



**TOBACCO-RELATED DISEASE
RESEARCH PROGRAM**

Tobacco Control, Research, and Education:

**Joining Forces
to Address
New Challenges**



October 27-29, 2015
Sheraton Grand Sacramento Hotel



Compendium of Abstracts

POSTER SESSION: How Tobacco Causes Disease

(DAY-1: Tuesday, October 27, 5:35-6:30PM)

Abstract# 1-19

1-**Thirdhand Smoke Causes DNA Damage and Cell Transformation in vitro**

Bo Hang^{1*}, Altaf H. Sarker¹, Yurong Huang¹, Jian-Hua Mao¹, Kelly S Trego¹, Ahmed Chenna³, Christopher Havel⁴, Anthony Iavarone⁵, Saikat Saha⁶, Peyton Jacob, III⁴, Tapas K. Hazra⁶, Suzaynn Schick⁴, Dyvia Sharan¹, Amy Min¹, Virender K. Rehan⁷, Mohamad Sleiman², Hugo Destailats², Lara Gundel²

¹Department of Molecular and Cell Biology, Life Sciences Division, and Indoor Environment Department, ²Environmental Energy Technologies Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720

⁶Monogram Biosciences Inc, South San Francisco, CA 94080

A long-term goal of our research is to understand the potential cancer risk of exposure to thirdhand smoke (THS), a newly described health risk. We have discovered that THS and its specific constituent NNA (1-(N-methyl-N-nitrosamino)-1-(3-pyridinyl)-4-butanal) can cause significant cellular changes at realistic concentrations. THS causes genotoxic damage in various human cell lines that increases the risk of cancer, including DNA double strand breaks (leading to genetic instability), formation of DNA adducts and oxidative damage to DNA (leading to mutations). THS exposure to human lung cells led to colony formation in soft agar assays, suggesting that it can promote anchorage-independent growth of these cells, an accurate and stringent in vitro indicator of neoplastic transformation and abnormal growth that can lead to cancer. In mechanistic studies, we have recently found that NNA can readily modify both 2-deoxyguanosine (dGuo) and 2-deoxycytidine (dCyt) in in vitro reactions. In the reaction of NNA with dGuo, several adducts have been identified, including 8-oxo-2'-deoxyguanosine (8-oxo-dG), a novel bulky dG adduct 1,N2-NNA-dG, and a DNA sugar damage, forming 5' & 3'-methyl-dG. These results provide evidence for DNA damaging potential of NNA, which, in part, may contribute to THS-induced adverse health effects in humans. In addition, the NNA-specific DNA adduct(s) identified may be used as a specific biomarker of THS exposure. In conclusion, the findings of our study have demonstrated for the first time that exposure to THS and NNA is genotoxic in human cell lines, with the tendency to cause cell transformation.

2-**Insulin Resistance Stimulated by Third-Hand Smoke Exposure is decreased by Treatment with Antioxidant Agents**

Neema Adhami, Cristina Flores and Manuela Martins-Green

Cell Biology and Neurosciences Department, University of California, Riverside

Third-hand smoke (THS) is the accumulation of secondhand smoke (that contains thousands of toxins) on environmental surfaces; these molecules age with time, becoming progressively more toxic. Exposure to THS can occur by ingestion, inhalation and dermal absorption. Children living in the homes of smokers are at most risk, because they crawl on the floor, touch parents clothing/hair, furniture and other household objects and then place their hands in their mouth. We show that exposure of C57/BL6 mice to THS results in oxidative stress with elevated presence of H₂O₂ and SOD activity and reduction in the activity of the antioxidant enzymes catalase and glutathione peroxidase. We also observe increased lipid peroxidation, protein nitrosylation and DNA damage as well as increased circulating glucose, leading to hyperglycemia despite the fact that insulin is also elevated. In addition, the insulin signaling mechanism involving the IR-IRS-PIP3-AKT axis is dysfunctional leading to insulin resistance. To determine whether the THS-induced oxidative stress is responsible for these effects we treated the exposed mice with the antioxidants N-acetyl cysteine and Alpha-tocopherol for 5 months. As a result, fasting blood glucose levels dropped, the levels of insulin were reduced, H₂O₂ levels and SOD activity were lower, while GPx and catalase activity were increased. Furthermore, lipid peroxidation and protein nitrosylation in antioxidant treated mice are also lower. These results show that insulin resistance in THS-exposed mice is induced by increased oxidative stress in the muscle, a major peripheral organ involved in glucose metabolism, and that treatment with antioxidants alleviates/reverses damage.

3-

Identification of cytotoxic chemicals in third hand smoke

1 V. Bahl, 2 M. Sleiman, 3 S. Schick, and 1 P. Talbot

1University of California, Riverside; 2Lawrence Berkeley National Laboratory; 3
University of California, San Francisco

Extracts of THS-exposed terry cloth were cytotoxic in an MTT assay for cell viability. Following further aging, extracts lost cytotoxicity, suggesting that cytotoxicity was caused by volatile organic chemicals. A group of volatile compounds found in THS headspace was screened using the MTT assay; three were cytotoxic and acrolein was the most potent. A live cell imaging assay showed that acrolein killed cells at high doses and inhibited proliferation at non-lethal doses. Gene expression array analysis revealed that acrolein inhibited proliferation by blocking two phases in the cell cycle, at concentrations that are within the dose range that individuals inhale in areas contaminated by THS. These results indicate that inhalation of THS could impair respiratory cells and increase morbidity.

4-**Third-Hand Smoke Alters Balance of Stress Hormones Resulting in Non-Obese Type-2 Diabetes Involving Mitochondrial Dysfunction**

Neema Adhami and Manuela Martins-Green

Cell Biology and Neuroscience Department, University of California, Riverside

Third-hand smoke (THS) is the accumulation of secondhand smoke on environmental surfaces, becoming more toxic with time. THS can be found in places where smoking has taken place and is a danger to health, in particular to infants and young children. New data are emerging on the effects of these "stealth" toxicants on metabolism. We show here that non-obese THS-exposed mice on normal diet develop metabolic syndrome with increased fasting blood glucose, hyperinsulinemia and decreased expression of insulin-signaling molecules. The onset of metabolic syndrome is associated with imbalance in key metabolic hormones. We find increases in corticosterone (cortisol in humans) and epinephrine, two hormones that are elevated when people are exposed to different kinds of stress such as THS toxins. At the same time, the hormone adiponectin, that modulates glucose regulation and fatty acid metabolism, is significantly decreased in THS-exposed mice. This type of hormonal imbalance is usually associated with obesity and bad diet, that, in the muscle, a highly metabolic tissue, shuts down insulin signal transduction pathways through downregulation of key insulin signaling proteins IR, AKT, PI3K and GLUT 4, as we observe in THS-exposed mice. Furthermore, this hormonal state leads to mitochondrial dysfunction by reducing the levels of active AMPK and PGC-1 α , master regulators of mitochondrial biogenesis and function. Indeed, THS-exposed mice have decreased ATP levels and increased lactate levels, two biomarkers of mitochondrial function. We speculate that mitochondrial dysfunction caused by these hormonal alterations leads to poor metabolism and insulin resistance in the absence of poor diet.

5-**Thirdhand Cigarette Smoke Triggers Stress Induced Mitochondrial Hyperfusion in Neural Stem Cells**

Vasundhra Bahl¹, Kimberly Johnson¹, Julian Hartzell¹, Suzaynn Schick² and Prue Talbot¹

¹ University of California, Riverside; ² University of California, San Francisco

Little is known about health effects of thirdhand smoke (THS) on postnatal brains, which are adversely affected by secondhand smoke. Mouse neural stem cells (mNSC), derived from neonatal brain, were used to evaluate the impact of THS on cell survival and mitochondrial stress. mNSC were exposed to solutions of THS extracted from cotton fabric exposed to smoke from about 133 cigarettes, and cytotoxicity was evaluated using the MTT assay. THS inhibited cell proliferation and survival dose dependently, indicating that THS exposure could adversely affect brain cells. Effects of non-lethal doses of THS on mitochondrial morphology and membrane potential were studied using MitoTracker Red. Compared to controls, cells treated with THS had larger/ fewer mitochondria with altered morphology and increased mitochondrial membrane potential (MMP). ATP production and oxidative stress increased significantly (demonstrated by chemiluminescence and fluorescence) in THS treated cells. These data indicate that THS triggers stress induced mitochondrial hyperfusion (SIMH) in mNSC. This response was not reversed when exposure stopped. Longer exposure resulted in a loss of MMP suggesting mitochondrial function was compromised. SIMH can either rescue mitochondria through fusion of healthy and unhealthy mitochondria or cause cells to die if they are overwhelmed by stress. SIMH could affect the differentiation potential of stem cells at doses that do not affect cell proliferation or survival.

