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Summary of the 2017 Alcohol and Immunology Research Interest Group (AIRIG) meeting

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Abstract

On June 24, 2017, the 22nd annual Alcohol and Immunology Research Interest Group (AIRIG) meeting was held as a satellite conference during the annual Research Society on Alcoholism (RSA) Scientific Meeting in Denver, CO. The 2017 meeting focused broadly on mechanisms that

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link alcohol to tissue injury and inflammation, and how this research can be translated to improve human health. Two plenary sessions comprised the meeting, which first explored the association between alcohol and trauma/tissue injury, and finished with a discussion of alcohol and mucosal inflammation. The presentations encompassed diverse areas of alcohol research, from effects on the brain, to airway and pulmonary systems, to gut barrier disruption. The discussions also thoughtfully highlighted how current laboratory and clinical research can be used to prevent or treat alcohol-related morbidity and mortality.

Keywords

Alcohol; Inflammation; Trauma; Mucosa; Tissue Injury

Introduction

Nearly six percent of all global mortality can be attributed to alcohol use, including 88,000 deaths in the United States, making it the fourth leading cause of preventable death in the U.S. (National Institute on Alcohol Abuse and Alcoholism, 2017). Alcohol misuse contributes to over 200 different diseases and health injuries, including alcohol dependence, liver cirrhosis, and some cancers (World Health Organization, 2014). It has been shown that binge alcohol ingestion can have noticeable pro-inflammatory immune-modulating effects after only 20 minutes (Afshar et al., 2015b), but the mechanisms that contribute to chronic pathologies remain to be fully understood. The focus of the 2017 AIRIG meeting centered on immune pathways and systems involved in tissue and organ dysfunction and the inflammatory response at mucosal sites following alcohol exposure. Specifically, the meeting was divided into two plenary sessions, the first with oral presentations in the area of alcohol and trauma/tissue injury and the second with oral presentations related to alcohol and mucosal inflammation.

Alcohol and Trauma/Tissue Injury

Dr. Elizabeth J. Kovacs, Director of Burn Research and the Alcohol Research Program in the Department of Surgery at the University of Colorado Denver, and Dr. Joe Wang, Program Director for the Division of Metabolism and Health Effects at the National Institute on Alcohol Abuse and Alcoholism (NIAAA), began the 2017 AIRIG meeting with words of welcome and appreciation for the attendees' dedication to the advancement of alcohol-related immunology research. The welcoming remarks were followed by the first plenary session chaired by Drs. Michael McCaskill (Tulane University) and Philip Roper (Loyola University Chicago), which focused on how alcohol affects tissues and contributes to traumatic injury. Dr. Patricia E. Molina from Louisiana State University Health Sciences Center opened the session with her talk titled "Alcohol-neuroimmune interactions in traumatic brain injury." Traumatic brain injury (TBI) is a debilitating condition in military and civilian populations (Faul, Wald, & Coronado, 2010; French, 2009), characterized by an early and sharp rise in neuroinflammation followed by a protracted secondary wave of sustained neuroinflammation that is associated with lasting neurological and behavioral deficits that include increased incidence of anxiety and depression, stress, and pain

