that increased susceptibility to *K. pneumoniae* is, in part, mediated by the intestinal microbiota, as animals recolonized 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 recolonized 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 recolonized 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 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 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.

2275

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

Bryce J. Marquis, Eugenia Carvahlo, Nicholas Hurren, Robert R. Wolfe and Elisabet 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 nondiabetic male and female subjects ages 50–75 years with elevated plasma TG levels (130–500 mg/dL) were recruited to participate in an acute (5 h) 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 metabolomic 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 anaplerotic 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, Inés Pineda-Torra, Edward A. Fisher and Michael J. Garabedian

OBJECTIVES/SPECIFIC AIMS: Accumulation of cholesterol-laden macrophages in arterial walls leads to atherosclerosis. LXRs induce expression of genes that are atheroprotective in macrophages including CCR7, a chemokine receptor that promotes their emigration from the plaque. CCR7 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 diabetes. 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.

2295

A novel in vivo zebrafish model of hematopoietic stem cell-driven regeneration of blood

Samima Sultana Habbsa, Mia McKinstry, Sara Payne, Christian Mosimann 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 (drl) promoter (drl:CFP-NTR), which restricts NTR expression to blood cells. Co-expression analyses of drl:CFP-NTR with known markers of other blood types including HSPCs (runx1 + 23:mCherry), erythroid cells (gata1:dsRed), and lymphoid cells (rag2:RFP), revealed drl:CFP-NTR was restricted to HSPCs and erythrocytes. To delineate the regeneration potential of embryonic HSPCs, we exposed drl: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 drl+ and gata1+ cells was evaluated over a 7-day recovery period. RESULTS/ANTICIPATED RESULTS: Following MTZ exposure, the nadir of drl+ cell ablation occurs at 2 days post MTZ (dpM) treatment. During the renewal phase of blood regeneration, we first observe recovery of drl+ cells by about 4 dpM, while more mature blood cells like gata1+ erythrocytes 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.

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 HealtheRx recruitment Versus usual practice. METHODS/STUDY POPULATION: CommunityRx is a health information technology, integrated with electronic medical record (EMR) platforms, that generates personalized referrals ("HealtheRxs") for community-based programs and services that

https://doi.org/10.1017/cts.2017.36 Published online by Cambridge University Press

address basic and other health-related self-care needs. The target population included people ages 18 and older, English speaking, living in 1 of 16 ZIP codes on Chicago's south and west sides (106 mi^2) who received care at ≥1 of 28 CommunityRx partner sites and had a diagnosis of asthma or COPD. Between December 2015 and December 2016, information about pulmonary research participation opportunities was included on the HealtheRxs of eligible patients contemporaneously with usual registry recruitment methods. Usual methods, used since 2010 by the PRR group, included public advertisements requiring the patient to call the research team for more information and education of eligible patients identified during routine clinical care with a Pulmonary/Critical Care clinician or when enrolling in a pulmonary clinical trial. We hypothesized that, compared with usual recruitment practices, the HealtheRx recruitment strategy would increase the rate and decrease the per subject cost of patient recruitment to a prospective registry. Total annual recruitment costs for each method were calculated and divided by the number of consented PRR enrollees per method. RESULTS/ANTICIPATED RESULTS: Between December 22, 2015 and December 15, 2016 13,437 HealtheRxs (8762 for asthma, 3842 for COPD, and 833 for both asthma and COPD) were generated with the recruitment advertisement. In total, 41 patients responded to the ad and participated in the phone survey. In which 15 (36.5%) participants self-reported a diagnosis of asthma only (65% of all HealtheRxs with advertisement were for asthma only), 9 (22%) reported a diagnosis of COPD only (28.5% of all HealtheRxs with advertisement were for COPD only), and 17 (41.5%) reported diagnoses of both asthma and COPD (6.2% of all HealtheRxs with advertisement were for asthma and COPD). Most participants were female (n = 28), non-Hispanic black (n = 37), and not employed (n = 39). The median age was 57. The majority (n = 31) had never participated in health or medical research and was not aware of current opportunities to participate in research (n = 25). All 41 participants expressed interest in joining PRR and were mailed a blank PRR consent form and a prepaid return envelope with their incentive check for the telephone survey. To date, 5 participants returned a signed consent form via mail and were enrolled in PRR. During the same period, 4 patients enrolled in PRR via usual recruitment methods. The cost per subject to enroll in PRR was $364.40 using the HealtheRx recruitment and $4590 using usual practice. DISCUSSION/SIGNIFICANCE OF IMPACT: NIH has called for innovation in research recruitment methodologies to increase enrollment especially of people who are under-represented in clinical trials research. This study demonstrates the feasibility and efficiency of using an EMR-integrated recruitment method to enroll people of under-represented minority groups to a research registry.