6-

Immunophenotyping of Second Hand Smoke-Related Asthma Using Mass Cytometry

Rebecca N. Bauer, R. Sharon Chinthrajah, Sandra Andorf, Benjamin Hobson, Rachel L. Miller, Kari C. Nadeau

Department of Medicine, Stanford University; Department of Medicine, Columbia University

Second hand smoke (SHS) exposure is associated with increased risk of asthma development and worse asthma symptoms, suggesting that SHS exposure promotes a more severe form of asthma. Recent studies suggest that there are many subtypes of asthma defined by the types of immune cells in the airway and blood, and that therapies specific to each subtype may better treat asthma. The objective of this research is to understand how SHS exposure alters immune cells that may worsen asthma. We assessed SHS and asthma related changes in immune cells from the blood using mass cytometry. This technique uses antibodies to measure expression of up to 40 immune markers on a single cell to identify types of immune cells that associate with asthma or SHS exposure. Asthmatic volunteers were defined by history of asthma diagnosis and breathing tests suggestive of asthma. Lifetime SHS exposure was determined by questionnaire. Our results show that SHS exposure affects T cells in the blood and that the effect of SHS exposure on these immune cells differs in asthmatics and non-asthmatics. We found that in non-asthmatics, but not asthmatics, lifetime SHS exposure was associated with more inflammatory T cells and a corresponding increase in production of the inflammatory mediator, IFN γ , by T cells. Results from our ongoing studies may unveil diagnostic markers of SHS-related asthma that could help doctors determine the most appropriate asthma treatment. Improved understanding of how SHS impacts asthma will lead to more informed regulations and promotional material to control SHS exposure.

7-

Effect of THS Toxins on Wound Healing Response Mechanisms, Leading to Impaired Healing

Sandeep Dhall, Raquelle Alamat, Anthony Castro, Joao Pedro Silva, and Manuela Martins-Green

Department of Cell Biology and Neuroscience University of California Riverside,
Riverside, California 92521

It has been shown that smokers have impaired healing, especially after surgery. However, it is not known whether Third Hand Smoke causes the same problems. It is known that 88M US nonsmokers >3 years old living in homes of smokers are exposed to THS toxicants and show blood cotinine levels of >0.05ng/ml, suggesting susceptibility to developing impaired healing. We show that mice living under conditions mimicking THS exposure in humans display impaired healing. These wounds have increased superoxide dismutase, H₂O₂, and significantly lower glutathione peroxidase activity, while catalase activity is unchanged. This leads to excessive oxidative-stress-induced damage, including significantly elevated protein nitration, lipid peroxidation, and DNA damage. Importantly, elevated DNA damage in non-wounded skin indicates that THS toxin exposure over time leads to alterations in DNA that potentially affect cutaneous wound healing. This damage is most likely due to the presence of tobacco specific nitrosamines (TNSAs). In order to demonstrate that redox imbalance is critical in THS-induced impaired healing, exposed mice were treated with antioxidants α -Tocopherol and N-acetylcysteine for a month before wounding. This decreased reactive oxygen species levels. However, high levels of cellular and molecular damage were still present. THS wounds also showed presence of leaky blood vessels, hyperactive platelets and "fibrin cuffs", and abnormal hemostasis and thrombogenesis. Furthermore, THS-exposed mice had lower levels of inflammatory cytokines with decreased influx of inflammatory cells early after injury. These findings strongly suggest that THS toxicants affect wound healing by altering critical wound response mechanisms that are only partially reversed by antioxidants.

8-

Metabolomics reveals metabolic changes in male reproductive cells exposed to thirdhand smoke

B. Xu, MJ. Chen, MM. Yao, XL. Ji, ZL. Mao, W. Tang, SL. Qiao, SF. Schick, JH. Mao, B. Hang, YK. Xia

Lawrence Berkeley National Laboratory, Nanjing Medical University, University of California, San Francisco

Thirdhand smoke (THS) is a new term for the toxins in cigarette smoke that linger in the environment long after the cigarettes are extinguished. The effects of THS exposure on male reproduction have not yet been studied. In this study, metabolic changes in two male germ cell lines (GC-2 and TM-4) were analyzed after THS treatment for 24 hours. THS-loaded chromatography paper samples were generated in a laboratory chamber system and extracted in DMEM. At a paper:DMEM ratio of 50?g/ml, cell viability in both lines was normal, as measured by the MTT assay and markers of cytotoxicity, cell cycle, apoptosis and ROS production were normal as measured by quantitative immunofluorescence. Metabolomic analysis was performed on methanol extracts of GC-2 and TM-4 cells using gas chromatography-time-of-flight mass spectrometry (GC-TOF MS). Glutathione metabolism in GC-2 cells, and nucleic acid and ammonia metabolism in TM-4 cells, was changed significantly by THS treatment. Reverse Transcription-Polymerase Chain Reaction (RT-PCR) analyses of mRNA for enzyme genes Gss and Ggt in GC-2 cells, and TK, SMS and Glna in TM-4 cells reinforced these findings, showing changes in the levels of enzymes involved in the relevant pathways. In conclusion, exposure to THS at very low concentrations caused distinct metabolic changes in two different types of male reproductive cell lines, indicating potential hazardous effects of THS on male reproduction.

9-

Assessing exposure to thirdhand smoke (THS) in humans: The need for a comprehensive approach

Peyton Jacob, III, Christopher Havel, Lisa Yu, Neal L. Benowitz

University of California, San Francisco

The objective of our studies is to assess exposure to THS, by developing biomarkers and environmental tracers that can be measured using mass spectrometric methods. Tobacco smoke is a complex mixture of particles and gases. Thousands of compounds have been identified in tobacco smoke, including potent carcinogens and other toxic substances. Some are specific to tobacco, but others are not. If a study requires measuring nicotine exposure, concentrations of nicotine metabolites in biological fluids can be used as biomarkers to estimate exposure. However, if a study requires measuring exposure to THS, exposure assessment is not so simple. Distinguishing THS exposure from secondhand smoke (SHS) exposure is a challenging problem. The changes that occur as SHS evolves into THS are mainly changes in distribution in the environment, rather than conversion of SHS components into unique substances specific to THS, that could be used to distinguish THS exposure from SHS exposure. The main differences are in the ratios of compounds due to different fates in the environment after release from burning cigarettes. Although a unique biomarker or environmental tracer is a possibility and is under investigation, at the present a comprehensive approach in which a number of biomarkers and environmental tracers are measured is probably the best approach. Exposure assessment is essential for evaluating the public health impact of THS. In this presentation, biomarkers and environmental tracers developed by and under investigation by the California Consortium on Thirdhand Smoke will be discussed.

10-

Post-natal exposure to thirdhand cigarette smoke affects body mass and immunological function in mice

Bo Hang, Yurong Huang, Antoine M. Snijders, Suzaynn Schick, Christopher Havel, Peyton Jacob III, and Jian-Hua Mao

Lawrence Berkeley National Laboratory, University of California, San Francisco

Thirdhand smoke (THS) is the fraction of cigarette smoke that persists in indoor environments after smoking. We have investigated the effect of THS exposure between birth and weaning on body mass and blood cell populations in C57BL/6J mice. 100% cotton terrycloth was repeatedly exposed to controlled concentrations of secondhand smoke. Newborn mice were bedded on this THS-laden cloth together with standard bedding until weaning at 3wks, and then switched to only standard bedding. Control animals were housed separately in standard bedding. The mice were weighed at 5,8,12 and 17wks. A complete blood cell count was done by HemaVet950FS and specific lymphocytes were assessed by FACS with cell specific markers at 17wks. At weaning, THS-treated male and female mice had significantly lower body mass than control mice. After weaning, THS-treated mice gained significantly more body mass to catch up to the controls after 5wks. In THS-exposed mice, neutrophil, eosinophil and basophil counts, mean platelet volume, and proportion of myeloid and T-suppressor cells were significantly higher at 17wks, while hematocrit, mean cell volume, red cell distribution width and platelet count were significantly lower, suggesting that THS may cause bone marrow damage and inflammation. Our results demonstrate that THS exposure during a critical window-of-susceptibility can affect development and induce persistent changes in immune function potentially contributing to the adverse impacts on human health.

11-

Partitioning of Nicotine and Nitrosamines in Thirdhand Smoke Particulate Matter

Suzaynn Schick, PhD, Aaron Whitlatch, BS, Adam Whitlatch, BS, Peyton Jacob, PhD, Christopher Havel, PhD

Department of Medicine, University of California, San Francisco

Aged secondhand cigarette smoke was created by passing machine generated smoke through a stainless steel chamber at 2 air changes per hour. Thirdhand cigarette smoke (THS) was created by closing the ventilation through this chamber for 12 hours and then flushing the chamber with conditioned, filtered air. Particle samples were collected isokinetically on 47 mm filter membranes, extracted with 50% methanol:1% HCl and analyzed by LC-MS/MS. The THS particles contained significantly higher concentrations of nicotine, nicotelline and myosamine per milligram than SHS and lower levels of the higher molecular weight molecules nicotelline and NNK. SHS particles contained 9.7ug nicotine per mg PM, and THS particles contained 99ug/mg PM. NNN and NNA were not detectable in the THS particle samples. We believe that these findings are due partly to re-entry of nicotine and the other volatile alkaloids myosmine and bipyridine from the interior of the SAC, and the fact that as tobacco smoke ages it becomes more acidic, which increases the partitioning of basic substances into the particulate matter. The surfaces in the smoke aging chamber have high levels of THS from previous experiments and constitute a source from which chemicals can reenter the aerosol phase during the overnight incubation period that creates the THS aerosol. Over time, THS chemicals with lower molecular weight and higher volatility, like nicotine, are more likely to desorb from interior surfaces and interact with airborne particles than chemicals with higher molecular weight, like NNK and nicotelline.