sensitivity, as well as anhedonia and impulse control deficits (Faden, 1993; Riggio, 2011; Werner & Engelhard, 2007). These TBI sequelae promote alcohol abuse in humans through unknown mechanisms (Bombardier, Temkin, Machamer, & Dikmen, 2003; Graham & Cardon, 2008). Because post-TBI alcohol exposure is detrimental to overall recovery through sustained neuroinflammation and excitatory glutamate signaling (Mayeux, Teng, Katz, Gilpin, & Molina, 2015), Dr. Molina's overall aim is to understand the underlying mechanisms leading to escalation in alcohol drinking post TBI. It has been previously shown that modulation of endocannabinoid tone by systemic administration of JZL184, a monoacylglycerol lipase inhibitor that prevents degradation of the endocannabinoid 2-Arachidonoylglycerol (2-AG), is sufficient to attenuate neuroinflammation and improve neurobehavioral recovery (Katz et al., 2015). Therefore, Dr. Molina's group tested the hypothesis that post-TBI endocannabinoid degradation inhibition would improve neurobehavioral outcomes, including escalation of alcohol drinking. Adult male Wistar rats were trained to self-administer alcohol in a thirty-minute, free-choice, two-lever fixed ratio (FR1) operant paradigm and subjected to a mild to moderate "single-hit" TBI produced by fluid percussion. The rats were divided into sham TBI+vehicle, or TBI+JZL184 (16 mg/kg intraperitoneally, delivered thirty minutes post TBI), and allowed to self-administer alcohol for two weeks post TBI before sacrifice and brain collection for biochemical analysis. Results showed that a single injection of JZL184 post TBI decreases motivation to drink, attenuates neuroinflammation, rescues dysregulated glutamatergic signaling, and attenuates neuronal hyperexcitability at the site of injury (Mayeux, Katz, Edwards, Middleton, & Molina, 2017). JZL184-administered TBI animals had significantly improved cognitive performance, significantly attenuated pain sensitivity deficits, and significantly attenuated anxiety-like behavior compared to vehicle-injected TBI animals. These data demonstrate that modulation of endocannabinoid tone post TBI has potential therapeutic benefits that persist throughout the acute recovery period (fourteen days post TBI). Dr. Molina's group speculates that TBI-induced synaptic hyperexcitability at the site of injury may contribute to the development of negative affective behaviors including anxiety-like behavior and escalation of alcohol self-administration post TBI.

Dr. Majid Afshar from Loyola University Chicago presented his work in a talk titled "Alcohol biomarkers to examine organ dysfunction in injured patients." Alcohol misuse occurs in nearly a quarter of trauma patients, contributes to worsening organ dysfunction, and is associated with deleterious outcomes (Afshar, Netzer, Murthi, & Smith, 2015a; Silver et al., 2008). The dysregulated immune response from alcohol persists even after blood alcohol is no longer detectable in critically ill trauma patients (Chen et al., 2013; Fitzgerald et al., 2007; Li, Kovacs, Schwacha, Chaudry, & Choudhry, 2007). Blood alcohol concentration (BAC) does not characterize the drinking patterns of trauma patients and self-report methods cannot be assessed in patients with severe injury. Therefore, it remains a challenge to identify patients with alcohol misuse in a timely manner so that targeted interventions may be provided. The Alcohol Use Disorders Identification Test (AUDIT) is a self-report tool and the current standard for identifying alcohol misuse in trauma settings (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). However, severely injured patients may not be capable of providing AUDITs until much later in their care when the institution of timely interventions may have lapsed. In addition, indirect blood biomarkers, like γ -

Glutamyltransferase (GGT), Mean Corpuscular Volume (MCV), Carbohydrate Deficient Transferrin (CDT), Aspartate Aminotransferase (AST), and Alanine Aminotransferase (ALT) are confounded by age, gender, organ dysfunction, and nonalcohol-related illnesses and have not proven useful in clinical application (Gough et al., 2015). Direct alcohol biomarkers such as Phosphatidylethanol (PEth) show promise to augment current methods in identifying patients with alcohol misuse (Wurst et al., 2015). PEth homologues are a group of phospholipids formed in the red blood cell membrane in the presence of alcohol by phospholipase D. The advantages of using PEth as an alcohol biomarker are: (1) it has a half-life of 3 to 5 days (detectable up to 28 days), and has demonstrated a dose dependent correlation with single use as well as heavy daily drinking patterns; (2) the sensitivity of PEth has greatly improved with recent development and validation of the liquid chromatography-mass spectrometry assay (Schrock, Thierauf, Wurst, Thon, & Weinmann, 2014); (3) PEth is independent of mental status or recall bias, unlike self-report methods such as the AUDIT; and (4) it is not affected by age, sex, race, comorbidities, and organ dysfunction. Dr. Afshar reported that a cutoff of 250 ng/ml demonstrated good negative and positive predictive values for identifying alcohol misuse in critically-ill patients. Ongoing studies in Dr. Afshar's laboratory aim to provide additional validation for the clinical application of PEth in the critically-ill, and as a tool to better identify alcohol misuse and patients at-risk for complications and organ dysfunction.

