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groups. Concerning to liver damage, any of the evaluated immune cell parameters displayed association with fibrosis or hepatitis severity.

Conclusion: Although in chronic HCV infection the lymphocyte frequency was not modified, an altered T cell differentiation profile was evident. The co-infected condition distorted lymphocyte frequencies and enhanced T cell activation. This deteriorated immune profile may condition T cell response against antigens, including vaccines.

UMP. 010

Effect of iron-limiting conditions on virulence gene expression in pathogenic Leptospira spp.

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Background: Leptospirosis is considered an important re-emerging disease of worldwide distribution, and aetiologically caused by pathogenic *Leptospira* species. Iron, with its wide redox potential, is inherently important for the growth of most living organisms. Consequently, attempts by hosts to limit unbound iron result in pathogens developing systems to overcome such conditions which invariably reflects in increased virulence. In this study, the effects of iron-limiting conditions on the expression of virulence-associated genes in *Leptospira interrogans* Portlandvere and *Leptospira borgpetersenii* Jules were examined.

Methods & Materials: To assess the effect of iron-limitation, bacteria in EMJH were exposed to 10, 20 and 40 μM bipyridyl (metal chelator) at each of three temperature conditions, 30 °C, 37 °C, and 30 °C upshifted to 37 °C. Gene expression was analyzed by endpoint PCR and quantitative RT-PCR in biological replicates.

Results: Endpoint RT-PCR indicated marginally higher transcription among Portlandvere compared to Jules grown under iron-limitation at upshift temperature and similar transcription rates between both species grown at 30 °C and 37 °C. Differential *lenA*, *sph2*, *lipL41*, *lipL32* and *loa22* expressions in iron-limited Jules and Portlandvere highlighted the integration of the pathogens' response to temperature and iron-limiting conditions. In particular, changes in iron availability resulted in increased *loa22* expression in both L. Portlandvere ($p = 0.02$) and L. Jules ($p = 0.05$). Further, reduced iron conditions resulted in concomitant increases in *sph2* and *lipL32* in Jules at 37 °C, and a decrease in *lipL41* transcripts in both L. Jules and L. Portlandvere at 37 °C.

Conclusion: These data suggest that there is tight co-regulation of virulence genes by iron and temperature, and that species differences could account for some differences in gene expression in L. Jules and L. Portlandvere in iron-limiting conditions.

UMP. 011

Role of binge ethanol consumption in the pathogenesis of sepsis

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Background: Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Comorbid conditions, as acute ethanol exposure, typically suppresses innate immunity and increases the risk of mortality in patients with sepsis. However, the interrelationship between the acute use of ethanol on neutrophil migration during an acute inflammatory response remains uncertain. Thus, in the present study we addressed the role of acute ethanol exposure in the course of sepsis and in neutrophil migration to the inflammatory site.

Methods & Materials: Adult female Swiss mice were used. Sepsis was induced by cecal ligation and puncture model (CLP). A triple puncture was made using a 26-gauge and 21-gauge, respectively, to induce sub-lethal sepsis and moderate sepsis. Animals were randomly divided in groups. Sub-lethal sepsis: Water + Sub-Lethal Sepsis Group and Ethanol + Sub-Lethal Sepsis Group. Moderate sepsis: Water Group; Ethanol Group; Water + Moderate Sepsis Group; Ethanol + Moderate Sepsis Group. Ethanol was administered via gavage in a dose of 4 g/kg, 30 minutes before sepsis induction.

Results: Our results demonstrate that animals pretreated with ethanol and submitted to sub-lethal sepsis showed changes in clinical score, but these changes were insufficient to increase the mortality rate. In moderate sepsis model, the Ethanol + Moderate Sepsis Group had a reduction in the migration of total leukocytes and neutrophils to the peritoneal cavity when compared with Water + Moderate Sepsis Group. Moreover, the Ethanol + Moderate Sepsis Group presented reduction in the delta of mean arterial pressure as compared with the others groups. These findings are related to a decrease in the survival rate of these animals, since the groups Water + Moderate Sepsis Group and Ethanol + Moderate Sepsis Group showed, respectively, 60% and 20% survival with changes in clinical score by the end of the evaluation.

Conclusion: Thus, we concluded that acute ethanol exposure alters the outcome of sepsis, with consequent increase in mortality rate and susceptibility to moderate sepsis.

UMP. 012

Targeting Vascular Leakage for Novel Biomarker Diagnosis and Therapy of Severe Pulmonary Infections

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Background: Persistent vascular leakage is a cardinal feature of major and severe infections, such as influenza and associated bacterial superinfections. These infections kill millions of individuals yearly, most commonly from complications affecting the vasculature such as acute respiratory distress syndrome and pulmonary

edema. Newly emerged and re-emerging infections that threaten public health globally, such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and Ebola fever, also involve vascular leakage as an important factor of morbidity and mortality. We hypothesize that using therapy targeting on pathologically important vascular leakage regulators, morbidity and mortality from severe pulmonary infections can be improved by reducing excessive inflammation while not weakening host immune defence against secondary infections.