12-

StemCellQC: A Toolkit for Evaluating the Effects of Tobacco Products Including Electronic Cigarettes on Prenatal Development

Atena Zahedi, Sabrina Lin, Vincent On, Prue Talbot

Cell Biology and Neuroscience Department, IGERT in Video Bioinformatics Program,
University of California, Riverside

The objective was to develop a video bioinformatics platform, StemCellQC?, to address the need for automated tools for evaluating the effects of toxicants, such as cigarette smoke (CS) and electronic cigarette (EC) aerosol, on prenatal development. Human embryonic stem cells (hESC) are an excellent model for studying the effects of tobacco products on young embryos. StemCellQC? was specifically designed extract biological information from phase-contrast videos of pluripotent stem cell cultures and to classify the health of hESC colonies. This non-invasive, unbiased toolkit can significantly reduce analysis time, resources, and eliminate the need for invasive labeling. To validate the software, hESC were treated with 0.1 puff equivalent (PE) Marlboro Red (MR) sidestream (SS) smoke to induce a heterogeneous population of healthy, unhealthy, and dying hESC colonies. 24 morphological and dynamic features were analyzed and several cellular processes were successfully identified to be altered in the treated group. MR SS smoke significantly inhibited colony growth (area, perimeter, major axis length, and number protrusions) and motility (mean square displacement), and induced increased apoptosis (brightness to total area ratio) in treated colonies. From these data, StemCellQC? provided both user-specified and classifier-determined analysis in cases where the effects on stem cells were not intuitive or anticipated. Video analysis algorithms allowed assessment of biological phenomena.

13-**Harm Reduction Tobacco Induces Skeletal Teratogenicity via Oxidative Stress**

Sparks NRL(1), Martinez IKC(2), and zur Nieden NI(2)

(1)Environmental Toxicology Graduate Program, (2) Department of Cell Biology, University of California, Riverside, Riverside

Tobacco use during pregnancy increases the risk of fetal abnormalities such as improper development of bone. An alternative to maternal smoking is the use of 'harm reduction' tobacco products such as ultra-filtered cigarettes (Lights) and chewing tobacco (Snus). However, it remains to be elucidated the molecular mechanisms and detrimental effects of harm reduction tobacco products on the inhibition of bone. Here we aim to understand the molecular mechanisms of how harm reduction tobacco can cause bone teratogenicity using human embryonic stem cell (hESC) derived osteoblasts. Teratogenic doses of Camel and Camel Blue smoke solutions and Snus tobacco extracts (STE) inhibited osteoblast calcification. Camel, Camel Blue and STE generated excessive levels of reactive oxygen species (ROS), O₂- and H₂O₂, and coupled with decreased superoxide dismutase and catalase enzyme activity. Osteoblast inhibition was reversed by co-administration of antioxidants: ascorbic acid, vitamin E or glutathione reduced ethyl ester. Nuclear activation of FoxO, which regulates MnSOD and catalase, was mis-regulated upon cellular exposure to the harm reduction tobacco products. Moreover, TWIST1, crucial for bone specification, nuclear protein levels were downregulated. These data suggests that products like Camel Blue and STE may inhibit embryonic bone development by excess ROS and modulation of transcription factors, TWIST1 and FoxO, activation necessary for osteoblast specification and production.

14-

The effects of chronic Cigarette Smoke Extract exposure on somatic withdrawal in adolescent rats

D. D. Reynaga, A. Rezk, C. Pon, D. Ghobrial, F. M. Leslie

Pharmacology, University of California - Irvine, Irvine, CA

Adolescence is a sensitive period of development where the initiation of smoking typically occurs. Human adolescents are especially sensitive to withdrawal exhibiting symptoms of dependence soon after smoking initiation. In adult rodents discontinuation of chronic nicotine administration results in the development of many of the same characteristic withdrawal symptoms as humans. However, whereas human adolescents have an increased sensitivity to the effects of smoking cessation, rodent adolescents experience little to no somatic withdrawal symptoms after chronic nicotine exposure. This discrepancy may be due to the lack of other non-nicotine smoke constituents in current preclinical models. The goal of this study is to determine whether adolescent rats show spontaneous somatic withdrawal symptoms after chronic exposure to CSE, and to investigate the involvement of nicotinic acetylcholine receptors (nAChRs) in CSE cessation-induced withdrawal using mecamylamine, a nonselective and noncompetitive nAChR antagonist, to precipitate withdrawal. Adolescent rats were treated with saline, nicotine or CSE (1.5 mg/kg/day nicotine content; i.v) for 10 days. Following the last day of drug treatment, spontaneous or precipitated somatic signs of withdrawal were scored. Adolescent rats showed spontaneous somatic withdrawal after CSE exposure but not after chronic nicotine. Mecamylamine (1 mg/kg; s.c.) administration precipitated withdrawal after chronic CSE exposure. This provides evidence that non-nicotine constituents in CSE mediate withdrawal processes, possibly via nAChRs.

15-**Antenatal Antioxidant Prevents Nicotine-Mediated Hypertensive Response in Rat Adult Offspring**

Daliao Xiao, Xiaohui Huang, Yong Li, Chiranjib Dasgupta, Lei Wang and Lubo Zhang

Center for Perinatal Biology, Division of Pharmacology, Loma Linda University
School of Medicine

Our previous studies demonstrated that perinatal nicotine exposure increased blood pressure (BP) in offspring. However, the underlying mechanisms were unclear. The present study tested the hypothesis that perinatal nicotine-induced programming of hypertensive response is mediated by enhanced reactive oxygen species (ROS) in the vasculature. Nicotine was administered to pregnant rats via subcutaneous osmotic minipumps in the absence or presence of a ROS inhibitor, N-acetyl-cysteine (NAC) in the drinking water. Experiments were conducted in 8-month old male offspring. Nicotine treatment resulted in a significant increase in arterial ROS productions in offspring, which was abrogated by NAC. Angiotensin II (Ang II)-induced BP responses were significantly higher in nicotine-treated group than in saline control group, and NAC treatment blocked the nicotine-induced increase in BP response. In consistence, the nicotine treatment significantly increased both Ang II- and PDBu (Prkc activator)-induced arterial contractions in offspring, which were blocked by the NAC treatment. In addition, acetylcholine-induced arterial relaxations were significantly decreased in the nicotine-treated offspring, compared with those in the control animals. These were also inhibited by NAC. The results demonstrate that inhibition of ROS blocks the nicotine-induced increase in arterial reactivity and BP response to vasoconstrictors in adult offspring, suggesting a key role of increased oxidative stress in nicotine-induced developmental programming of hypertensive phenotype in male offspring.

16-

Maternal smoking during pregnancy and risk of cancer among young children: a population-based study

Julia E Heck, Zuelma A. Esquivel, Andrew S Park, Myles Cockburn, Beate Ritz

UCLA, University of Southern California

Smoking is the leading cause of cancer worldwide, and maternal smoking is a plausible cause of some childhood cancers. Most studies on parental smoking and childhood cancer are based upon parental interview, but these may be subject to selective participation and recall biases. In 2007, California began collecting maternal smoking information on the birth certificate. Data on smoking and other pregnancy and birth-related factors are abstracted by hospital clerks from the medical record, reported by the mother's medical provider, or self-reported by mothers. We linked California birth certificates (births 2007-2011) with California Cancer Registry cases (diagnoses 2007-2012) for children ages five or younger at diagnosis. We examined risk for pediatric cancers using unconditional logistic regression, with adjustment for the race/ethnicity of the mother. Our analysis examined ever smoking during any point in pregnancy. Overall, 2.6% of women smoked at some point in their pregnancies. We observed an increased risk for astrocytoma [Odds Ratio (OR)=2.0, 95% confidence interval (CI) 1.0-4.2] and retinoblastoma (OR=2.6, 95% CI 1.2-5.7) with maternal smoking during pregnancy. We did not observe associations between maternal smoking and other cancer types. Our findings support a role for maternal smoking in astrocytoma and retinoblastoma.

