removing contaminants from stormwater runoff. The field test will demonstrate the removal efficiencies attained by the system for TSS, TP, Cu, Zn and other pollutants. This will then be used to confirm that the system meets stormwater regulations which require the removal of a minimum 80% of the total suspended sediment load and treatment of nutrients to the maximum extent feasible. The field testing program will collect discrete samples from the influent and effluent of the BayFilter. These samples will be analyzed using standard EPA protocols for total suspended solids (TSS), particle size distribution (PSD), nutrients as well as metal concentrations. Removal efficiencies will be calculated based on this data using standard scientific methods. Precipitation and flow records will be aquired during these events as well. The testing program is anticipated to take 12-18 months to complete and will include at least 15 qualifying storm events. BayFilter systems to be monitored will treat the stormwater runoff from Trinity Episcopal Church property in Fredericksburg, VA. Stormwater runoff from the paved area transports dissolved, colloidal, suspended and settleable solids in a heterogeneous mixture, which includes metals, organic compounds and nutrients. These constituents result from atmospheric deposition, traffic activities, vehicular wear, pavement degradation and deicing, landscape maintenance and littering. The nutrient load from the site is expected to vary seasonally.

ASSESSING WATER QUALITY OF CEDAR CREEK USING BENTHIC MACROINVERTERBRATES. John V. Stevens, Briana L. Barron, James E. Bisset, Linden E. Lewis, Daniel A. Milhon, Cory M. Miller, Benjamin S. Sawyer, Amy L. Smith & Woodward S. Bousquet. Environmental Studies Department, Shenandoah University, Winchester Virginia 22601. In the spring and fall of 2010, Shenandoah University researchers assessed the water quality of Cedar Creek in Frederick and Shenandoah Counties, Virginia. They used the Environmental Protection Agency's Rapid Bioassessment Protocols (RBPs) to select sampling sites and collect specimens. In addition to choosing three representative sites on the creek's main stem, the researchers selected two locations on ecologically distinct tributaries: Paddy Run (a cold-water montane stream), and Meadow Brook (a warm-water valley stream). Analysis was performed with the Virginia Stream Condition Index (VSCI), a multimetric measure based on the diversity, pollution tolerance and feeding categories of the invertebrates collected. A majority of the sites had a VSCI water quality score of >73, placing them in the excellent category. Only Meadow Brook was rated as severely impaired (avg. VSCI score = 32.2), most likely due to surrounding agricultural and residential development. These findings affirm previous studies that rated Cedar Creek's overall water quality as among the best in the Shenandoah Valley region, using chemical, physical and fish community data. Best management practices should be implemented to protect this beautiful, high-quality watershed.

Medical Science

THE ROLE OF α5 NICOTINIC ACETYLCHOLINE RECEPTORS IN ACUTE AND CHRONIC ALCOHOL BEHAVIORS IN MICE. Anton J. Dawson & M. Imad

Damaj. Dept. of Pharmacology & Toxicology, Virginia Commonwealth University, Richmond, VA 23298. The high incidence of nicotine dependence in alcoholics suggests that nicotinic acetylcholine receptors (nAChRs) may be involved in both nicotine and alcohol dependence. Genetic studies suggest that the α5 nAChR-coding gene is significantly associated in both nicotine and alcohol dependence phenotypes, but virtually no studies have investigated this receptor subtype with regard to alcohol's effects *in vivo*. We hypothesized that the α5□nAChRs mediate some acute and chronic behavioral effects of alcohol in alcohol preferring C57BL/6J mice lacking α5 gene expression (α5 KO mice). We tested their response to alcohol's acute effects including initial sensitivity and functional tolerance through the loss of righting reflex assay, anxiolysis using elevated plus maze, hypothermia, and locomotor depression. For chronic effects, we chose to study alcohol intake and preference using two-bottle choice and aspects of alcohol reward using conditioned place preference. Our results showed that α5 KO mice, indeed respond differentially to acute and chronic ethanol exposure. These data suggest that α5 nAChRs may exert differential effects on the acute and chronic effects of alcohol and may, therefore, represent a potential therapeutic target for the treatment of alcohol and nicotine co-abuse in the future.

FACTORS RELATED WITH ACTIVE LIVING FOR INDIVIDUALS IN THE WESTERN REGION OF USA. S. Tiraphat, Q. Zhang, J.G. Behr, & L. Shepherd. Old Dominion University, Norfolk, VA 23529. Adequate physical activity is a major contributor to a healthy living and prolonging life. Among extreme geographic diversity of the US, the disparity in physical activity (PA) has remained substantially across the region, with the Western part having the highest activity prevalence. It is a challenge to study and identify what factors influence on active lifestyle of people in the Western area. Objective: this study is to investigate the influences of individual and environmental contexts on the odd of being physically active of people in the Western region. Method: data from 2007 BRFSS is obtained and linked with external environmental data sources from US Census Bureau, USDA, and NORSIS databases. A two-level logistic regression is analyzed. Outcome variable is meeting PA recommendation according to CDC guideline (yes / no). Individual-level variables include demographic factors, socio-economic conditions, lifestyle, and health status. Environmental -level variables as a county scale include physical activity built environments (local facilities, green area, and outdoor activity resources), educational context, crime rate, and natural amenity. Results: At the individual level, White, male, consuming more fruits and vegetables, more satisfied with life, higher income, higher education, better health, and younger are significantly positive with the meeting PA recommendation. At the county level, outdoor activity resources and educational context are the significant predictors of the meeting PA. This study emphasizes the advantage of built environments especially outdoor activity resources on active living of people in the Western part.

REGIONAL GENE EXPRESSION CHANGES ASSOCIATED WITH INCREASED VOLUNTARY ETHANOL CONSUMPTION DUE TO DEPRIVATION IN C57BL/6J AND C57BL/6NCRL MICE. J.A. Warner, R.T. Khisti & M.F. Miles, Virginia Commonwealth University. The alcohol deprivation

effect (ADE) is an increase in ethanol consumption after abstinence and is considered a rodent model of relapse in human alcoholics. This study used microarray analysis to identify changes in gene expression in nucleus accumbens, prefrontal cortex, and ventral midbrain of C57BL/6NCrl mice after ethanol deprivation. Nearly 800 mRNA transcripts were significantly regulated, including several primary targets of ethanol, with most regulation in NAC. Analysis revealed over-represented biological processes, cell signaling pathways, and transcription factor binding sites, as well as novel coordinately regulated gene networks, with the common theme of neuroplasticity. Areas highly represented included calcium, sodium, potassium, and chloride currents, transcription and translation, neuronal remodeling, and control of cell fate. Components of GABA, glutamate, opioid and serotonin systems were regulated. Binding sites for diverse transcription factors, including CREB, were over-represented. Novel gene networks were identified related to gene expression, protein trafficking, and cellular function and maintenance. Regulated genes likely alter neuronal function by modulating excitability, protein turnover, and connectivity, and represent novel targets for further development of pharmacological and genetic therapies for relapse in alcoholism.

