that increased susceptibility to K. pneumoniae is, in part, mediated by the intestinal microbiota, as animals colonized 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-dysbiosis colonized 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 colonized 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 increased liver steatois (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 suggest 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.

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Control of atherosclerosis regression by LXRα S198 phosphorylation
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OBJECTIVES/SPECIFIC AIMS: Accumulation of cholesterol-laden macrophages in arterial walls leads to atherosclerosis. LXRα induces expression of genes that are atheroprotective in macrophages including CCRT, a chemokine receptor that promotes their emigration from the plaque. CCRT expression has been shown to be negatively regulated by phosphorylation of LXRα at S198 and is reduced in diabetic mice that show impaired plaque regression. I hypothesized that LXRα phosphorylation at S198 diminishes macrophage emigration from atherosclerotic plaque and contributes to impaired regression in atherosclerosis. 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 LXRx 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.

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A novel in vivo zebrafish model of hemato poetic stem cell-driven regeneration of blood
Samina Sultana Habbas, Mia McKinstry, Sara Payne, Christian Molsimann and Teresa Bowman

OBJECTIVES/SPECIFIC AIMS: Hematopoietic stem and progenitor cells (HSPCs) function to maintain steady state production of new blood cells and to rapidly respond to blood cell loss. Little is known regarding how HSPCs develop the ability to sense and respond to blood cell loss during embryogenesis. Gaining insight into the robust ability of HSPCs to regenerate blood during early development may allow us to develop therapies to rejuvenate this capacity at any stage. METHODS/STUDY POPULATION: We generated a new hematopoietic-specific and inducible cell ablation zebrafish model to uncover the origins of regenerative capacity in HSPCs during development. These transgenic zebrafish express a cyan fluorescent protein (CFP)-nitroreductase (NTR) fusion construct under the control of the draculin (dr) promoter (dr:CFP-NTR), which restricts NTR expression to blood cells. Co-expression analyses of dr:CFP-NTR with known markers of other blood types including HSPCs (runx1 + 23:mCherry), erythrocytoid cells (gata1+I:DsRed), and lymphoid cells (rag2:AFP), revealed dr:CFP-NTR was restricted to HSPCs and erythrocytoids. To delineate the regeneration potential of embryonic HSPCs, we exposed dr:CFP-NTR transgenic zebrafish embryos to Metronidazole (MTZ), which results in selective ablation of only NTR-expressing blood cells. Embryos were treated from 2 to 3 days postfertilization and recovery of dr+ and gata1+ cells was evaluated over a 7-day recovery period. RESULTS/ANTICIPATED RESULTS: Following MTZ exposure, the nadir of dr+ cell ablation occurs at 2 days post MTZ (dpM) treatment. During the renewal phase of blood regeneration, we first observe recovery of dr+ cells by about 4 dpM, followed by more mature blood cells like gata1+ erythrocytoids show a delayed recovery at about 6 dpM. Our results suggest that HSPCs can respond to injury as early as 2 days of life and that the HSPC-driven regeneration of embryonic blood cells occurs in a hierarchical fashion, similar to regeneration of the adult blood system. DISCUSSION/SIGNIFICANCE OF IMPACT: We have established a quantitative method for in vivo real-time monitoring of embryonic and larval blood regeneration. A significant advantage of our system is that we can use these insights to guide an in-vivo drug screen for factors that accelerate HSPC-driven blood regeneration in a complex biological environment.

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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 Registry (PR) at the University of Chicago using HealthNetRx recruitment. METHODS/STUDY POPULATION: CommunityRx is a health information technology, integrated with electronic medical record (EMR) platforms, that generates personalized referrals ("HealthNetRx") for community-based programs and services that