17-**Epigenetics of Transgenerational Transmission of Perinatal Nicotine-Induced Asthma**

Virender K. Rehan

LABioMed at Harbor-UCLA Medical Center

The transgenerational transmission (TGT) of perinatal nicotine-induced asthma has been described, but the molecular mechanisms involved remain unknown. Using a well-published rat model of perinatal nicotine-induced asthma phenotype, both global and pathway-specific alterations in DNA methylation and histone acetylation in germ cells and lung fibroblasts were determined. Our key findings include that in comparison to the control group, with perinatal nicotine exposure only to F0 rats, 1) F1 through F3 rat pups demonstrated the asthma phenotype in a gender-specific manner, with more pronounced and selective airway effects in males; 2) global DNA methylation increased in the testes, decreased in the ovaries, without any change in the lung; 3) PPAR α promoter methylation increased, whereas Wnt 5a promoter methylation decreased in testis; 4) H3 acetylation increased in the lungs and testes, but didn't change in the ovaries; and 5) importantly, almost all of these changes were blocked by the concomitant administration of PPAR α agonist rosiglitazone during the perinatal period. These data provide novel insights to the pathogenesis of asthma resulting from smoke exposure during pregnancy, set the stage to develop innovative, targeted preventive interventions and test these exciting findings in humans, and finally, provide probably the strongest experimental evidence to raise public awareness of the ever-lasting effects of smoke exposure during pregnancy on many ensuing generations.

18-

The effect of metabolic syndrome on high density lipoprotein function

Mark S. Borja, Ph.D.; Bradley Hammerson; Olga V. Savinova, Ph.D.; Gregory C. Shearer, Ph.D.; Michael N. Oda, Ph.D.

Children's Hospital Oakland Research Institute

Objective: Metabolic syndrome (MetSyn) is associated with a host of cardiovascular risk factors including increased waist circumference, triglycerides, blood pressure, fasting glucose, and reduced high density lipoprotein cholesterol (HDL-C). Changes in HDL function, especially the ability to participate in reverse cholesterol transport, are more indicative of the atheroprotective properties of HDL compared to HDL-C alone. In this study, we determine the association of HDL-apolipoprotein A-I (apoA-I) exchange, a measure of HDL remodeling/apoA-I exchange, with MetSyn and its individual components. **Method and Results:** We analyzed HDL-apoA-I exchange (HAE) in the plasma of 60 well-characterized subjects with MetSyn and 14 healthy control subjects. HAE measurements were obtained using electron paramagnetic resonance (EPR) following incubation of plasma with lipid free apoA-I containing a methanethiosulfonate spin label. HAE positively correlated with plasma HDL-C and apoA-I levels, and inversely correlated with fasting blood glucose levels, blood pressure, BMI and triglycerides. Multiple linear regression showed that HAE was significantly correlated with MetSyn ($r^2 = 0.57$, $P < 0.0001$), though MetSyn subjects on statins exhibited significantly higher HAE compared to subjects not on statins. **Conclusions:** MetSyn has a significant negative impact on HDL remodeling/ apoA-I exchange, as measured by HAE. HAE is a strong identifier of MetSyn status even after adjusting for individual components of MetSyn.

19-**Impact of the Proteostasis Network Cigarette-Smoke induced COPD**

Chia Yin Chang, Darren M. Hutt, William E. Balch

The Scripps Research Institute, Department of Chemical Physiology, 10550 North Torrey Pines Road, La Jolla, CA 92037

Given the global impact of chronic obstructive pulmonary disease (COPD) in the smoking population, it is crucial to discover new therapeutic options for managing lung pathophysiology. We now appreciate that cigarette smoke (CS) can induce the misfolding and aggregation of the cystic fibrosis transmembrane conductance regulator (CFTR), a crucial anion channel found in lung epithelial cells that maintains ion and fluid homeostasis on the airway surface. Mutations in the CFTR gene cause cystic fibrosis (CF), an inherited disease that has very similar symptoms to those of COPD including mucus accumulation, exacerbations and recurrent bacterial lung infection, leading to the recent proposal that a defect in wild-type (WT) CFTR could be a major contributing factor to COPD and CS induced pathophysiology. We have found that CS condensate (CSC), the tar of cigarette smoke, can reduce CFTR levels by 50-70% in cultured lung epithelial cells. To identify the underlying trigger for loss of WT CFTR, we screened an extensive siRNA library targeting factors that manage CFTR folding and its misfolding in human inherited disease that, when silenced, could potentially impact the response of WT CFTR to CSC, restoring CSC-induced downregulation of CFTR to normal levels found in healthy cells. We have now discovered several components of the protein folding network, referred to as the proteostasis network (PN), that strongly impact both folding and degradation of WT CFTR in response to CSC, some of the top hits being known proteostasis regulators that have been previously implicated in the correction of mutant CFTR protein folding found in cystic fibrosis. Our studies not only systematically reveal how the proteostasis network affects WT CFTR protein stability and maturation in the healthy lung, but also have identified novel therapeutic targets that could mitigate the onset and progression of COPD in response to CS.

***POSTER SESSION: "Bridging the Gap between
Discovery and Policy by Research"***

(DAY-1: Tuesday, October 27, 5:35-6:30PM)

Abstract #20-28

20-

Acute Cardiovascular Toxicity of Hookah (Waterpipe) Smoking versus Perceived Risk

Mary Rezk-Hanna; Michael D. Nelson; Florian Rader; O'Neil Mason; Shomari Hogan; Ryan Rosenberry; Avery Schwartz; Donal

School of Nursing, University of California Los Angeles, CA; Heart Institute, Cedars-Sinai Medical Center, Los Angeles

Hookah smoking is an explosive yet unregulated epidemic of tobacco abuse that is heavily marketed as a healthier alternative to cigarettes. To test if the acute cardiovascular effects of hookah smoking outweigh perceived risk, we asked 34 healthy young adult hookah smokers to rate effects of hookah smoking on heart health on a scale from -10 (extremely unhealthy) to +10 (extremely healthy). Then, in a custom-built smoking chamber, we measured heart rate, BP, pulse wave velocity (PWV), skin and muscle blood flow as well as sympathetic nerve activity before, during, and after a typical 30- minute hookah smoking session. The new major findings are two-fold: 1) Subjects rated hookah as having no effect on heart health (-1.4+1.0), while rating cigarettes as extremely harmful (-9.6+0.2); yet, 2) Hookah smoking increased heart rate by +22 bpm (from 67+3 to 89+4).

21-

Indoor vaping: chemical characterization and health impacts

JM Logue (1), M Sleiman (1,2), V N Montesinos (3), ML Russell (1), MI Litter (3), LA Gundel (1), H Destailats (1)

(1): Lawrence Berkeley National Laboratory, USA; (2): Clermont Université, France; (3): CNEA, Argentina

Electronic cigarette (e-cigarette) use has increased exponentially, particularly among young adults. While the risks and/or benefits associated with e-cigarettes remain uncertain, marketing campaigns highlight the advantages of using these devices indoors to overcome restrictions imposed on conventional tobacco products. This study is characterizing mainstream and exhaled e-cigarette vapor for a variety of popular e-cigarettes and e-liquids under realistic conditions using a room-sized chamber and bench-scale experiments. We identify and measure the levels of harmful indoor pollutants (e.g., aldehydes) and particles emitted during vaping to evaluate the persistence of these contaminants and their potential impact on indoor air quality. Levels and patterns of non-users' exposure to exhaled vapor will be estimated under various scenarios, using simple modeling tools that incorporate key inputs such as concentrations, ventilation rate, vaping frequency and occupancy. An initial health impact assessment of secondhand vaping (SHV) will be performed using a metric (Disability-adjusted life years) that is commonly used by the World Health Organization to estimate the global burden of disease. The primary impact of the proposed research is to generate science-based information regarding the impacts of e-cigarette SHV that can be used for public education as well as policy-making. Outcomes of this study will also be disseminated to the public by developing a science-based fact sheet to better educate Californians on vapor composition and potential health risks of e-cigarettes.

22-**Thirdhand Smoke: Quantifying Risks and Developing Policies for Control**

Jonathan M. Samet and Heather L. Wipfli

Department of Preventive Medicine, Keck School of Medicine and the USC Institute for Global Health

The University of Southern California (USC) component of the Thirdhand Smoke (THS) Consortium has the overall objective of integrating the evidence obtained from the subprojects and external investigators to establish a scientific foundation for advancing control policies. We focus on the following three objectives: 1) to provide scientific evidence either for or against clear and significant health risks to humans as a result of exposure to THS, 2) to design an evidence-based approach to THS exposure risk policies, policy implications and issues, 3) to disseminate any evidence related to the health risks of THS to the California tobacco control stakeholders as well as general public, including any recommendations on potential approaches to risk elimination. In addressing the risks of THS, the complexities of separating risks of secondhand smoke (SHS) and of THS merit consideration. In order to focus attention on the problem of THS, a characterization of the risks associated with THS exposure alone is needed, as THS exposure likely now takes place in many places where smoking once took place but is no longer allowed, e.g., homes and vehicles.

The USC team will play a central role in the process of evidence gathering, integration, and interpretation in order to elaborate the foundation for evidence-based policy. We will also pursue an agenda of policy formulation by drawing on experts from multiple sectors, establishing a set of working groups and ending with a “policy summit” with the goal of reviewing policy approaches. We plan a systematic review of all of the evidence on THS and interpretation of this evidence within a risk assessment framework as a basis for policy elaboration.