THE CENTRAL MECHANISMS OF GASTRIN-RELEASING PEPTIDE-INDUCED ANOREXIA. C. R. Dougherty & M. A. Cline. Dept. of Biology, Radford University, Radford, VA 24142. Recently our laboratory demonstrated that intracerebroventricular (ICV) injection of gastrin-releasing peptide (GRP), a member of the bombesin family, caused primary anorexigenic effect in broiler chicks. Currently the central mechanisms behind the anorexigenic effect of GRP are poorly understood. We hypothesized that this effect is likely mediated through similar neurotransmitters that are known to be involved in hypothalamic appetite regulation. c-Fos immunoreactivity was used in order to visualize changes in neuronal activity in regions primarily associated with satiety and appetite regulation as a result of ICV administration of GRP. We are currently in the process of further studying the central mechanisms of GRP via real-time PCR. Further investigation into the central mechanisms of GRP-induced anorexia could have significant implications in the management of obesity if pharmaceutical applications are pursued.

OPIOID AND HIV-1 ASSOCIATED NEURODEGENERATION: POSSIBLE REGULATION BY THE $P2X_4$ RECEPTOR IN PRIMARY MOUSE STRIATAL CELLS. M.E. Sorrell, S. Zou, P.E. Knapp, and K.F. Hauser, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298. HIV-1-associated neurocognitive disorders (HAND) are seen in up to 50% of AIDS patients and individuals who abuse opiates can have an increased incidence of HAND with more severe symptoms. Microglia play a role in HIV-1 neuropathogenesis since activation produces cytokines, chemokines, and other inflammatory molecules that can lead to neuronal injury and death. Recently, morphine has been reported to increase microglial motility by modifying $P2X_4$ signaling. This is important because mu opioid receptor agonists can increase HIV-1 replication, potentiate the release of oxyradicals and glutamate, and increase cytokine production in HIV-1 Tat-exposed microglia. To examine whether HIV-1 and/or

opioid-induced microglial activation and neurotoxicity are mediated via purinergic signaling, co-cultures of primary neurons and mixed glia from mouse striatum were treated with vehicle, Tat and/or morphine ± TNP-ATP, which blocks $P2X_{1-7}$ receptors. Individual neurons were repeatedly tracked for 72 hours and neuron survival vs. time was assessed. In neurons co-exposed to Tat ± morphine, treatment with TNP-ATP significantly blocked Tat-mediated neurotoxicity. Further neuron survival studies showed that TNP-ATP dose dependently prevented Tat and morphine toxicity, both when treated in combination and separately. Our data implicates that the activation of P2X receptors are critical in opiate and HIV neurotoxicity, while further work needs to be done to verify the role of the $P2X_4$ receptor in our HIV and opioid model.

THE IMPACT OF ADOLESCENT NICOTINE EXPOSURE ON DRUG DEPENDENCE IN ADULTHOOD. Mai Alajaji, M.S. & M. Imad Damaj, Ph.D Department of Pharmacology & Toxicology Virginia Commonwealth University, Richmond, VA 23298. Smoking among adolescents is a strong predictor of future drug abuse and dependence in adulthood. A number of studies have suggested that adolescents pre-exposed to nicotine may suffer permanent disruption of the brain's reward systems through changes in dopamine receptor function. We hypothesize that nicotine exposure during adolescence causes long lasting neurobiological alterations that increase the likelihood of cocaine use in adulthood. Conditioned place preference data showed that a 7-day exposure to 0.5 mg/kg of nicotine altered cocaine-induced responses. In contrast, neither 1 day exposure nor a low dose of nicotine (0.1 mg/kg) elicited this effect. A follow-up study was undertaken to determine if this enhancement generally applies to other drugs of abuse. Pre-exposure to 0.5 mg/kg nicotine during early adolescence demonstrated significant enhancement to d-amphetamine and morphine preference in a CPP model. Similar to the effects seen with reward, exposure of early adolescent mice to nicotine also enhanced acute locomotor activity and locomotor sensitization to cocaine in adulthood. Our data strongly suggest that nicotine intake during adolescence may act to cross-sensitize the brain to cocaine's long-term changes in the brain. Further research will be required in order to more fully examine the mechanisms of action for the observed changes in cocaine rewards.

CHANGES IN GENE EXPRESSION DURING IMCD3 CELL DIFFERENTIATION. Brittany N. Abbatiello & Deborah L. Zies, Dept. of Biol. Sci., Univ. of Mary Washington, Fredericksburg, VA. Renal Cell Carcinoma (RCC) accounts for 90% of kidney cancer cases and is extremely difficult to treat. Understanding the mechanisms by which renal cells become de-differentiated during the transformation process is an important step in understanding this deadly disease. Identification of the genes involved in kidney cell differentiation may lead to a better understanding of the de-differentiation process. Therefore, the goal of this study is to identify genes involved in the differentiation of kidney cells. We determined growth conditions for undifferentiated and differentiated IMCD3 cells. Cells were plated into 6 well plates and duplicate wells were lysed each day for 9 days. RNA was collected, converted to cDNA, and QPCR was performed for Glyceraldehyde 3-Phosphate Dehydrogenase (GAPDH) and Epithelial sodium channel subunit alpha

(ENaCα). GAPDH expression did not change over time. IMCD3 cells were determined to be differentiated when QPCR results correlated with expected increase in expression of ENaCα. The RNA from undifferentiated samples (day 4) and differentiated samples (day 7) were compared in a microarray experiment. Bioinformatic analysis of the results identified four candidate genes, neuronal guanine nucleotide exchange factor (NGEF), roundabout homolog 1 (ROBO1), transforming growth factor 1 beta (TGFB1), and brain derived neurotropic factor (BDNF). These genes differ in expression between undifferentiated and differentiated cells and have functions known to be associated with development or differentiation. Future studies will characterize these genes to determine if they play a role in cell differentiation or cancer cell de-differentiation.