Dr. Lisbeth A. Boule, a post-doctoral fellow in Dr. Elizabeth J. Kovacs' laboratory at the University of Colorado Denver, presented her work titled "Alcohol intoxication in aged mice alters pulmonary inflammatory responses." An increasingly common behavior in the elderly is alcohol consumption, as 40% of those >65 years of age drink alcohol (National Institute of Alcohol Abuse and Alcoholism, 2016), and the effects of alcohol ingestion in this population may be more potent in part due to their slowed ability to metabolize alcohol (Kinirons & O'Mahony, 2004; Mangoni & Jackson, 2004; Meier & Seitz, 2008). In addition, the elderly experience a greater prevalence of infection, and increased morbidity and mortality due to infection, which may be attributed to the effects of low-grade chronic inflammation that increases with age (Fung & Monteagudo-Chu, 2010; Van der Horst Graat, Terpstra, Kok, & Schouten, 2007). To test her hypothesis that alcohol consumption will have a more potent negative impact on immunity in older subjects, Dr. Boule used a mouse model of alcohol intoxication and infection. Briefly, young and aged mice were given vehicle or 1 g/kg body weight ethanol via oral gavage, which resulted in a blood alcohol concentration of approximately 100 mg/dL at the time of bacterial infection (30 minutes post ethanol treatment). Dr. Boule showed that intoxicated, aged mice had worse pulmonary pathology 24 hours after infection, including increased cellularity, alveolar wall thickening, and larger inflammatory foci than comparably treated young mice. In parallel experiments, isolated alveolar macrophages from young and aged mice given vehicle or ethanol were stimulated with bacterial products *in vitro*. After stimulation, alveolar macrophages from young mice given ethanol produced 50% less interleukin (IL) 6 and tumor necrosis factor (TNF) α than those from young mice given vehicle. Additionally, stimulation-induced production of IL-6 by alveolar macrophages was reduced even further (>90%) when macrophages were isolated from aged mice given ethanol. In contrast, ethanol-mediated changes in the production of neutrophil chemoattractants KC (CXCL1 [chemokine (C-X-C motif) ligand 1]) and

RANTES (CCL5 [chemokine (C-C motif) ligand 5]) by alveolar macrophages followed a different pattern. Specifically, alveolar macrophages from young mice given ethanol produced less of these chemokines compared to young mice given vehicle control, whereas alveolar macrophages from aged mice given ethanol produced higher levels of both chemokines compared to all other groups of mice. In summary, Dr. Boule showed that aging and ethanol intoxication skew alveolar macrophage function, such that there is decreased production of pro-inflammatory cytokines and increased levels of neutrophil chemoattractants; these consequences likely contribute to the infection-mediated morbidity and mortality observed in aged individuals.

Niya Morris, a Ph.D. student in the laboratory of Dr. Mashkoor A. Choudhry at Loyola University Chicago Health Sciences Division, discussed the role of hypoxia inducible factor 1 α (HIF-1 α) in impaired microRNA biogenesis in intestinal epithelial cells (IEC) in her talk titled “Role of HIF-1 α in gut barrier disruption following ethanol and burn injury.”