Characterization of the risks of THS is needed to inform the public and key stakeholders about the basis for concern and action, and to motivate policies to mitigate exposures. To develop this foundation and a suite of policy approaches, the USC subproject will do the following:

1. Year 1: We will continue to explore policy issues with engagement of experts from multiple relevant disciplines. At the end of the year, we will hold a multidisciplinary conference to review the white papers and to formulate potential policy approaches to addressing THS.
2. Year 2: We will carry out a series of systematic literature reviews on THS. All members of the consortium will be participants in various phases of the review process.
3. Year 3: We will complete a risk assessment based on the systematic review and the exposure assessment. With the risk assessment and the systematic reviews, we will build on the work in the first year to propose evidence-based policy approaches for limiting THS exposure. One critical step in the third year will be development of tool kits that set out practical guidance for addressing THS in key sectors, such as real estate.

23-

Volatile constituents of thirdhand smoke: Chemical composition and health impacts

M Sleiman (1,2), JM Logue (1), W Luo (3), JF Pankow (3), LA Gundel (1), H Destailats(1)

(1)Lawrence Berkeley National Laboratory, USA; (2) Clermont Université, France;
(3) Portland State University, USA

Deposition, re-suspension and chemical reactions taking place in timescales from minutes to months can influence how human health is affected by exposure to thirdhand smoke (THS). We identified and quantified airborne THS pollutants available for respiratory exposure, identified environmental tracers and estimated health impacts to nonsmokers. The approach combined laboratory measurements with an exposure and impact assessment methodology that computed disability-adjusted life years lost. While the commonly used SHS tracers 3-ethenylpyridine (3-EP) and nicotine were removed by sorption to surfaces within 2 hours after smoking, other volatile organic compounds (VOCs, e.g. furans, carbonyls and nitriles) persisted in the gas phase for at least 18 hours. The concentration ratios of acetonitrile to 3-EP increased substantially with aging and may provide a useful metric for differentiating freshly emitted (SHS) from aged smoke (THS). The levels of acrolein, methacrolein, and acrylonitrile exceeded concentrations considered harmful by the State of California. Exposure to PM_{2.5} contributed more than 90% of the predicted harm. Acrolein, furan, acrylonitrile, and 1,3-butadiene were considered to be the most harmful VOCs. Depending on which criteria are used to establish the separation between SHS and THS, between 5% and 60% of the predicted health damage could be attributed to THS exposure. Understanding the dynamics of THS will contribute to design optimal policies and practices to protect non-smokers and optimize remediation methods for environments that have been impacted by THS.

24-

Thirdhand Smoke Pollution and Exposure in Ex-Smokers' Homes

Georg E. Matt¹, Penelope J. E. Quintana², Eunha Hoh², Joy M. Zakarian³, Kayo Watanabe³, Dale A. Chatfield⁴

¹San Diego State University, Department of Psychology, San Diego, CA, U.S.A. ²San Diego State University, Graduate School of Public Health, San Diego, CA, U.S.A. ³San Diego State University Research Foundation, San Diego, CA, U.S.A. ⁴San Diego State University, Department of Chemistry, San Diego, CA, U.S.A.

Thirdhand smoke (THS) consists of SHS pollutants that accumulate in indoor environments where tobacco has been smoked. THS ages and reacts with other pollutants (e.g., HONO, ozone), leading to a dynamically changing mixture of chemical compounds. THS exposure may occur via inhalation, dermal transfer, or ingestion. This study examined homes of smokers who quit smoking to quantify changes in level and composition of THS pollutants in household dust and air and on surfaces over time, the extent to which nonsmoking residents remained exposed to THS, and the association of THS pollution with relapse. Samples were collected before the smokers quit, and at one week, and one, three, and six months after cessation. At six months, the homes showed significantly elevated levels of nicotine in dust and on surfaces and of tobacco-specific nitrosamines (TSNA) in dust. Nonsmokers' urinary cotinine levels remained above 6 ng/ml three to six months after cessation. At three months, exposure to TSNA as measured by the metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) remained elevated in nonsmokers at 56% of baseline levels and 72% of levels found one week after cessation. Residents of homes of former smokers continued to be exposed to a variety of tobacco smoke toxicants long after successful smoking cessation. Findings also raise the possibility that relapse may be mediated or moderated by the continued low level exposure to nicotine as well as other odorant compounds in a smoker's home that serve as triggers.

25-

Persistent Thirdhand Smoke Toxicants in Indoor Environments

Penelope J. E. Quintana¹, Georg E. Matt², Eunha Hoh¹, Joy M. Zakarian³, Kayo Watanabe³, Melbourne F. Hovell¹

¹San Diego State University, Graduate School of Public Health, San Diego, CA, U.S.A.

²San Diego State University, Department of Psychology, San Diego, CA, U.S.A. ³San

Diego State University Research Foundation, San Diego, CA, U.S.A.

Our project focuses on characterizing levels of known and newly identified toxicants in field-based real-world measures of thirdhand smoke (THS). Real-world field measures are critical to understanding the health risks of THS. First, exposure risk through house dust and surfaces to vulnerable populations such as small children can be directly assessed in environments where they live and spend time. Second, real-world samples are critical for characterizing THS exposure as the component reactive pollutants change over time. We will chemically characterize THS in order to identify potentially hazardous or toxic constituents that may be present in THS, and identify relevant and specific biomarkers in exposed participants that could serve as indicators of exposure. We will characterize levels of highly mutagenic and toxic polycyclic aromatic hydrocarbon (PAH)-related compounds (e.g., oxy-PAHs) in THS dust samples using a new multi-analyte analysis method developed in our laboratory. Many of these samples come from homes with small children, who are likely most at risk, and the homes represent an ethnically diverse, low income community. We hypothesize that production and aging of THS in real-world environments results in a spectrum of toxic compounds in dust and surfaces that potentially pose significant risks to vulnerable groups, and that certain signature patterns of chemicals can serve as THS markers and biomarkers.

26-

Toward Smoke-Free Casinos: The Win-River Experience

Georg E. Matt¹, Penelope J. E. Quintana², Eunha Hoh², Zohir Chowdhury², Teaba S. Theweny², Anh V. Nguyen², Joy M. Zakarian³, Kayo Watanabe³, Francisco O. Buchting⁴, Neil E. Klepeis², Narinder Dhaliwal⁵, Melbourne F. Hovell²

¹San Diego State University, Department of Psychology, San Diego, CA, U.S.A. ²San Diego State University, Graduate School of Public Health, San Diego, CA, U.S.A. ³San Diego State University Research Foundation, San Diego, CA, U.S.A. ⁴Buchting Consulting, Oakland, CA, U.S.A. ⁵ETR Associates, Sacramento, CA, U.S.A.

While California Labor Code prohibits smoking in places of employment, it does not apply to casinos located on sovereign tribal lands. We measured tobacco smoke pollutants and human exposure to thirdhand smoke (THS) before and after a tribal casino in Northern California implemented a 100% smoking ban, and again after the ban was reversed. Before and after the ban, levels of surface nicotine and airborne particles were significantly higher in areas where smoking was permitted pre-ban vs. areas that were nonsmoking. In smoking areas, surface nicotine levels persisted for several months following the ban at high levels indistinguishable from pre-ban levels. By six months after the ban, the median surface nicotine level in smoking areas was still 2.5 to 5 times the levels observed in our previous studies of homes where residents were actively smoking indoors. Airborne fine and ultrafine particles levels significantly declined in smoking areas of the casino after the ban. This study shows the promises and limitations of indoor smoking bans. THS persisted at significantly elevated levels as long as six months after active smoking had ceased, and patrons and employees were exposed to THS pollutants. The findings provide strong support for the implementation of 100% smoke-free policies to protect nonsmoking casino patrons and employees and highlights that these policies must be accompanied by efforts to remove the reservoirs in which THS pollutants are stored.

27-

Chemical and cellular toxicity of atmospherically-oxidized tobacco smoke

Alam Hasson, Jason Bush, Krish Krishnan, Divine Yang, Justin Vang, Robyn Verhalen, Erik Rangel, Carrie Tambo and Kathryn Patterson

Department of Chemistry, California State University, Fresno; Department of Biology, California State University, Fresno

In this work, we have investigated the hypothesis that chemical processing of environmental tobacco smoke by atmospheric oxidants can increase the environmental health risks of exposure to tobacco smoke. The chemical composition of gas- and particle-phase smoke were examined using gas chromatography-mass spectrometry, proton transfer reaction mass spectrometry and nuclear magnetic resonance spectroscopy. Cellular toxicity was investigated with the WST-1 assay using three cell lines. We observe substantial changes in the chemical composition of gas and particulate SHS when exposed to ozone. A large mass fraction of particulate-phase organics react with ozone to form gas-phase products. We also identify several possible chemical marker for atmospherically-processed SHS in the atmosphere. In-vitro measurements demonstrate a significant increase in the toxicity of smoke particles when they react with ozone.