ASPECTS OF ETHANOL RESPONSE IN *C. ELEGANS.* J. Alaimo, A. Davies & J. Bettinger, Pharm/Tox, VCU, Richmond VA 23298. Alcohol abuse is a disorder with a poorly understood etiology that includes both genetic and environmental influences. One factor found to influence drinking behavior is variation in genes encoding ethanol metabolism machinery. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are two major enzymes involved in the ethanol metabolic pathway. We directly tested the effects of altering the function of these enzymes on ethanol responsive behaviors in the nematode, *C. elegans*. Through homology searches we have identified two ADH-like enzymes that are encoded by *sodh-1* and *H24K24.3*. We have found that at 200mM and 400mM exogenous ethanol, worms lacking SODH-1 are hypersensitive to the initial effects of ethanol relative to wild type, but knockdown of *H24K24.3* caused no significant behavioral changes at either dose. We tested if this sensitivity to ethanol reflected an increase in internal ethanol concentrations and found that tissue concentration is increased in *sodh-1* mutants, but not in *H24K24.3* mutants. Moreover, *sodh-1* and *H24K24.3* mutants develop acute tolerance to ethanol suggesting that these components of the alcohol metabolism machinery are dispensable for this process. The *C. elegans* genome encodes 13 ALDH enzymes that are highly conserved between worms and humans. We have found that knockdown of either *alh-6* or *alh-13* results in altered ethanol sensitivity at 400mM exogenous ethanol, but internal tissue concentrations trend towards an increase relative to wild type. This suggests that the lack of ALDH function may cause a buildup of acetaldehyde, which would be converted by ADH into ethanol. Collectively, we find that altered ethanol metabolism in worms results in a mild effect on ethanol response behaviors.

GENE NETWORKS OF ALCOHOL DEPENDENCE. S.P. Farris, K.L. Shelton, & M.F. Miles. Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond VA 23298. The molecular mechanisms underlying alcohol abuse and alcoholism are largely unknown, however, divergent patterns in gene expression are critical molecular endophenotypes regulating the risk of developing alcohol dependence. Using a mouse model of intermittent ethanol self-administration we have conducted Weighted Gene Co-expression Network Analysis (WGCNA) of medial prefrontal cortex (PFC) to identify gene expression networks associated with ethanol intake. WGNA revealed a significant correlation of ethanol intake to myelin-associated gene expression. Prior work from our laboratory and others' have

identified decreased expression of myelin in the PFC of alcoholics. Additionally, our laboratory has shown myelin gene expression may be a latent factor influencing acute ethanol sensitivity which influences long-term drinking behavior. Therefore, we hypothesized a myelin network functions in acute ethanol behavioral sensitivity. Using the cuprizone model of demyelination in C57BL/6J male mice we determined that differential expression of a myelin gene network impacts the duration for the loss of righting reflex, a phenotypic measure of acute ethanol behavioral sensitivity. Cuprizone treated mice and controls exhibited no difference in blood ethanol concentrations, suggesting the phenotypic impact of ethanol administration is a pharmacodynamic effect of myelin and not due to non-specific effects on the pharmacokinetics of ethanol. Our results suggest myelin may be a molecular endophenotype influencing acute behavioral sensitivity and the risk of developing alcohol dependence. Supported by NIAAA grants U01 AA016667 to MFM and F31 AA018615 to SPF.

GENE EXPRESSION OF GASTRIC CYTOKINES AND HORMONES IN OBESITY ASSOCIATED LIVER INFLAMMATION. R. Mehta[1,2], A. Birerdinc[1,2], L. Wang[1,2], N. Hossain[2,3], A. Afendi[2,3], V. Chandhoke[1,2], Z. Younossi[1,2,3]& A. Baranova[1,2], [1]Molecular and Microbiology Department and Center for the Study of Genomics in Liver Diseases, George Mason University, Fairfax, VA, USA. [2]Translational Research Institute, Inova Health System, Falls Church, VA, USA. [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church, VA, USA. Obesity is one of fastest growing global epidemics. Obesity is a complex multisystem disease resulting from a failure in the normal homeostatic mechanisms which regulates food intake, fat storage, and energy utilization. Further in obesity, there is interplay of substances produced by various organs, including visceral adipose, liver, muscle and gastric tissues. Obesity is strongly associated with numerous degenerative conditions, particularly non-alcoholic fatty liver disease (NAFLD). Consequently, deregulation of genes involved in energy homeostasis and expenditure may play an important role in not only obesity, but also the pathogenesis of the diseases stemming from this condition. Soluble molecules produced by gastric tissues and their receptors may play a role in the pathogenesis of obesity-related NAFLD. In this study, we assessed the association of gastric tissue gene expression of obesity related genes and inflammatory cytokines with NAFLD in obese patients. We demonstrate a correlation of gastric CNR1 and cytokines with hepatic inflammation. This data indicates that gastric tissue may play a previously unexplored role in the pathogenesis of obesity associated NAFLD. With further validation in a larger cohort, the differentially expressed genes detected in this study may provide novel mechanistic insights into the pathology of NAFLD.

DYNAMICS OF SUBSTRATE INTERACTIONS IN tRNA (m^1G37) METHYLTRANSFERASE: IMPLICATIONS FOR DRUG DISCOVERY. M. K. Palesis[1], J. C. Hackett[2], & W.M. Holmes[3], Departments of [1]Pharmacology and Toxicology, [2]Medicinal Chemistry, and [3]Microbiology, Virginia Commonwealth University, Richmond, VA 23298. The bacterial enzyme t-RNA (m^1G37) methyltransferase (TrmD), a potential antimicrobial drug target, methylates the G37 nucleotide of tRNA using S-adenosyl methionine (SAM) as the methyl donor. This

methylation reduces the occurrence of frame shift mutations during protein translation. Molecular dynamics simulations of TrmD implicate secondary structural elements which may contribute to active site accessibility. Substrate-enzyme interactions were studied using Isothermal Titration Calorimetry (ITC). Molecular dynamics simulations together with ITC data suggest cooperativity between two active sites on the enzyme. To further investigate this cooperativity, a series of experiments have been initiated. Because SAM is a ubiquitous substrate for many different methyltransferases in the cell, analogs of this ligand may not be suitable for drug development. It is therefore important to understand the structural elements involved in the mechanism of action which will subsequently enable a more targeted approach to the development of new antimicrobial drugs.