MicroRNAs (miRs) are small noncoding RNAs that regulate gene expression by binding to the 3' untranslated region (UTR) sequences of their targets, resulting in messenger RNA (mRNA) degradation or translational repression. To mediate their gene silencing ability, miRs require two maturation steps. Following transcription by RNA polymerase II, the newly formed primary microRNA undergoes nuclear cleavage by Drosha, forming a precursor miRNA (pre-miR). The pre-miR is exported into the cytoplasm where it is cleaved by Dicer prior to formation of the microRNA-induced silencing complex (miRISC) with Argonaute (Finnegan & Pasquinelli, 2013; He & Hannon, 2004). Dysregulation of microRNA biogenesis has been shown to diminish miR expression and impair intestinal barrier function (Gaulke et al., 2014; McKenna et al., 2010). A recent study from the Choudhry laboratory reported that alcohol and burn injury results in a significant reduction in microRNA biogenesis proteins Drosha (52%) and Argonaute-2 (49%), which coincided with reduced miR expression (Morris et al., 2017). Furthermore, the combined insult of alcohol and burn injury results in increased gut leakiness and bacterial translocation one day after injury, possibly due to diminished microRNA biogenesis and miR expression (Rendon, Li, Akhtar, & Choudhry, 2013). Both microRNA expression and biogenesis are negatively impacted by hypoxia (Rupaimoole et al., 2014), which occurs in the intestine as blood flow is redistributed to more vital organs following alcohol and burn injury (Choudhry, Ba, Rana, Bland, & Chaudry, 2005). Similarly, HIF-1 α (a marker of hypoxia) is significantly elevated in IECs following alcohol and burn injury. To investigate the role of HIF-1 α in microRNA biogenesis following alcohol and burn injury, mice were gavaged with approximately 2.9 g/kg alcohol 4 hours before receiving a 12.5% total body surface area full-thickness burn injury. Immediately following the burn injury, mice received normal saline resuscitation with or without PX-478, an inhibitor of HIF-1 α . Ms. Morris' preliminary findings suggest that treatment of mice with a HIF-1 α inhibitor improves microRNA biogenesis following alcohol and burn injury.

Alcohol and Mucosal Inflammation

The second plenary session was chaired by Dr. Marisela Agudelo (Florida International University) and Holly Hulsebus (Ph.D. student in Dr. Elizabeth J. Kovacs' lab at the University of Colorado Denver); the session began with Dr. Ali Keshavarzian from Rush

University Medical Center, who presented his work entitled, “Alcohol-induced gut leakiness to endotoxin and systemic inflammation.” Excessive alcohol consumption can deleteriously impact multiple organs (Wang, Zakhari, & Jung, 2010). However, only a subset of alcoholics develop organ damage such as cirrhosis (Gao & Bataller, 2011), suggesting that excessive alcohol consumption is required but not sufficient for alcoholic organ damage. Multiple studies have demonstrated that inflammation is the required co-factor for alcoholic organ damage (Wang et al., 2010), most likely triggered by alcohol-induced dysbiosis and gut leakiness to endotoxins (Engen, Green, Voigt, Forsyth, & Keshavarzian, 2015).