28-

Tobacco Prevention Toolkit: For a Nicotine Free Adolescence

Bonnie Halpern-Felsher, Malena Ramos, Stephen Smuin, Ira Sachnoff, & Cherrie Boyer

Stanford University, University of California at San Francisco

School-based tobacco education efforts have had mixed results. The goal of this project was to address the gaps identified by our school partners and stakeholders to identify what's missing from school-based tobacco prevention programs, and then incorporate these missing aspects into new programs and delivery strategies in order to reduce and prevent middle and high school students' tobacco use, including cigarettes, cigars, chew, hookah and all electronic tobacco products. We conducted focus groups with students, parents, educators, and school administrators to obtain input on new directions for school-based tobacco control efforts. We also held working group meetings with local and state-level educators, school administrators and researchers to work on content and activities for the toolkit. Analyses of the data led to the development of 5 modules: nicotine addiction, positive youth development, information for parents, communicating about school policies and efforts, and preventing use of e-cigarettes/vapes. Each module contains relevant information and activities that can be implemented by any educator teaching tobacco prevention and education. This Toolkit will primarily sit online, hosted at Stanford University. Each module and activity contains hyperlinks to additional information, graphics, handouts, and PDFs that educators, parents and youth will find easy to access and utilize. We are also holding trainings to teach interested parties about this Toolkit.

***POSTER SESSION: "Scientific Perspectives on
Electronic Cigarettes"***

(DAY-1: Tuesday, October 27, 5:35-6:30PM)

Abstract #29-38

29-

Investigating Perceptions of Electronic Nicotine Delivery Systems with Young Journalists: Reporting on Participatory Research Processes

Alison Chopel, DrPH; Pamela Ling, MD MPH; Rachel Grana, PhD
Public Health Institute; UCSF School of Medicine

Objective: This study aims to understand the marketing and promotion of e-cigarettes in Oakland, in order to inform interventions to reduce youth nicotine use and to counter misleading marketing messages perpetuated by tobacco and e-cigarette companies. **Methods:** This Community-Based Participatory Research study is designed and implemented in conjunction with Youth Radio, a youth media training program. Using a modified photovoice process, a visual and narrative data collection method, youth and adult co-investigators will collect and present data, which will be analyzed according to an inductive-deductive analysis process that incorporates social phenomenological and grounded theory approaches. **Results:** A partnership was established between academic and community organizations with both youth and adult participants. Research topics were generated and prioritized, and the consensus was to focus on messages about electronic cigarettes, how youth are exposed to these messages, and how they respond. Youth expressed interest in increasing their knowledge of e-cigarette products, how and why these products are used, and identifying what kinds of messages lead to youth e-cigarette use, and what messages might discourage it. **Conclusion:** PIs and youth co-researchers will comment on the processes used to build youth's capacity, and to work collaboratively to develop research questions and generate knowledge. The goal of this research is to increase understanding and support of adolescent health and well-being in California through youth leadership development.

30-

Addiction in a bottle: A call to action for nicotine regulation

B. Davis¹; I. Cordova¹; E. Omaiye¹; M. Dang¹; J. Kim; A. Razo¹; E. Nothnagel²; M. Chen¹; and P. Talbot¹

¹Dept. of Cell Biology and Neuroscience; ²Dept. of Botany and Plant Sciences; University of California, Riverside, CA, 92521

Introduction: Nicotine is addictive, toxic and teratogenic. This presentation addresses the need for regulation of accurate labeling of nicotine concentrations on bottles of electronic cigarette (EC) refill fluids, DIY fluids, and DIY flavorings. **Methods:** Nicotine concentration was quantified using high performance liquid chromatography (HPLC) in 115 electronic cigarette refill fluids from three counties and in 30 DIY flavoring products sold for use with EC. Data were compared to manufacturer labeled concentrations. **Results:** 70.8% of the refill fluids that were labeled to contain nicotine had concentrations that deviated by more than $\pm 10\%$ from the label (American E-Liquid Manufacturing Standards Association's tolerance level). Two DIY bottles of nicotine contained 105.9 and 134.7 mg/ml and had no label. Four of 30 DIY flavoring products with no indications of nicotine on their labels had up to 20 mg/ml of nicotine. Finally, nine bottles of a brand of refill fluid purchased in Nigeria and labeled 0% nicotine all contained nicotine, while the same products purchased in the USA did not have nicotine. **Conclusions:** These data show that nicotine is widely distributed in EC refill fluid products in containers that often are inaccurately labeled. Ad libitum access to nicotine in EC refill products poses important public health and safety issues. Most dangerous of these is unintended exposure to nicotine from products believed to be nicotine free, such as refill fluids.

31-

Electronic Cigarette Aerosol from a Vape Shop is distributed to Adjacent Businesses

Careen Khachatoorian¹, Jessica Miranda Bustamante¹, Peyton Jacob² and Prue Talbot¹

¹Dept. of Cell Biology & Neuroscience, UC Riverside, CA 92521 ²Dept. of Psychiatry, UC San Francisco, CA 94143

Electronic cigarette (EC) exhaled aerosol residue (ECEAR) is composed of EC aerosol exhale that settles on indoor surfaces. The purpose of this study was to characterize the ECEAR chemicals in an indoor field site (salon) located in a smoke-free mini mall. The field site is adjacent to a vape shop where EC are used and the salon proprietor has experienced adverse health effects due to EC aerosol exposure. The salon has negative pressure relative to the vape shop, and air from the vape shop is drawn into the salon. Various types of fabric were exposed to salon air then extracted into aqueous medium and analyzed by LC/MS-MS to quantify nicotine, nicotine derivatives, and tobacco specific nitrosamines (TSNAs). All fabrics placed in the salon, but not unexposed control fabrics, contained nicotine, its derivatives, and TSNAs. Short-term exposures (1 day) of fabrics placed at the front of the salon where EC aerosol enters contained these chemicals, which increased in concentration with longer exposures (3 months). Chemical analysis of the air conditioner filter used inside the salon showed the presence of nicotine and its derivatives demonstrating redistribution of chemicals in the ventilation system. These data indicate that vape shops in multi-users buildings can distribute EC aerosol to adjacent businesses where nicotine, TSNAs and nicotine derivatives accumulate. When developing legislation for indoor use of EC, it is important for policy makers and legislators to consider the distribution of EC aerosols in multi-user buildings.

32-

Surmounting the Challenges of Studying Electronic Cigarettes in Humans

Holly R. Middlekauff, Kacey Peters

University of California Los Angeles

Controversy about the increasingly popular electronic cigarettes (ECs) is growing, but there remains a glaring lack of scientific data regarding EC health effects. Upon initiating studies of the health effects of EC, we surmounted many barriers to performing these much needed studies. Administrative Resistance originated from many sources, including the UCLA IRB and even, surprisingly, co-investigators, largely due to concerns about ethics of enrolling nicotine-naïve subjects. This resistance was dealt with successfully using a forthright approach. Recruitment: In order to recruit EC users, we have advertised via social media, as well as UCLA websites. We have placed fliers at vape bars and smoke shops. On-line EC advocacy sites, including sites purportedly supporting EC research, have been contacted, but thus far have not posted our study information. Recruitment is slow, but steady. Methodology: The heterogeneity of EC devices presents its own challenges to scientific study. We have overcome this lack of standardization by choosing one popular brand of EC (Greensmoke®), and one flavor (tobacco). Further, we use a standardized EC topography for every study. EC exposure each session is monitored by pre/post nicotine blood levels, and measurements of exhaled particulates. In conclusion, studying ECs in humans is challenging. These challenges originate from both sides of the EC controversy, as well as from the unregulated, and thus non-uniform, nature of the EC itself.

33-**Characteristics of Secondhand Vapor Emissions from Electronic Cigarettes Use in Humans**

Holly R. Middlekauff, Yifang Zhu, Eon S. Lee, Tongke Zhao, Che-Hsuan Lin, Kacey Peters

Controversy about the increasingly popular electronic cigarettes (ECs) is growing, but there remains a glaring lack of scientific data regarding EC health effects. Upon initiating studies of the health effects of EC, we surmounted many barriers to performing these much needed studies. Administrative resistance originated from many sources, including the UCLA IRB and even, surprisingly, co-investigators, largely due to concerns about ethics of enrolling nicotine-naïve subjects. This resistance was dealt with successfully using a forthright approach. Recruitment: In order to recruit EC users, we have advertised via social media, as well as UCLA websites. We have placed fliers at vape bars and smoke shops. On-line EC advocacy sites, including sites purportedly supporting EC research, have been contacted, but thus far have not posted our study information. Recruitment is slow, but steady. Methodology: The heterogeneity of EC devices presents its own challenges to scientific study. We have overcome this lack of standardization by choosing one popular brand of EC (Greensmoke®), and one flavor (tobacco). Further, we use a standardized EC topography for every study. EC exposure each session is monitored by pre/post nicotine blood levels, and measurements of exhaled particulates. In conclusion, studying ECs in humans is challenging. These challenges originate from both sides of the EC controversy, as well as from the unregulated, and thus non-uniform, nature of the EC itself.