COMBINING CANNABINOIDS AND RADIATION THERAPY IN BREAST CANCER. S.M. Emery, E. Sumner, A. Lichtman & D.A. Gewirtz, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298. Numerous reports have shown that in several preclinical models cannabinoids have the potential for improving the effectiveness of cancer treatment. Given that cannabinoids are already used as a palliative treatment during cancer therapy, we investigated whether select agents could enhance the effectiveness of radiation, which is used in treatment of breast cancer. We assessed the impact of Win55, 212-2 (Win2), a full efficacy cannabinoid agonist, as well as Cannabidiol (CBD) and Δ9- Tetrahydrocannabinol (THC) in combination with radiation in MCF-7 (human p53 wild type), MDA-MB-231 (human p53 mutant), and 4T1(mouse p53 null) breast tumor cell lines as well as in MCF-10a cells, a human non-transformed cell line. Win2 significantly enhanced the antiproliferative actions of radiation (2 Gy) in MCF-7, MDA-MB-231 cells as well as 4T1 cells but not in MCF-10a cells. Unexpectedly, CBD and THC did not produce the same effect as Win2, suggesting differences between the compound classes. We also were able to show in MCF-7 cells that when using Win55,212-3 the inactive enantiomer of Win2 there was no effect alone as well as no enhancement with the combination. Our data indicates that Win2 (but not THC) has the potential to enhance current radiation therapy used against breast cancer.

miRNAs AND THEIR TARGET GENE EXPRESSION IN THE VISCERAL ADIPOSE TISSUE OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) PATIENTS. H. Sharma[1,2], M. Estep[1], N. Hossain[1], H. Elarainy[1], Z. Goodman[2,3], V. Chandhoke[2], A. Baranova[2,3], Z. Younossi[1, 2, 3], [1]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church VA, [2] School of Systems Biology, George Mason University, Manassas, VA and [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church , VA. There are many biological molecules involved in the pathogenesis of Non-Alcoholic Steatohepatitis (NASH) and its progression from NAFLD. miRNAs are known to inhibit the translation of their target mRNA. At least 113 species of miRNAs are differentially expressed in patients with NASH within visceral adipose. In this study, we set out to measure the differential levels of expression for six miRNA target genes and the components of the miRNA processing apparatus in patients with simple steatosis vs NASH. We discovered that while in NASH patients expression levels increase for only two

pre-processed miRNAs, for miRNA processing enzymes mRNA level increase throughout the pathway. When the expression levels of several NASH-related genes were studied, we observed concerted changes in the expression levels of the target genes (increased) and levels of miRNA responsible for regulation of these genes (decreased). This observation suggests that regulation by miRNA may be involved in the pathogenesis of NASH. These results warrant additional research in order to establish the precise role of the miRNA regulated genes and their miRNA regulators.

THE ROLE OF CCR5 IN HIV-1 TAT AND MORPHINE MEDIATED NEURODEGENERATION. E.M. Podhaizer[1], Y. Zhang[2], P.E. Knapp[1,3], & K.F. Hauser[1], Depts. of [1]Pharmacology & Toxicology, [2]Medicinal Chemistry, [3]Anatomy & Neurobiology, Virginia Commonwealth University, Richmond VA, 23298. Injection drug use, such as heroin abuse, is closely linked to both the spread and pathogenesis of HIV-1. The effects of HIV-1 Tat, in models of HIV-1 infection, have been shown to be worsened with the addition of morphine and include measures of neurotoxicity, dendritic pathology, and astrocyte calcium and cytokine/chemokine release. CCR5 has been suggested to be involved in Tat-induced signaling through Tat's effects on pro-inflammatory CCR5 ligand secretion. Additionally, morphine and the mu opioid receptor have been shown to regulate CCR5 ligand secretion and both receptor expression and protein levels. Thus, it was hypothesized that inhibition of CCR5 would be protective against neurodegeneration and glial inflammatory signaling. Neurotoxicity was examined in neuronal-mixed glial co-cultures treated with morphine (500 nM), Tat (100 nM), or the combination, in the presence or absence of the CCR5 antagonist maraviroc (50 nM). Maraviroc pretreatment prevented the synergistic neurotoxic effects of collective Tat and morphine treatment. CCR5 inhibition in cultures heavily enriched in astrocytes suppressed both RANTES and MCP-1 chemokine production, but had no effect on TNF-α. This data suggests that CCR5 is a critical convergence point of Tat and morphine signaling. *Supported by NIH P01 DA019398 & T32 DA007027.*

NADPH OXIDASE-MEDIATED INFLAMMASOME ACTIVATION BY ELEVATED HOMOCYSTEINE IN MOUSE PODOCYTES AND GLOMERULI. J. M. Abais, C. Zhang, M. Xia, K. Boini, L. A. Laperle, A. M. Thacker & P-L. Li, Department of Pharmacology & Toxicology, Virginia Commonwealth University, Richmond VA 23298. Hyperhomocysteinemia (hHcys) is an important pathogenic factor contributing to the progression of end-stage renal disease. Recent studies in our laboratory have found that Hcys can activate the inflammasome, potentially turning on the inflammatory response. Hcys is also known to activate nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, and this present study was designed to test whether NADPH oxidase-mediated redox signaling contributes to Hcys-induced inflammasome activation in podocytes. Confocal microscopy showed that Hcys caused a 2.5-fold increase in colocalization between the 3 major inflammasome components - NALP3, apoptosis-associated speck-like protein (ASC), and caspase-1. Furthermore, Hcys increased caspase-1 activity, IL-1β, and superoxide production, and all of these changes in podocytes were significantly blocked by inhibition of NADPH oxidase using apocynin, $gp91^{phox}$ peptide, and $gp91^{phox}$ siRNA. *In vivo*, $gp91^{phox}$ knockout mice protected against inflammasome

formation and dysfunction induced by hHcys. These results suggest that Hcys-induced NADPH oxidase activation is importantly involved in turning on NALP3 inflammasomes, making both NADPH oxidase and the inflammasome potential therapeutic targets for preventing Hcys-induced glomerular sclerosis.