Methods & Materials: By using monoclonal antibody and knockout mouse model of angiopoietin-like 4 (ANGPTL4), a novel regulator of vascular permeability, we investigated the effects of vascular leakage modulation in mouse models of influenza pneumonia and secondary pneumococcal pneumonia. To further validate our findings in animal and in vitro models, multi-center clinical studies involving hundreds of patient samples from hospitals in China, Singapore, France and Japan were also conducted.

Results: Both viral and bacterial pulmonary infections stimulated the upregulation of ANGPTL4 expression in lung tissue, via a direct IL6-STAT3-mediated mechanism. ANGPTL4 enhances pulmonary tissue leakiness and exacerbates infiltration-induced lung damage. Anti-ANGPTL4 antibody therapy significantly reduced lung edema and protected lung tissue integrity. Surprisingly, while reducing excessive inflammation by restricting immune cell infiltration from blood vessels, anti-ANGPTL4 treatment also enhanced the function of innate immune cells, especially during secondary bacterial infection when the immune defense against bacteria was suppressed by primary influenza infection. Anti-ANGPTL4 treatment thus resulted in significant improvements on immune functions and lung tissue integrity in mice with secondary pneumococcal pneumonia. In our clinical sample analysis, ANGPTL4 has shown great potential as a biomarker to predict the severity of pneumonia, and guide the strategies to triage and treat pneumonia patients.

Conclusion: Improving vascular integrity may provide an effective alternative or adjunctive strategy to combat severe pulmonary infections. ANGPTL4 is a promising target for designing diagnostic biomarker and therapeutic applications for the management of pulmonary infections.

https://doi.org/10.1016/j.ijid.2018.04.3686

UMP. 013

Vimentin-mediated activation of NLRP3 inflammasome in the mice brains infected with human Enterovirus 71

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Background: The severe infection of human enterovirus 71(EV71) is associated with childhood neuropathology. It has been reported that the infection of host cells by EV71 is dependent on the cell surface vimentin (VIM) as an attachment receptor for EV71. Moreover, VIM is identified as a key regulator of NLRP3 inflammasome which is responsible for pyroptosis and autophagy of host cells. Thus, VIM-induced activation of NLRP3 may contribute to the development of severe central nervous system (CNS) infection by EV71. However, the pathogenesis of EV71 CNS infection remains unknown. Therefore, it is important to elucidate the molecular mechanism of EV71 inducing VIM-associated activation of inflammasome in CNS infection.

Methods & Materials: In order to explore whether VIM-mediated activation of inflammasome play an important role in the EV71 CNS infection, the VIM knockout mice (VIM$^{-/-}$, 3 to 5 days old) and the wild-type (WT, same age) infected by using identified strain of EV71 isolated from a pharyngeal swab specimen of a 3-year-old male diagnosed as severe hand-foot-and-mouth disease were detected by RT-PCR. EV71-induced histopathological alterations were also observed. Then, the levels of caspase-1 and IL-1β were examined by ELISA and Western blot to determine the activation of NLRP3 in mice.

Results: As shown in these results, the exhibited limb paralysis rates of VIM$^{-/-}$ mice and WT mice were $(19 \pm 4)\%$ and $(55.7 \pm 7.7)\%$ ($P < 0.05$, n = 30) respectively. The level of viral RNA in VIM$^{-/-}$ mice was lower as compared to that of WT mice ($P < 0.05$, n = 10), and the morphological changes and neurons death in brains of VIM$^{-/-}$ mice were less than that of WT mice. Furthermore, the level of IL-1β and caspase-1 in the CNS was significantly decreased in VIM$^{-/-}$ mice when compared to WT mice ($P < 0.05$, n = 5).

Conclusion: In this report, we demonstrated for the first time that EV71 could activate NLRP3 inflammasome induced by VIM. These might lead to the development of EV71 CNS disease.

https://doi.org/10.1016/j.ijid.2018.04.3687

UMP. 017

Biofilm formation in carbapenemase-producing Pseudomonas spp. and Acinetobacter baumannii clinical isolates

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Background: Biofilm involving infections are difficult to eradicate, mainly because bacteria forming these communities are more resistant to antimicrobials compared to their planktonic counterparts. Among 65-80% of healthcare infections are caused by microorganism that form biofilms in tissues or inanimate surfaces.

An additional concern is present when bacteria are associated with multiple drug-resistant determinants due to the difficulty in its eradication. Multidrug resistant *Pseudomonas* spp. and *Acinetobacter* spp. have arisen as important opportunistic pathogens, and have been described as successful biofilm producers.

The aim of this work was to assess the capability of clinical isolates carbapenemase-producing *Pseudomonas* spp. and *Acinetobacter calcoaceticus-baumannii* complex to produce biofilm in abiotic surfaces.

Methods & Materials: Forty-four non-duplicate carbapenemase-producing isolates were studied: 14 *P. aeruginosa* (bla_{VIM-2} n = 11, bla_{KPC-2} n = 3), 9 bla_{VIM-2}-producing *P. putida*, and 21 bla_{OXA-23}-producing *A. baumannii*. The strains were obtained