silva-Flannery, PhD[2]; Timothy Flietstra, MS[2]; Colleen Kraft, MD, MSc[3]; Aneesh K Mehta, MD, FIDSA, FAST[3]; G. Marshall Lyon III, MD[3]; Jay Varkey, MD[3]; Bruce Ribner, MD, MPH, FIDSA, FSHEA[3]; Stuart Nichol, PhD[4]; Sherif Zaki, MD/PhD[2] and Christina Spiropoulou, PhD[2]; [1]University of Pittsburgh, Pittsburgh, Pennsylvania, [2]US CDC, Atlanta, Georgia, [3]Emory University School of Medicine, Atlanta, Georgia, [4]Viral Special Pathogens Branch, Centers for Disease Control and Prevention, Atlanta, Georgia

Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM

Background. Ebola virus disease (EVD) is associated with elevated cytokine levels that are more pronounced in fatal cases. This type of hyperinflammatory state is reminiscent of other inflammatory disorders, such as macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH). These are both part of a spectrum of rheumatologic phenomena characterized by both macrophage and T-cell activation. These disorders can be secondary to infection, malignancy, underlying rheumatologic disorder, or, paradoxically, immune deficiency.

Methods. Two cohorts of EVD patients were evaluated with respect to common plasma markers of HLH/MAS. Immunohistochemistry was used to evaluate tissue macrophages and viral antigens in various tissues from fatal cases of EVD.

Results. Neither fibrinogen nor soluble IL-2 receptor were significantly different between fatal and nonfatal cases. However, elevated levels of triglycerides, ferritin and sCD163, a marker of macrophage activation were noted in patients with EVD and they correlated with disease severity and a fatal outcome. Furthermore, significant immunoreactivity for CD163 + cells in host tissues was observed in fatal cases, predominantly in areas of extensive immunostaining for EBOV antigens.

Conclusion. These data suggest that host macrophage activation contributes to EVD pathogenesis and that directed anti-inflammatory therapies could be beneficial in the treatment of EVD.

Disclosures. **All authors:** No reported disclosures.

647. Characterization and Development of Human Monoclonal Antibodies to Pneumococcal Serotype 3

Rachelle Babb, PhD[1] and Liise-Anne Pirofski, MD, FIDSA[2]; [1]Department of Medicine, Einstein College of Medicine, Bronx, New York, [2]Department of Medicine, Division of Infectious Diseases, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York

Session: 65. Pathogenesis and Immune Response
Thursday, October 4, 2018: 12:30 PM