ROLE OF ALPHA7 NICOTINIC ACETYLCHOLINE RECEPTOR IN A MURINE DEXTRAN SULFATE SODIUM-INDUCED COLITIS MODEL. S. AlSharari, H. Akbarali, & M.I. Damaj. Department of Pharmacology & Toxicology, Virginia Commonwealth University, Richmond, VA 23298. Substantial evidence suggests an association between cigarette smoking and the incidence and severity of ulcerative colitis (UC), a common human inflammatory bowel disease (IBD). Nicotine seems to be a key mediator of this response as has been demonstrated by the use of transdermal patches and nicotine enemas. The mechanism through which nicotine acts is not well understood. Identification of nAChR subtypes and their role in UC would lead to better understanding of the disease and the development of better pharmacological treatment of UC. We investigated the role of α5, α6, α7 and β2 nAChR subtypes in a murine model of UC in which dextran sulphate sodium (DSS) to induce colitis in C57 mice and measured a Disease Activity Index (DAI). In addition, α7 KO mice displayed a significantly increased in DAI value (diarrhea, irritation around the anal area, hematochezia, and loss of body weight) compared to their WT littermates. Furthermore, treatment with PHA-543613, a selective α7 agonist, significantly reduced DAI signs in DSS-treated mice compare with vehicle DSS-treated mice. Moreover, we use PNU-120596, a positive allosteric modulator, and Choline chloride, an α7 nAChR full agonist, were both reduced DAI signs in DSS-treated mice. These results suggest that α7 nAChR has a protective role in colitis.

THE ROLE OF 2-AG ENDOCANNABINOID NEUROTRANSMISSION IN NICOTINE REWARD AND WITHDRAWAL. P. Muldoon, A. Lichtman, & M.I. Damaj, Ph.D. Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298. Nicotine is the main addictive component of tobacco that plays a major role in dependence. Emerging evidence suggest that the endogenous endocannabinoid system may modulate these effects. 2-AG is the most abundant endocannabinoid in the brain, required for retrograde transmission and exerts its action via CB1 receptors. We hypothesize that 2-AG neurotransmission is altered during Nicotine Dependence (ND). We first evaluated 2-AG levels in relevant brain regions after acute administration of nicotine (1, 2mg/kg s.c.) using liquid chromatography-mass spectrometric (LC-MS) method. Next, assessed the effect of repeated nicotine injections (2 times a day for 7 days) on 2-AG levels in LC-MS. Unfortunately, in either treatment group we did not see an effect of nicotine on 2-AG neurotransmission. However, this effect could be due to the sensitivity of the assay. Secondly, there could be a dilution of effects since we take whole tissue. We then wanted to measure the effect of enhanced 2-AG via MAGL inhibition by JZL184 in ND. JZL184 is a potent and selective inhibitor of MAGL. Nicotine reward in the mouse was evaluated in an unbiased conditioned place preference paradigm (CPP) in induction. Our results showed that degradation of MAGL dose-dependently decreased nicotine preference compared to nicotine control in our CPP paradigm. Finally, we assessed JZL184's effect on nicotine

withdrawal. Our results verified that JZL184 dose-dependently decreased somatic signs. Our results suggest that MAGL inhibition may be a therapeutic target in ND. P50DA005274

DETERMINING RAI1 BINDING SITES WITHIN *CLOCK*. C.A. Bax[1], S. Williams[2], S. Elsea[2], & D.L. Zies[1], Department of Biological Sciences, [1]University of Mary Washington, Fredericksburg, VA 22401, [2]Virginia Commonwealth University, Richmond, VA 23284. Smith-Magenis Syndrome (SMS) is a neurobehavioral disorder characterized by mental retardation, sleep disturbances, obesity and self injurious / attention seeking behavior. The major symptoms of SMS are caused by haploinsufficiency of the retinoic acid-induced 1 *(RAI1)* gene, which is thought to be a transcription factor involved in the regulation of many other genes. A Chromatin Immunoprecipitation-microarray chip (ChIP-chip) experiment was conducted to determine genes regulated by RAI1. One of the genes identified was Circadian Locomotor Output Cycles Kaput (*CLOCK*). The purpose of this project was to confirm RAI1 as a regulator of *CLOCK* and identify specific binding sites within the gene. Transient transfection and luciferase assays were performed. A statistically significant increase in transcription of luciferase was seen when RAI1 was cotransfected with the regulatory region of *CLOCK*. No significant drop in luciferase levels was seen when the shortened *CLOCK* construct was cotransfected with RAI1. Therefore, the binding site is located within the 227 bases that were not removed by the deletion. The identification of a specific RAI1 binding site would enable researchers to identify other genes regulated by RAI1. Knowing the cohort of genes regulated by RAI1 would provide a better understanding of the specific function of *RAI1* and the downstream effects that lead to the symptoms of SMS.

BOTH POLYCYSTIC OVARY SYNDROME (PCOS) AND NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) ARE DISEASES OF METABOLIC SYNDROME SPECTRUM. T.P. Tran[1,2], A. Baranova[1,2], A. Birerdinc[1,2] & Z.M. Younossi[2,3], [1]Betty and Guy Betty Center for Integrate Research, Iona Health System, Falls Church VA 22042, [2]Center for the Study of Genomics in Liver Diseases, Molecular and Microbiology Department, George Mason University, Fairfax VA 22030, [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church VA 22042. Obesity has been widely known to cause non-alcholic fatty liver disease (NAFLD) and aggravate polycystic ovary syndrome (PCOS). Insulin resistance (IR), a hallmark of metabolic syndrome is observed in 50–80% of women with PCOS and patients with NAFLD. Here, we performed a systematic review using PubMed-search for peer-reviewed articles related to PCOS and NAFLD. Based on the association of PCOS and other metabolic abnormalities, such as IR, hyperandrogenism, obesity and NAFLD, the candidate genes have been proposed for PCOS. Closer scrutiny of these genes places most of their proteins at the crossroads of three highly inter-related conditions: metabolic syndrome, obesity and NAFLD. We showed that the prevalence of both PCOS and NAFLD rises proportionally to the degree of IR and increases in the mass of adipose tissue. These conditions often co-exist and may respond to similar therapeutic strategies. We suggest that it is appropriate to consider PCOS as the ovarian manifestation of

metabolic syndrome, similarly to NAFLD that was earlier proposed as the hepatic manifestation of metabolic syndrome.