Keshavarzian’s group has shown that alcoholics with liver disease exhibit gut leakiness to endotoxins, while alcoholics without organ damage have normal intestinal permeability (Keshavarzian et al., 1999). His group also showed that a subset of alcoholics had dysbiosis with a decreased abundance of Bacteroidetes and Clostridia, and an increased abundance of pro-inflammatory Proteobacteria (Mutlu et al., 2009). Alcohol disrupts the intestinal barrier through both a direct effect on tight junctional proteins (Elamin, Masclee, Dekker, & Jonkers, 2013) and indirectly through dysbiosis (Llorente & Schnabl, 2015). Keshavarzian’s group and others have shown that alcohol not only impacts microbiota composition (Engen et al., 2015; Mutlu et al., 2009), but also microbiota function, with decreased production of the short chain fatty acid (SCFA) butyrate (Couch et al., 2015). SCFAs are required to maintain intestinal barrier integrity and low levels of butyrate result in disruption of intestinal barrier function (Hamer et al., 2008). Further, several animal studies have provided a causal link between dysbiosis/gut leakiness and organ damage. For example, ameliorating dysbiosis with prebiotics or probiotics prevented alcoholic steatohepatitis (ASH) (Forsyth et al., 2009; Keshavarzian et al., 2001). Further, transplantation of stool from patients with alcoholic hepatitis into alcohol-fed mice caused severe ASH compared to stool transplantation from control subjects (Llopis et al., 2016). Recent data from Keshavarzian’s lab suggest that disruption of circadian rhythms promotes alcohol-induced dysbiosis and gut leakiness (Summa et al., 2013; Swanson et al., 2016; Voigt et al., 2014), and could therefore be a susceptibility factor for alcohol-induced, gut-derived inflammation. Disrupted circadian rhythms are common in western societies, affecting at least 30% of the population through shift work and social jet lag (Roenneberg, Allebrandt, Merrow, & Vetter, 2012; Zelinski, Deibel, & McDonald, 2014), which intriguingly correlates to that fact that 30% of alcoholics develop dysbiosis, gut leakiness, and clinically relevant organ damage (Gao & Bataller, 2011). These discoveries will help identify potential novel therapeutic targets to prevent/treat alcohol-associated pathologies.

Dr. Jay K. Kolls from the University of Pittsburgh School of Medicine presented his work in a talk titled “Alcohol and type 17 immunity in the respiratory tract.” Type 17 immunity has been shown to be critical for mucosal protection against extracellular bacteria and fungi, in part by regulating the expression of neutrophil-recruiting chemokines and antimicrobial proteins (Chen et al., 2016; Conti et al., 2016). Using an acute model of ethanol administration in mice, Dr. Kolls’ group has shown a perturbed clearance of *Streptococcus pneumoniae* in the lung, which was associated with reduced expression of *il23a* and *il17a*. Further, they found that IL-17 receptor (IL-17R) signaling regulates the expression of both CXCL1 and CXCL5 in lung epithelium, and reduced levels of these chemokines are observed in acute-ethanol treated mice (Chen et al., 2016). Interestingly, neither recombinant

IL-23 nor IL-17 could rescue these mice, suggesting that ethanol also perturbed IL-17R signaling in this model. However, rescue with CXCL1 and to a lesser extent CXCL5, restored bacterial clearance in ethanol-treated mice (Trevejo-Nunez et al., 2015). Taken together, these data suggest that ethanol can inhibit type 17 immune responses but this defect can be overcome by restoring chemokine gradients in lung tissue.