34-

Heating coil temperature and mainstream particle characteristics under different puff conditions

Tongke Zhao, Shi Shu, Yifang Zhu
University of California Los Angeles

Heating coil temperature is an important factor affecting the electronic cigarette (EC) mainstream particle characteristics. High heating coil temperature can potentially cause chemical decomposition and metal leaching, both of which makes the mainstream particles more hazardous to the EC users. However, there is limited measurement data of EC heating coil temperature, let alone how it is affected by puff topography and how it in turn affects mainstream particle characteristics. This study established a practical and robust method for measuring heating coil temperature and mainstream particles simultaneously. The heating coil temperature was measured by inserting a thermocouple probe through the tip hole on the EC cartridge and making direct contact with the heating coil. Particle concentrations and size distributions were measured by a scanning mobility particle sizer. Experiments were conducted to investigate the effects of variable puff durations (i.e., 2, 3, 4 and 5 s) and puff flow rates (i.e., 0.5, 1, 1.5, and 2 L/min) on EC heating oil temperature and related mainstream particle size distributions. The results show that the peak heating coil temperature increases as puff duration increases and puff flow rate decreases. Similar trend was observed for the count median diameter of the mainstream aerosol. The particle number concentration is greater for longer puff duration and/or higher puff flow rate. These results provide better understanding of how an EC works and highlight the need to carefully characterize exposures in future EC related health effect studies.

35-**Disposable Electronic Cigarettes and Electronic Hookahs: Evaluation of Design, Performance, and Metal Emissions**Monique Williams¹, Sanjay Ghai¹, Krassimir Bozhilov², and Prue Talbot¹¹Department of Cell Biology & Neuroscience, University of California, Riverside, CA,
²Central Facility for Advanced Microscopy and Microanalysis

The purpose of this study was to evaluate the design, performance, and metal emissions of disposable electronic cigarettes and electronic hookahs. All brands had similar design and basic components: wires, solder joints, air-tubes, a mouthpiece, fluid, and fibers. The airflow rates required to produce aerosol and aerosol absorbance were lower for button-activated models (3 mL/s; 0.41-0.55 absorbance) than for airflow activated models (7-17 mL/s; 0.48-0.84 absorbance). Pressure drop was lower across button-activated products (6-12 mmH₂O) than airflow-activated products (15-67 mmH₂O). While button-activated models lasted 200 puffs and airflow-activated models often lasted 400 puffs, none of the models lasted the advertised number of puffs. Puff number was limited by battery life, which was shorter in button-activated models. For elemental analysis of the aerosol, 21 of 35 elements were detected in the aerosol. Fourteen elements were consistently higher in concentration in aerosol than in cigarette smoke. Four elements were lower in the aerosol than conventional cigarette smoke. In summary, while all brands were similar in design, performance varied and was differentiated mainly by the way the aerosol was produced rather than by product type. All brands contained metals in their aerosols and some metals were higher than in cigarette smoke. These data suggest quality control in manufacturing varies among brands and show a need for further evaluation of aerosol metals.

36-**The Impact of E-cigarette Exposure on Pulmonary Epithelial Cell Transformation and Gene Expression**

SJ Park¹, LM Tran¹, TC Walser¹, R Li¹, Y Lin¹, MC Fishbein¹, JD Minna³, ME Lenburg², A Spira², SM Dubinett¹

¹ University of California Los Angeles, ² Boston University, ³ University of Texas Southwestern

Since the electronic cigarette (ECIG) is designed to deliver nicotine without combusting tobacco, they are widely advertised to be a safer alternative to tobacco cigarettes (TCIGs). However, the potential health risks and carcinogenicity of ECIGs have not previously been evaluated. In this study, we assess the impact of ECIG exposure on the carcinogenic potential of immortalized human bronchial epithelial cells on a background of silenced p53 and activated KRAS, mutations often observed in the airway of current and former smokers at risk for lung cancer. Our preliminary results demonstrate that exposure to clinically relevant concentrations of ECIG vapor-conditioned media enhance the cancer-associated behavior of at-risk airways with a demonstrated capacity for malignant transformation. We observed enhanced colony growth in anchorage independent assays and increased cell invasion-associated morphological changes in three-dimensional air-liquid interface models. In addition, we found that mutant epithelial cells exposed to ECIG vapor-conditioned media induces airway gene expression changes that are similar to those seen with TCIG exposure. Annotation of the deregulated genes revealed several enriched gene sets observed in clinical lung and breast cancer. We will further identify gene candidates to evaluate their role in driving the malignant transformation of airway epithelial cells. These studies will contribute to our understanding of the impact of ECIG exposure on lung carcinogenicity.

37-**Electronic cigarette Use and Respiratory Symptoms in Adolescents**

Jessica L. Barrington-Trimis, PhD; Kejia Wang, MPH; Robert Urman, MS; Tess Cruz, PhD; Jimi Huh, PhD; Jennifer Unger, PhD; Chih-Ping Chou, PhD; Adam M. Leventhal, PhD; Tamika D. Gilreath, PhD; Mary Ann Pentz, PhD; Kiros Berhane PhD; Rob McConnell, MD

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California; School of Social Work; University of Southern California, Los Angeles, California

Background: A widely held opinion is that electronic (e-) cigarettes and other electronic nicotine delivery devices are likely to be less harmful to users than combustible tobacco products. Although components of e-cigarette aerosol have known pulmonary toxicity, there has been little study of either the toxicology or epidemiology of e-cigarettes. We examined the association between e-cigarette use and chronic bronchitic symptoms and wheeze among adolescents, among whom the rate of e-cigarette use has been rapidly increasing. **Methods:** Questionnaire data were obtained for 2097 adolescents in grade 11 or 12 participating in the Children's Health Study in schools in 12 Southern California communities. The risk of bronchitic symptoms (chronic cough and phlegm or bronchitis) and wheeze associated with e-cigarette use was assessed in models adjusted for gender, ethnicity, education, income, community, and secondhand and lifetime personal combustible cigarette smoking history. **Results:** There were 502 participants (24.1%) who reported ever having used an e-cigarette, of whom 196 (9.4%) reported having used an e-cigarette during the last 30 days (current users). Past and current e-cigarette users were twice as likely to report bronchitic symptoms (odds ratio (OR) past=2.0 [95% CI 1.6, 2.6]; OR_{current}=1.7 [95% CI 1.2, 2.5]). Risk increased with frequency of current e-cigarette use (OR=1.5 [95% CI 0.91, 2.5] for 1-2 days; OR=2.0 [95% CI 2.5, 3.4] for 3 or more days in previous month) compared with never users. This frequency-response relationship was attenuated by adjustment for lifetime or current cigarette smoking dose. However, risk of bronchitic symptoms among past e-cigarette users was robust to control for smoking and in analyses restricted to never smokers. There were no associations between e-cigarette use and wheeze. **Conclusions:** Adolescent e-cigarette users had increased rates of bronchitic symptoms. Further investigation is needed to determine the long-term effects of e-cigarettes on lung health.

38-**E-cigarette use, Smoking Cessation, and Change in Smoking Intensity in the 2010/2011 TUS-CPS Longitudinal Cohort**

Yuyan Shi, John Pierce, Martha White, Maya Vijayaraghavan, Wilson Compton, Kevin Conway, Anne Hartman, Karen Messer

Moore's UC San Diego Cancer Center, University of California, San Diego

Objective: To test whether ever-use of e-cigarettes among early adopters was associated with: 1) increased cigarette smoking cessation; and 2) reduced cigarette consumption. **Design, Setting and Participants.** Prospective cohort study using a representative sample of U.S. smokers (N=2,454) from the 2010 Tobacco Use Supplement to the Current Population Survey, who were re-interviewed 1 year later. Multivariate regression was used to adjust for demographics and baseline cigarette dependence level. **Results:** In 2011, an estimated 12% of adult U.S. smokers had ever used e-cigarettes, and 41% of these reported use to help quit smoking. Smokers who had used e-cigarettes for cessation were about half as likely to be quit for 30+ days at follow-up, compared to never-users who tried to quit (11.1% vs 21.6%; OR_{adj}=0.44, 95%CI=0.2-0.8). Smokers who used pharmaceutical aids for quitting were about 30% less likely to be quit for 30+ days, compared to those quitting without pharmaceutical aids (16.0% vs 22.4%; OR_{adj}=0.67, 95%CI=0.5-0.9). Among heavier smokers at baseline, ever-use of e-cigarettes was not associated with change in smoking consumption. Lighter smokers who had ever used e-cigarettes for quitting had stable consumption. **Conclusions and relevance.** Among early adopters, ever-use of e-cigarettes for quitting smoking was not associated with improved abstinence, nor with reduced consumption among heavier smokers.