THE ROLE OF NEURONAL NICOTINIC ACETYLCHOLINE RECEPTORS IN MORPHINE DEPENDENCE. Lindsay M. Kondo & M. Imad Damaj, Dept. of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond VA 23298. Opiate addiction is a growing concern in today's society. Opiate users show little success in maintenance treatments and improved clinical therapies are needed. Evidence suggests that neuronal nicotinic acetylcholine receptors (nAChRs), which contribute to nicotine dependence, may also influence morphine dependence. We used two complementary approaches, genetically modified mice and pharmacological ligands, to study the involvement of α6* nAChRs (* denotes additional subunits). In the first experiment, α6* knockout (KO) mice and wild type (WT) littermates were injected twice a day with ascending doses of morphine (20, 40, 80, 100 mg/kg morphine, s.c.) for 8 days. On day 9, mice received a pretreatment of morphine two hours before naloxone challenge (2 mg/kg, s.c.) and abstinence signs were observed for 30 minutes including jumps, paw tremors, head shakes, ptosis, backing, and diarrhea. We observed that the KO mice showed an increased intensity of withdrawal signs in comparison to the WT controls. To complement our transgenic approach, we used a peptide-like α6β2* selective antagonist, α-conotoxin MII-[H9A;L15A]. In this study, mice were injected three times per day for three days with ascending doses of morphine (50, 75 and 100 mg/kg morphine, s.c.). On day 4, mice received a morphine pretreatment followed by an injection of α-conotoxin MII-[H9A;L15A] (12 pmol, i.c.v.) 5 minutes before naloxone. MII-[H9A;L15A] treatment enhanced the intensity of global somatic withdrawal signs ($p<0.05$). Taken together, these results suggest that α6* nAChRs offer a novel target for the treatment of physical morphine dependence.

AUTOLOGOUS PLATELET-RICH PLASMA (PLATELET GEL) ENHANCES BLOOD FLOW IN LARGE SOFT TISSUE WOUNDS IN VIVO AND REDUCES BACTERIAL GROWTH IN VITRO. B.F. Host, F. Li & B. Hargrave, Center for Bioelectrics, Old Dominion University, Norfolk VA 23508. Platelet-rich plasma (PrP) enhances the process of wound healing in soft tissues. Platelets in whole blood were concentrated 7-10 times using a Harvest Technologies Concentrator. Concentrated platelets were then placed into a sterile pulsing cuvette and activated by exposure to a 30-kV/cm electric field for 5 pulses, with each pulse having a duration of 300 ns. With the animal under a surgical plane of anesthesia, a 3x8 cm surgical wound was created on the dorsal surface of each animal, and the autologous platelet-rich plasma (formed from rabbit blood) was applied directly to the wound site. To assess the return of blood flow to the wounded area, the wound was imaged using a Moor Instruments Laser Doppler Imager just prior to the creation of the wound, and also post-operatively on days 0, 3, 7, 14, and 21. The wounds of 4 animals were treated with saline and these animals served as our controls. The wounds of 6 animals were treated with PrP. Results are reported as the mean ± standard deviation. Our current data suggest that the return of blood flow to the distal region of the wound was significantly greater in the PrP-treated animals than in the control animals treated with saline.

IDENTIFICATION OF GENES THAT MEDIATE ETHANOL-INDUCED ACUTE FUNCTIONAL TOLERANCE IN *C. ELEGANS*. Ka-Po Leung, M. Bolling, J. Gardner, A. Davies & J. Bettinger, Deptartment of Pharmacology and Toxicology, VCU, Richmond, VA 23298. Alcohol abuse and alcoholism are prevalent diseases in our society. There are few adequate treatments available, in part because the molecular mechanisms behind the development of alcoholism are still unclear. We know from human genetics studies that there is a significant genetic component that influences disease susceptibility, and that an individual's development of acute functional tolerance (AFT) after alcohol consumption are strong predictors of lifetime development of addiction. We have taken a genetic approach to study the development of tolerance to ethanol. We used *C. elegans* as a behavioral model for the study of alcohol responses because of its simple nervous system and conserved neurobiology. We performed a genetic screen looking for mutations in genes that are required for the development of AFT to ethanol. Previous studies have shown that the gene NPR-1, a G protein-coupled neuropeptide receptor in *C. elegans* that is homologous to the mammalian neuropeptide Y (NPY) receptor, negatively regulates the development of AFT; animals that lack NPR-1 function develop tolerance to ethanol at a faster rate relative to animals with intact NPR-1. We used an inactivated *npr-1* gene strain, *npr-1(0),* as a sensitized background for a phenotypic screen to identify animals that are unable to develop AFT. We have identified a mutation, *bet11*, that causes mutant animals to be defective in the development of AFT. Identifying the genes that are responsible for alcohol-induced development of AFT will provide a better understanding of the mechanisms that cause alcohol abuse and alcoholism.

THE GALACTOLIPID SULFATIDE IS A NEGATIVE REGULATOR OF CELL PROLIFERATION. S.A. Freeman, A.D. Pomicter & J.L. Dupree, Department of Anatomy and Neurobiology, Virginia Commonwealth University, School of Medicine, Richmond VA, 23284. Myelin is an electrically insulating sheath that oligodendrocytes wrap around neurons, greatly increasing the speed and efficiency of electrical signaling between neurons. Unlike other membranes, myelin is lipid rich and composed of approximately 70% lipid. Myelin is also unique in that it contains an abundance of galactolipids. The two most prominent myelin galactolipids are galactocerebroside and its sulfated derivative sulfatide, made by the enzyme cerebroside sulfotransferase (CST). The CST null mouse exhibits an increased population of oligodendrocytes due to enhanced proliferation and decreased cell death in the spinal cord, but the mechanism of these changes is not known. The goal of this project is to determine if the inhibition of sulfatide results in increased proliferation in Madin Darby canine kidney (MDCK) cells, a sulfatide expressing, immortal cell line. In separate experiments, we will utilize sodium chlorate to block sulfatide production. The sulfatide antibody O4 and bromodeoxyuridine (BrdU) will be used to examine the amounts of sulfatide and proliferation, respectively. Preliminary results suggest that MDCK cells treated with sodium chlorate exhibit an elevated cell population via a mechanism favoring increased proliferation, and additionally, sodium chlorate treated cells show decreased morphologic complexity, which is consistent with findings in the CST null mouse. Understanding the complex

factors that regulate oligodendrocyte proliferation is critical for future production of therapeutics for multiple sclerosis patients.