Dr. Samantha M. Yeligar from Emory University/VA Medical Center presented her work titled “Alcohol-induced Nox microRNA down-regulation causes alveolar macrophage phagocytic dysfunction.” Patients with alcohol use disorders (AUDs) are 2-4 times more susceptible to developing respiratory infections than non-alcoholics (Moss et al., 2003). During chronic alcohol consumption, alveolar macrophages exhibit impaired microbial phagocytosis and clearance (Yeligar, Mehta, Harris, Brown, & Hart, 2016). Alcohol-induced alveolar macrophage immune dysfunction is mediated by increases in oxidative stress (Brown, Ping, Harris, & Gauthier, 2007). NADPH oxidases (Nox) 1, 2, and 4 are the primary sources of oxidative stress in the alveolar macrophage. Nox1 and Nox2 primarily produce superoxide, and Nox4 primarily produces hydrogen peroxide (Brown & Griendling, 2009). The experimental models used in Dr. Yeligar’s studies included (a) alveolar macrophages isolated from an *in vivo* model of chronic alcohol consumption in which male C57BL/6J mice were fed with and without ethanol in their drinking water (20% wt/v) for 12 weeks, and (b) the MH-S mouse alveolar macrophage cell line was treated with and without ethanol (0.08%) for 3 days as an *in vitro* model of chronic ethanol exposure (Yeligar, Harris, Hart, & Brown, 2012; Yeligar, Harris, Hart, & Brown, 2014; Yeligar et al., 2016). Compared to control, ethanol increased expression of Nox1, Nox2, and Nox4, enhanced oxidative stress as measured by intracellular reactive species production and extracellular hydrogen peroxide generation, and impaired phagocytosis and lysosomal clearance of *Staphylococcus aureus* bacteria *in vivo* and *in vitro*. These ethanol-induced alveolar macrophage derangements were reversed with transfection of silencing RNAs for Nox1, Nox2, and Nox4 or utilization of Nox1 and Nox2 knockout mice (Yeligar et al., 2012). To determine how ethanol increases expression of Nox proteins, miRs that bind to the 3′-UTR of Nox1, Nox2, and Nox4, thereby targeting Nox mRNA for degradation, were investigated. Using *in silico* analysis, species-conserved binding sites for Nox-related miRs were identified. Ethanol downregulated the expression of Nox1-related miR-1264, Nox2-related miR-107, and Nox4-related miR-92a. MH-S cells transfected with miR-1264 mimic partially reversed ethanol-induced Nox1 and Nox4 mRNA levels, miR-107 mimic transfection partially reversed ethanol-induced Nox2 and Nox4 mRNA levels, and miR-92a mimic transfection completely reversed ethanol-induced Nox4 mRNA levels. Further, ethanol-induced alveolar macrophage oxidative stress and phagocytic dysfunction were mitigated by transfection with Nox-related miR mimics. Taken together, these data suggest that miRs-1264, -107, and -92a may provide novel therapeutic targets for the treatment of impaired alveolar macrophage immunity and mitigate increased susceptibility to respiratory infections in AUD patients.

The final research presentation was given by Michael E. Price, a Ph.D. student in the laboratory of Joseph H. Sisson at the University of Nebraska Medical Center, titled “Alcohol-driven redox imbalance and mitochondrial dysfunction in ciliated airway epithelial cells.” AUD has long been associated with increased prevalence and worse outcomes of airway disease. Cyclic AMP-dependent protein kinase (PKA) increases in airway ciliary

beat frequency are a key defense against inhaled pathogens and debris (Salathe, 2007). Prolonged alcohol exposure causes dysfunctional mucociliary clearance by rendering PKA and ciliary beat frequency desensitized to stimulation (Wyatt, Gentry-Nielsen, Pavlik, & Sisson, 2004). Sisson's group has previously demonstrated that concomitant feeding of antioxidants to alcohol-drinking mice preserved ciliary beat frequency responsiveness to stimulation (Simet, Pavlik, & Sisson, 2013). In other models of alcohol exposure, mitochondria are an important source of reactive oxygen species (ROS) (Liang, Harris, & Brown, 2014). Thus, Mr. Price hypothesized that alcohol promotes ROS and mitochondrial dysfunction in airway epithelial cells. To test this hypothesis, airway brushings from healthy human non-smoking control subjects (AUDIT < 5; n = 4) and nonsmoking subjects with AUD (AUDIT > 20; n = 6) were sampled from the Colorado Pulmonary Alcohol Research Consortium (CoPARC), and mRNA expression levels of select oxidant related proteins including TrxR1, TrxR2, TXN, XDH, ADH5, GPX2, SOD3, PRXDX1, PRXDX6, GPX3 and NME8, were assessed. To model alcohol exposure *in vitro*, superoxide dismutase (SOD) 1, SOD2, SOD3, catalase, and mitocatalase were overexpressed in the BEAS-2B cell line (immortalized human bronchial epithelial cells) and then treated with $\pm$ 100 mM alcohol for 24 h followed by $\pm$ isoproterenol. The outcomes measured included ROS using fluorescent probes mitoSOX and dihydroethidium (DHE) coupled with flow cytometry, mitochondrial function by measuring oxygen consumption rate (OCR) with Seahorse mitostress tests, and PKA activity. In airway brushings from AUD subjects, TrxR1 (p = 0.06) and XDH (p = 0.04) were increased, and SOD3 (p = 0.04) and NME8 (P = 0.08) were decreased compared to control subjects. Alcohol exposure in BEAS-2B cells resulted in increased mitoSOX and DHE detection at baseline compared to control. Interestingly, only mitoSOX was increased with alcohol exposure compared to control. Additionally, alcohol caused a 20% decrease in the maximum OCR and desensitized PKA activity when stimulated with isoproterenol compared to control cells. Importantly, overexpression of SOD1 restored maximum OCR and PKA responsiveness in alcohol-exposed BEAS-2B cells. Mr. Price concluded that alcohol shifts the redox balance in primary human airway epithelial cells to an oxidative phenotype, and alcohol impairs mitochondria function and increases mitochondrial-derived oxidants in BEAS-2B cells. These data implicate the mitochondria as a potentially important source of oxidants to cause PKA and cilia dysfunction.