2302

Downregulation of miR-1207-3p is correlated to upregulation of FNDC1, FN1, AR, and c-MYC in aggressive prostate cancer in men of African ancestry

Dibash K. Das, Akintunde T. Orunmuyi, Gabriel Olabiyi Ogun, S. Adekola Adebayo, A. Ayo Salako, Adeodat Ilboudo, E. O. Olapade-Olaopa and Olorunseun O. Ogunwobi

Department of Biological Sciences, Hunter College, New York, NY, USA

OBJECTIVES/SPECIFIC AIMS: Prostate cancer is the second most common cancer in the world for men. For reasons still unclear, aggressive PCa disproportionately affects males of African ancestry (MoAA). Incidence and mortality rates are highest in MoAA as they have consistently shown a 2.3–3.0-fold higher risk of mortality compared with Caucasian men. This aggressiveness of PCa may be due to specific biological factors. Studies have established that microRNAs (miRNAs), essential in post-transcriptional gene regulation, are dysregulated in PCa. miR-1207-3p is encoded at the PVT1 gene locus, which is located downstream of MYC on the 8q24 PCa susceptibility locus. The chromosomal region 8q24 is associated with aggressive PCa. Yet miR-1207-3p in PCa in MoAA has never been investigated. Moreover, studies have shown that PVT1/MYC co-operation is a fundamental feature in all cancers with 8q24 amplification and 98% of the 8q24 amplicons contained concurrent amplification of the MYC and PVT1 loci. Moreover, MYC has been linked to PCa aggressiveness, and has been reported to be downstream of androgen receptor (AR) in some PCa. However, the mechanisms regulating c-MYC have never been studied in MoAA. We have recently demonstrated that miR-1207-3p has prognostic value in PCa, and directly binds to the 3′ UTR of Fibronectin type III domain containing 1 (FNDC1) to regulate a novel FNDC1/fibronectin (FN1)/AR pathway upregulated in metastatic PCa. However, the relevance of this novel and clinically significant miR-1207-3p molecular pathway in PCa in MoAA is unknown. Therefore, we hypothesized that miRNA 1207-3p, encoded at the 8q24 PCa susceptibility locus, is a PCa biomarker with clinical applications in MoAA. Our specific aim was to assess the clinical relevance of miR-1207-3p, FNDC1, FN1, AR, and MYC expression in aggressive PCa in a cohort of West African Black males. METHODS/STUDY POPULATION: Consequently, we aimed to determine the expression profile of miRNA-1207-3p, FNDC1, FN1, AR, and MYC in histologically confirmed normal prostate (n = 24), benign prostate (n = 44) and malignant prostate tissue (n = 29) from prostatectomy or transrectal ultrasound-guided biopsies in patients recruited at the University College Hospital, Ibadan, Nigeria, a sub-Saharan Black African population. In total, 17 patients had tumor tissues with Gleason score ≥8. Tissues were collected in compliance with Institutional Ethics Board approved protocols. RNA extraction, cDNA synthesis, and quantitative-PCR were performed to analyze mRNA expression of miRNA-1207-3p, FNDC1, FN1, AR, and MYC. Statistical analysis were performed using SPSS software. All data were analyzed by the 1-way ANOVA test. Tukey post-hoc test was performed to determine the differences in mean expression between normal and tumor prostate tissues. $p < 0.05$ were considered significant. RESULTS/ANTICIPATED RESULTS: We discovered that miR-1207-3p is significantly underexpressed in prostate tumor tissues [0.09 ± 0.02, 95% CI (0.04, 0.136), $p = 0.000$] in comparison with normal prostate tissue in MoAA [0.92 ± 0.15, 95% CI (0.60, 1.244), $p = 0.000$]. This is the first description of miR-1207-3p differential expression in human clinical PCa in MoAA. In contrast, FNDC1 was significantly overexpressed in prostate tumor tissues [21.93 ± 8.21, 95% CI (4.97, 38.89), $p = 0.003$] in comparison with normal prostate tissues in MoAA [1.57 ± 0.45, 95% CI (0.625, 2.51), $p = 0.003$]. The same positive correlation with advanced disease held true for FN1 [tumor: 13.66 ± 3.53, 95% CI (6.38, 20.93), $p = 0.000$; normal: 1.07 ± 0.235, 95% CI (0.58, 1.56), $p = 0.000$], AR [tumor: 20.49 ± 6.74, 95% CI (6.50, 34.48), $p = 0.000$; normal: 0.94 ± 0.20, 95% CI (0.52, 1.36), $p = 0.000$], and c-MYC [tumor: 33.93 ± 8.43, 95% CI (16.53, 51.33), $p = 0.000$; normal: 1.94 ± 0.36, 95% CI (1.18, 2.70)]. The significantly increased mean expression for FNDC1, FN1, AR, and c-MYC in prostate tumor tissues in comparison with normal prostate tissues indicate that their overexpression is associated with increased risk of cancer progression in MoAA. DISCUSSION/SIGNIFICANCE OF IMPACT: These results show that the underexpression of miR-1207-3p and the overexpression of FNDC1, FN1, AR and MYC is associated with aggressive PCa in MoAA. miR-1207-3p, and it molecular target FNDC1, may be useful biomarkers for prognostication of PCa in MoAA.