THE RELATIONSHIP BETWEEN PHYSICIAN SPECIALIZATION AND COMMUNICATION EFFICACY. Amber Collier[1], Matthew Cronin[1], [1]School of Management, George Mason University, Fairfax, VA 22030. A central challenge in being an effective physician is communication; patients need reassurance and emotional support, and also need to be informed about risks and requirements of treatment. The challenge is for the physician to be compassionate and communicate complex information in a way that the patient can understand. As physicians become more specialized, these functions may become more difficult to perform. This presents a challenge as the patients who go see specialists often do so because their health conditions are more serious. If specialists are having greater difficulty with communication this could have significant effects on the patient's health outcome. Currently, there is no existing research that explores this area of communication and its corresponding relationships. Thus, this project aims to discover whether and how increased specialization negatively affects the quality of communication, and ultimately the patient's health. We plan to achieve this through survey scales that gauge different dimensions of communication and objective/subject health measures. If we find it does, we hope to be able to suggest mitigation measures.

COMPONENTS OF THE METABOLIC SYNDROME AND THEIR RELATION TO NAFLD IN MORBIDLY OBESE PATIENTS. C.T. Nguyenngo[1], A.Baranova[2,3], Z.Younossi[3], M.J. Estep[1,3], [1]Biology Department, College of Science, George Mason University, Fairfax, VA 22030, [2]School of Systems Biology, College of Science, George Mason University, Fairfax, VA 22030, and [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church, VA 22042. Non-alcoholic fatty liver disease (NAFLD) and its most severe form non-alcoholic steatohepatitis (NASH) are often referred to as the hepatic manifestations of metabolic syndrome. However, firm connections between individual components of metabolic syndrome and the progression of NAFLD have yet to be conclusively established. The aim of this study was to examine the relationship between lipid profiles and NAFLD progression in morbidly obese patients. Circulating concentrations of fasting glucose, HDL, LDL, Total cholesterol, and triglycerides was obtained using Cholestech-GLU kits. Descriptive statistics, Mann-Whitney U-tests, and Spearman correlations were calculated. Of the 416 NAFLD patients, 245 had progressed to NASH. Significant differences were seen between NASH and non-NASH NAFLD in circulating concentrations of HDL, Triglycerides, and Glucose. Diagnosis of NASH and circulating concentrations of HDL were negatively correlated, while NASH and Triglyceride levels and NASH and glucose levels were positively correlated. The individual components of metabolic syndrome are associated with stage of NAFLD progression to NASH.

LIVER FUNCTION IN HCV PATIENTS WITH DIFFERENT IL28B ALLELIC GROUPS. R. Guragain[1], A. Baranova[2, 3], Z. Younossi[3], & M. Estep[1, 3], [1]Bio. Dept., [2]School of Sys. Bio., George Mason University, Fairfax VA, and [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church VA. IL28B genotype is an important

host factor in treatment of Hepatitis C virus (HCV) infection. HCV patients could be either homozygous for "C" allele (CC-group), or homozygous for "T"/ heterozygous (non-CC-group). The success rate of achieving Sustained Viral response (SVR) in the CC-group is significantly higher. However, other host-related factors that affect liver function may also affect rates of SVR achievement. We examined distinctions in clinical parameters between CC-group and non-CC-group HCV patients. Blood samples and laboratory data were obtained for 56 patients who had undergone standard HCV treatment. DNA was extracted using QIAmp Minikit (Qiagen). Allelic discrimination was performed by tetra-primer PCR and electrophoresis. Spearmen correlations and Mann-Whitney tests were performed. Of the 23 patients that comprised the CC group, 15 had achieved SVR. Of the 33 non-CC-group patients, only 8 had achieved SVR. SVR negatively correlated with occurrence of significant steatosis ($r= -0.31$, $P=0.03$). Interestingly, among the patients that achieved SVR, those with CC genotype had significantly increased liver enzymes compared to non-CC-group (average ALT levels 59.75U/l and 35.4U/l, respectively ($P=0.007$)). Similar trends were observed for AST levels (86.91U/l vs. 63.8U/l ($P=0.02$)). Additionally, urine nitrogen was also significantly higher in the CC-group that achieved SVR (18.5mg/dl vs. 8mg/dl, ($P<0.001$)). The results support the hypothesis that factors affecting liver function such as steatosis may have a more significant impact on the achievement of SVR in the non-CC-group.

HOMA CALCULATOR TO CALCULATE RESISTANCE SCORE USING HOMEOSTASIS MODEL ASSESSMENT. L. Alomair[1], L. Wang[1], A. Birerdinc[1,2], J.M. Estep [2,3] & A. Baranova[1,2,3], [1]School of Systems Biology, College of Science, George Mason University, Fairfax, VA, USA, [2]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA, [3]Center for Liver Diseases, Inova Fairfax Hospital, Falls Church, VA, USA. Insulin is a protein that plays a major role in glucose metabolism. Insulin may be quantified in the serum as whole insulin or as C-peptide, where C-peptide is more stable to degradation in during sample processing and storage. C-peptide is a byproduct created when the hormone insulin is produced. Equimolar amounts of C-peptide and insulin are then stored in secretory granules of the pancreatic beta cells and both are eventually released to the portal circulation. Homeostasis Model Assessment (HOMA) scores are a combination of fasting insulin and glucose measurements in the serum. HOMA indices are used to assess insulin resistance (IR). Currently, there no publically available software to calculate HOMA scores using C-peptide data. Here we present a software tool capable of calculation of Homeostasis Model Assessment (HOMA) scores based on both fasting C-peptide and fasting insulin levels. Use of this tool will allow researchers to optimize their analysis of insulin resistance in human subjects.

