that increased susceptibility to K. pneumoniae is, in part, mediated by the intestinal microbiota, as animals reconstituted with an alcohol-induced dysbiotic intestinal microbial community have significantly higher lung burdens of K. pneumoniae (5 × 104 CFU vs. 1 × 103 CFU) independent of EtOH. We also found that increased susceptibility in alcohol-dysbiotic reconstituted animals was associated with a decrease in the recruitment and/or proliferation of CD4+ and CD8+ T-cells (1.5 × 109 cells vs. 2.5 × 109 cells) in the lung following Klebsiella infection. However, there were increased numbers of T-cells in the intestinal tract following Klebsiella infection, which may suggest that T cells are being sequestered in the intestinal tract to the detriment of host defense in the lung. Interestingly, mice reconstituted with an alcohol-dysbiotic microbiota had increased intestinal permeability as measured by increased levels of serum intestinal fatty acid binding protein (55 vs. 30 ng/mL). Alcohol-dysbiotic microbiota also induced liver steatosis (Oil Red O staining) and liver inflammation (>2-fold expression of IL-17 and IL-23). DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings suggest that the commensal intestinal microbiota support mucosal host defenses against infectious agents by facilitating normal immune responses to pulmonary pathogens. Our data also suggested that increased intestinal permeability coupled with increased liver inflammation may impair the recruitment/proliferation of immune cells in the respiratory tract following infection. The role of the microbiota during host defense will be important areas of future research directed at understanding the effects of microbial dysbiosis in patients with AUDs.

**2255**

**Essential amino acid supplementation improves lipid metabolism in older adults with elevated triglycerides**

*Bryce J. Marquis, Eugenia Carvalho, Nicholas Hurren, Robert R. Wolfe and Elizabet Borsheim*

**OBJECTIVES/SPECIFIC AIMS:** This study will assess the effect of essential amino acid (EAA) supplementation on plasma triglyceride (TG) in elderly adults. We will also explore the mechanisms mediating EAA mediated changes in fat metabolism and to suggest promising routes to refine therapy of hypertriglyceridemia.

**METHODS/STUDY POPULATION:** In total, 7 non-diabetic male and female subjects ages 50–75 years with elevated plasma TG levels (130–500 mg/dL) were recruited to participate in an acute (5h) and long-term (8 wk) EAA supplementation study. We measured changes in regional and whole body fat metabolism, including changes in body composition, plasma TG levels, whole body fat metabolic rates, tissue mitochondrial respiratory capacity, and metabolic profiles before and after supplementation. RESULTS/ANTICIPATED RESULTS: Long-term EAA supplementation decreased fasted plasma TG levels by 19% (p < 0.01). Metabolomics of skeletal muscle found acute EAA supplementation resulted in increased EAA metabolic products while long-term supplementation resulted in increased anaplerosis [flux into the tricarboxylic acid cycle (TCA) intermediate pool] and anaerobic substrates [propionyl (p < 0.01) and succinyl (p < 0.01) carnitine] and intermediates of long-chain fatty acid metabolism [stearoyl (p < 0.01) and myristoyl (p < 0.05) carnitine]. However, tissue level respiratory capacity appeared to be unaffected by EAA supplementation. DISCUSSION/SIGNIFICANCE OF IMPACT: EAA supplementation has potential to improve lipid metabolism and plasma TG levels in non-diabetic older adults. Mitochondrial metabolomics suggest that insufficient TCA pool size may limit tissue fatty acid oxidation and may provide an additional route for nutritional therapy.

**2290**

**Control of atherosclerosis regression by LXRα S198 phosphorylation**

*Elina Shrestha, Maud Voisin, Tessa J. Barrett, Hitoo Nishi, Inês Pineda-Torra, Edward A. Fisher and Michael J. Garabedian*

**OBJECTIVES/SPECIFIC AIMS:** Accumulation of cholesterol-laden macrophages in arterial walls leads to atherosclerotic plaques and contributes to impaired regression in atherosclerotic plaques. We hypothesized that LXRα phosphorylation at S198 diminishes macrophage emigration from atherosclerotic plaque and contributes to impaired regression in atherosclerotic plaques. METHODS/STUDY POPULATION: Inducible LXRα S198A phosphorylation deficient knock in mouse were used as donors for bone marrow transplantation into mice prone to develop atherosclerosis. Plaques were developed by placing mice on western diet; and regression was induced by lowering their lipid levels.

Aortic plaques were then analyzed by using morphometric, histological, and molecular analyses in control and diabetic mice expressing either LXRα WT or LXRα S198A during regression. RESULTS/ANTICIPATED RESULTS: Surprisingly, lack of phosphorylation increased plaque macrophage content and impaired regression under normoglycemic condition; however, it did not exacerbate diabetic regression. Plaques in diabetic mice were associated with increased LXRα S198 phosphorylation. Consistent with this, LXRα phosphorylation is enhanced in macrophages cultured under hyperglycemic conditions indicating glucose-dependent regulation of LXRα phosphorylation. Monocyte trafficking studies reveal that lack of phosphorylation and diabetes independently increase recruitment of monocytes in the plaque that might contribute to increased macrophage content. Importantly, I found that diabetes also increases macrophage retention in the plaque, which is reversed in the absence of phosphorylation. We predict that this increased retention results from inhibition of emigration of plaque macrophages through enhanced phosphorylation in diabetes. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings suggest that inhibiting LXRα phosphorylation could be beneficial in diabetic atherosclerosis to reverse the accumulation of macrophages in the plaque. This study imparts insight on regulation of plaque macrophage trafficking through LXRα S198 phosphorylation.

**2300**

**E-prescribing research participation: Feasibility of recruiting research participants using an EMR-integrated health information technology**

*Gillian Feldmeth, Leidy Gutierrez, Stacy Tessler Lindau, Jennifer A. Makelarski, Edward T. Naureckas and Julian Solway*

**OBJECTIVES/SPECIFIC AIMS:** To study the rate of recruitment to the Pulmonary Research Registry (PRR) at the University of Chicago using HealthCareRx, a community-based program and services that facilitates normal immune responses to pulmonary pathogens. Our data also suggested that increased intestinal permeability coupled with increased liver inflammation may impair the recruitment/proliferation of immune cells in the respiratory tract following infection. The role of the microbiota during host defense will be important areas of future research directed at understanding the effects of microbial dysbiosis in patients with AUDs.