2307

Resting state network profiles of Alzheimer disease and frontotemporal dementia: A preliminary examination

Joey Annette Contreras, Shannon L.. Risacher, Mario Dzemidzic, John D. West, Brenna C. McDonald, Martin R. Farlow, Brandy R. Matthews, Liana G. Apostolova, Jared Brosch, Bernard Ghetti and Joaquin GoÑi

Indiana University School of Medicine, Indianapolis, IN, USA

OBJECTIVES/SPECIFIC AIMS: Recent evidence from resting-state fMRI studies have shown that brain network connectivity is altered in patients with neurodegenerative disorders. However, few studies have examined the complete connectivity patterns of these well-reported RSNs using a whole brain approach and how they compare between dementias. Here, we used advanced connectomic approaches to examine the connectivity of RSNs in Alzheimer disease (AD), Frontotemporal dementia (FTD), and age-matched control participants. METHODS/STUDY POPULATION: In total, 44 participants [27 controls (66.4 ± 7.6 years), 13 AD ($68.5.63 \pm 13.9$ years), 4 FTD (59.575 ± 12.2 years)] from an ongoing study at Indiana University School of Medicine were used. Resting-state fMRI data was processed using an in-house pipeline modeled after Power *et al.* (2014). Images were parcellated into 278 regions of interest (ROI) based on Shen *et al.* (2013). Connectivity between each ROI pair was described by Pearson correlation coefficient. Brain regions were grouped into 7 canonical RSNs as described by Yeo *et al.* (2015). Pearson correlation values were then averaged across pairs of ROIs in each network and averaged across individuals in each group. These values were used to determine relative expression of FC in each RSN (intranetwork) and create RSN profiles for each group. RESULTS/ANTICIPATED RESULTS: Our findings support previous literature which shows that limbic networks are disrupted in FTLD participants compared with AD and age-matched controls. In addition, interactions between different RSNs was also examined and a significant difference between controls and AD subjects was found between FP and DMN RSNs. Similarly, previous literature has reported a disruption between executive (frontoparietal) network and default mode network in AD compared with controls. DISCUSSION/SIGNIFICANCE OF IMPACT: Our approach allows us to create profiles that could help compare intranetwork FC in different neurodegenerative diseases. Future work with expanded samples will help us to draw more substantial conclusions regarding differences, if any, in the connectivity patterns between RSNs in various neurodegenerative diseases.

https://doi.org/10.1017/cts.2017.36 Published online by Cambridge University Press