THE DISCRIMINATIVE STIMULUS EFFECTS OF NITROUS OXIDE IN MICE. Kellianne J. Richardson & Keith L. Shelton. Deptartment of Pharmacology & Toxicology, Virginia Commonwealth University, Richmond, VA 23298. Despite the high prevalence of clinical and illicit use, the *in vivo* actions of nitrous oxide are unclear. *In vitro* studies have shown that nitrous oxide alters the function of NMDA, $GABA_A$, and nicotinic acetylcholine receptors, among others. However, the receptor

system or systems responsible for the intoxicating, subjective effects of nitrous oxide are unknown. Our objective was to use drug discrimination in mice to assess the neurotransmitter systems responsible for producing the subjective stimulus effects of nitrous oxide. Sixteen male B6SJLF1/J mice are being trained to discriminate 10 min of exposure to 60% inhaled nitrous oxide from 100% oxygen. Discrimination training under conditions in which training and test sessions were done in room air after cessation of nitrous oxide exposure resulted in lengthy training requirements and poor stimulus control. As a result the procedure was modified to conduct discrimination training and testing while being concurrently exposed to nitrous oxide. Thirteen mice thus far have acquired the discrimination and begun substitution testing with increasing nitrous oxide concentrations. The results indicate that under proper training conditions nitrous oxide can serve as a discriminative stimulus. Further testing will be conducted using site-selective test drugs to determine the neurotransmitter systems responsible for the discriminative stimulus effects of nitrous oxide.

CHARACTERIZATION AND OPTIMIZATION OF THE SYNAPTONEUROSOME PREPARATION IN ORDER TO INVESTIGATE ETHANOL INDUCED ALTERATIONS TO THE SYNAPTIC TRANSCRIPTOME. Megan A. O'Brien & Michael F. Miles, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond VA 23298. It is well established that mRNA can be transported to neuronal distal processes, where it can undergo localized translation regulated in a spatially restricted manner in response to stimulation, potentially playing a role in synaptic plasticity that results in long-term adaptive brain responses. In order to investigate our hypothesis that ethanol behavioral sensitization results, at least in part, from alterations in the trafficking of mRNAs to distal processes, we have worked to optimize a protocol for obtaining synaptoneurosomes from the frontal pole of mice treated with repeated ethanol. In the protocol, fresh tissue undergoes homogenization and fractionation resulting in a pelleted fraction (P2) that should be enriched with vesicularized pre- and post-synaptic elements from which RNA and protein can be extracted. Characterization of the preparation through electron microscopy, western blotting, and quantitative PCR indicate synaptic enrichment of the putative synaptoneurosome fraction. Attempts to further isolate synaptoneurosomes were undertaken through an immunoaffinity purification scheme targeting the synaptic transmembrane protein, Neuroligin. We conclude that the synaptoneurosome preparation will provide us with samples enriched in synaptically localized mRNAs and proteins that will aid our investigation into the underlying molecular alterations that contribute to behavioral sensitization in response to repeated ethanol.

CHRONIC INHIBITION OF MONOACYLGLYCEROL LIPASE REDUCES THE INTENSITY OF PRECIPITATED WITHDRAWAL SIGNS IN OPIOID DEPENDENT MICE. R.A. Owens[1], D. Ramesh[1], B.F. Cravatt[2] & A.H. Lichtman[1], [1]Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA, 23298, [2]Scripps Research Institute, La Jolla, California, 92037. Chronic use of opioids can lead to dependence that results in a clinically significant withdrawal syndrome upon drug cessation. It has been shown that

Δ^9–tetrahydrocannabinol (THC) reduces opioid withdrawal signs in rodents via CB_1 receptors. **The** endocannabinoids, anandamide (AEA) and 2-arachidonyl glycerol (2-AG), also activate CB_1 receptors, but they are rapidly metabolized by their respective enzymes, fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL). Research from our laboratory suggests that acute administration of these catabolic enzyme inhibitors reduces naloxone-precipitated withdrawal signs in morphine-dependent mice. In the present study, we investigated whether the MAGL inhibitor JZL184 would retain its anti-withdrawal effects following repeated administration. ICR mice were implanted with 75 mg morphine pellets, and challenged 72 h later with the opioid receptor antagonist naloxone to precipitate withdrawal. The presence of somatic withdrawal signs such as such as jumps, front paw flutters, weight loss, and the occurrence of diarrhea were measured. As previously reported, acute treatment of THC (10mg/kg) significantly reduced the occurrence of jumps and diarrhea. Repeated treatment with high dose of JZL184 (40 mg/kg), but not the low dose (4 mg/kg), reduced all measured signs of opioid withdrawal. The results of the present study indicate that inhibitors of MAGL offer a promising target to treat opioid dependence.

LYSOPHOSPHATIDIC ACID UPREGULATES EXPRESSION OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA IN OVARIAN CANCER CELLS. J.K. Ngwainmbi, A. Mukherjee & F. Fang, Department of Biochemistry and Molecular Biology, Virginia Commonwealth University, Richmond, VA 23298. Ovarian cancer is the fifth most common cancer among women in the United States and it is the leading cause of death among all gynecological cancers. Most early stage ovarian cancers are detected incidentally on routine pelvic examinations, and five year survival rates of over 90% can be achieved for localized disease. Lysophosphatidic acid (LPA), is a soluble phospholipid made up of a single fatty acyl chain, a glycerol back bone and a free phosphate group. It stimulates proliferation, survival, migration and invasion of ovarian tumor cells by acting on its cognate G protein-coupled receptors. Previous studies by others suggest that LPA binds and activates *peroxisome proliferator-activated receptor gamma* (PPARγ), a nuclear transcription factor important in regulation of fat and energy metabolism. In the current study, we did not observe any evidence for direct interactions between LPA and PPARγ instead, we demonstrated that LPA induces the expression of PPARγ in ovarian cancer cells leading to an increase in its transcriptional activity. This work points to a novel mechanism for activation of PPARγ by LPA in mammalian cells.

Natural History & Biodiversity

TWELVE YEARS LATER: ECOLOGICAL COMMUNITIES OF THE ABRAMS CREEK WETLANDS IN WINCHESTER AND FREDERICK COUNTY, VIRGINIA. Briana L. Barron, James E. Bisset, Linden E. Lewis, Daniel A. Milhon, Cory M. Miller, Benjamin S. Sawyer, Amy L. Smith, John V. Stevens & Woodward S. Bousquet, Environmental Studies Department, Shenandoah University,