Summary

The 2017 AIRIG meeting, held during the RSA national conference, showcased research relating to alcohol's effects on various tissues, organs, and mucosal systems. Several presentations focused on possible therapeutic targets following alcohol-induced morbidity. For example, JZL184, a monoacylglycerol lipase inhibitor, can modulate endocannabinoid tone following traumatic brain injury, HIF-1 α inhibition can improve microRNA biogenesis and potentially attenuate gut leakiness following alcohol and burn injury, and fecal transplantation could confer resistance to alcoholic steatohepatitis in alcohol-fed mice. Other presentations focused on alcohol's effects on the respiratory tract and pulmonary systems. It was shown that aging and ethanol intoxication alter alveolar macrophages to produce less pro-inflammatory cytokines and more neutrophil chemoattractants, and it can also inhibit type 17 immune responses in the lung. Additionally, ethanol increased expression of Nox

proteins and enhanced oxidative stress while impairing phagocytosis of bacteria in the lung, and can shift human airway epithelial cells to an oxidative phenotype and impair mitochondrial function. Finally, it was shown that phosphatidylethanol could be used as a potential biomarker for identifying patients with alcohol misuse and determining organ dysfunction. Collectively, these data highlight the varied effects of alcohol on multiple tissue and organ systems – especially mucosal surfaces, and offer many potential pathways to investigate in future alcohol-related studies.

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Overview of the 2017 Alcohol and Immunology Research Interest Group (AIRIG) meeting

Session 1: Alcohol & Trauma/Tissue Injury

- Patricia E. Molina, M.D., Ph.D., Louisiana State University Health Sciences Center: *Alcohol-neuroimmune interactions in traumatic brain injury*
- Majid Afshar, M.D., M.S., Loyola University Chicago Health Sciences Division: *Alcohol biomarkers to examine organ dysfunction in injured patients*
- Lisbeth A. Boule, Ph.D., University of Colorado Denver: *Alcohol intoxication in aged mice alters pulmonary inflammatory responses*
- Niya Morris, Loyola University Chicago Health Sciences Division: *Role of HIF-1 α in gut barrier disruption following ethanol and burn injury*

Session 2: Alcohol & Mucosal Inflammation

- Ali Keshavarzian, M.D., Rush University Medical Center: *Alcohol-induced gut leakiness to endotoxin and systemic inflammation*
- Jay K. Kolls, M.D., University of Pittsburgh School of Medicine: *Alcohol and Type 17 immunity in the respiratory tract*
- Samantha M. Yeligar, Ph.D., Emory University/VA Medical Center: *Alcohol-induced Nox microRNA down-regulation causes alveolar macrophage phagocytic dysfunction*
- Michael E. Price, University of Nebraska Medical Center: *Alcohol-driven redox imbalance and mitochondrial dysfunction in ciliated airway epithelial cells*

Article Highlights

- Therapeutic targets for alcohol-induced morbidity
- Effects of alcohol on alveolar macrophages and airway epithelial cells
- Potential biomarkers for alcohol misuse and organ dysfunction