***POSTER SESSION: "Neuroscience of Nicotine
Dependence"***

(DAY-1: Tuesday, October 27, 5:35-6:30PM)

Abstract #39-45

39-**A Select Group of Substituted 2-Aminopyrimidines Exhibit Potent Cooperative Activities on Nicotinic Acetylcholine Receptors (nAChR) and the Acetylcholine Binding Protein (AChBP)**

Katarzyna Kaczanowska, Gisela Andrea Camacho, Adrienne Desens, Palmer Taylor Skaggs School of Pharmacy & Pharmaceutical Sciences, University of California, San Diego, La Jolla, Ca 92093

Through studies with ligand binding to AChBP, we have identified a series of 4,6 substituted 2-aminopyrimidines that associate with this soluble nAChR surrogate in a cooperative fashion, not seen for the classical nicotinic agonists and antagonists. With these ligands and AChBP, we have conducted crystallographic studies that show that this family of ligands bind at the classical agonist- antagonist site, displace epibatidine, but in so doing, exhibit unusual cooperative behavior and conformational state changes in the pentameric AChBP. Although this family of ligands typically had low affinity for nAChRs, we recently found a subset of structures that show K_d values and elicited responses EC₅₀'s as low as 60-80 nM, reflecting high affinity and selectivity for $\alpha 7$ -AChRs. Moreover, these compounds reveal unique binding determinants and bound poses for the ligand-AChBP complex. Current studies of these ligands are directed to their potency on $\alpha 7$ -nAChR and related ligand-gated ion channels, along with binding and crystallographic studies with the AChBP to design selectivity and guide us to the development of superior agents. Certainly more selective agonists than varenicline and the nicotine patch need to be developed for smoking cessation and as selective nAChR modulators; these 2-aminopyrimidines also may hold potential in treatment of schizophrenia, a disorder where resistance to nicotine abstinence prevails.

40-

Menthol potentiates nicotine reward, upregulates lower sensitivity nAChRs, and alone is a candidate chemical chaperone for $\alpha 4^*$ and $\alpha 6^*$ nAChRs

B J Henderson, T R Wall, B M Henley, C H Kim, W A Nichols, C Xiao, H A Lester
California Institute of Technology (Caltech), Pasadena, California

Smokers of menthol cigarettes have lower cessation rates than non-menthol smokers. Upregulation of $\alpha 4^*$ nicotinic acetylcholine receptors (nAChRs) is implicated in several aspects of nicotine addiction; and menthol cigarette smokers upregulate more than non-menthol smokers. It is unclear how menthol in cigarettes hinders cessation or modifies nAChRs. We demonstrate that menthol potentiates nicotine reward-like behavior in mice. In dopaminergic (DA) neurons, chronic low-dose menthol itself increases the number of $\alpha 4$ and $\alpha 6$ nAChR subunits, accelerates the decay of nicotinic responses, and reduces baseline firing rates. The upregulation does not occur in midbrain GABAergic neurons. Thus chronic menthol produces a cell-type selectivity of $\alpha 4^*$ nAChR upregulation complementing that of chronic nicotine alone. In neuroblastoma cells, persistent exposure to 0.5 μ M menthol alone also increases nAChR numbers and favors the formation of $(\alpha 4)_3(\alpha 2)_2$ nAChRs; this again complements the action of nicotine itself, which favors $(\alpha 4)_2(\alpha 2)_3$. Menthol alone also increases the number of $\alpha 6\beta 2$ receptors that exclude the $\alpha 3$ subunit. Combined with nicotine, menthol potentiates the upregulation and peak current amplitude of $\alpha 4^*$ nAChRs. Menthol upregulates AChRs through increased endoplasmic reticulum export, perhaps acting as a chemical chaperone for nAChRs. Thus, maintained exposure to menthol, alone, alters nAChRs and changes the firing properties of DA neurons; and when combined with nicotine, menthol.

41-

Activation of metabotropic glutamate receptor 7 attenuates nicotine taking and nicotine seeking in rats

Xia Li, Astrid Stoker, Athina Markou

Department of Psychiatry, University of California San Diego

The reinforcing and motivational aspects of nicotine taking and nicotine seeking are associated with increased glutamate transmission in the brain. Decreasing glutamate by targeting metabotropic glutamate receptors (mGluRs), such as mGluR2/3 and 5, has demonstrated efficacy in inhibiting nicotine taking and nicotine seeking. mGluR7 is another presynaptic inhibitory receptor involved in shaping synaptic responses. But its role in nicotine dependence is unknown. Here we assessed the role of mGluR7 in nicotine dependence in rats. Self-administration under fixed (FR) and progressive (PR) ratio schedules of reinforcement was used to study the reinforcing and motivational effects of nicotine. Cue-induced reinstatement of nicotine seeking was used as a model of relapse to nicotine consumption. Systemic administration of AMN082, an mGluR7 agonist, attenuated nicotine self-administration under FR and PR schedules, and blocked cue-induced reinstatement of nicotine seeking. Central injections of AMN082 into the ventral tegmental area (VTA) decreased nicotine taking and seeking, suggesting the involvement of VTA mGluR7 in nicotine dependence. Similarly, overexpression of VTA mGluR7 decreased nicotine self-administration and reinstatement. Our results indicate that activation of mGluR7 attenuated nicotine taking and nicotine seeking through a neural circuitry involving the VTA within the mesocorticolimbic system. Thus mGluR7 may be a promising target for treatment of nicotine dependence.

42-

A microRNA mediating a major transition in brain development potentially vulnerable to nicotine

Giordano Lippi and Darwin K. Berg

University of California, San Diego

MicroRNAs (miRs) are small non-coding RNAs that can serve as "regulatory hubs", repressing multiple mRNAs in parallel to coordinate complex events. Because miRs offer therapeutic targets for cocaine addiction, we wondered whether they might do the same for nicotine addiction. Early exposure to nicotine exerts long-lasting effects, including an increased propensity for addiction. We previously showed that endogenous nicotinic signaling normally helps drive the major transition in brain development going from a period of exuberant synapse formation to one of consolidation and pruning. Nicotine-induced aberrations in this key transition could be responsible for long-lasting behavioral effects. We find that endogenous nicotinic signaling elevates miR-101 at a time appropriate for mediating the transition. MiR-101 targets potentially relevant mRNAs, including the chloride transporter NKCC1 in a way that helps GABAergic transmission flip from excitation to inhibition as needed in the adult. Even transient blockade of miR-101 early in vivo substantially increases the levels of excitatory synaptic input, seizure-like events, and compromised spatial memory formation found later in the adult. Disruptions in spontaneous network activity emerge early and promote hyper-excitability circuits. Target-site blockers reveal multiple mRNAs, in addition to NKCC1, regulated in parallel by miR-101 to coordinate these events. The results provide new mechanistic insight into brain development and suggest opportunities for therapeutic intervention in pathways relevant for nicotine addiction.

43-

Pedunclopontine tegmental nucleus glutamate neurons in behavioral reinforcement: behavioral, electrophysiological and anatomical data using optogenetics

Ji-Hoon Yoo, Vivien Zell, Johnathan Wu, Navarre Gutierrez-Reed, Alex Johnson and Thomas Hnasko

University of California, San Diego

The objective of the study was to determine whether the pedunclopontine tegmental nucleus (PPTg) glutamate (GLU) neurons play a role in behavioral reinforcement, and to identify efferent projections of PPTg GLU neurons. We use optogenetic approaches to selectively target and activate GLU neurons in the PPTg. Cre-inducible AAV-DIO-ChR2-mCherry vector was injected into the PPTg of vesicular glutamate transporter type 2 (VGLUT2)-cre mice. ChR2-mCherry labelled terminals were observed in several brain areas including substantia nigra, ventral tegmental area, subthalamic nucleus and ventromedial hypothalamic nucleus. To demonstrate the presence of functional excitatory efferents from PPTg to VTA and SNc we performed electrophysiological recordings in midbrain slices. Short pulses of 473nm blue light led to glutamate-mediated excitatory postsynaptic currents within the ventral tegmental area and substantia nigra. The functional reinforcing properties of PPTg GLU neuron stimulation were assessed using operant reinforcement assays and optogenetic stimulation of PPTg glutamate neurons is sufficient to support striking positive behavioral reinforcement. Our results indicate a crucial role for GLU neurotransmission from PPTg to midbrain and other brain regions in behavioral reinforcement.

44-

Alpha2-Containing Nicotinic Acetylcholine Receptors Modulate Nicotine-Induced Hippocampal Dependent Learning and Memory Behavior in Mice

Shahrdad Lotfipour, Ph.D.

University of California Los Angeles

Nicotinic receptors are known to modulate hippocampal dependent learning and memory behavior. Using nicotinic receptor mutant mice, the current talk highlights the functional role for a selective nicotinic acetylcholine receptor subtype (alpha2-containing nAChRs), known for its ability to facilitate hippocampal dependent long-term potentiation (LTP). Using molecular genetic techniques in two separate mouse lines, we delete or enhance the functionality of alpha2-containing nAChRs and assess the behavioral consequences on nicotine-modulated hippocampal dependent learning and memory behavior. We hypothesize that changes in hippocampal nicotinic-facilitation of LTP should differentially influence nicotine-modulated learning and memory behavior in mice. Our results confirm that the deletion or enhancement of alpha2-containing nAChR function induces bidirectional nicotine-dependent learning and memory behavior. The deletion of alpha2-containing nAChRs results in nicotine-induced deficits, while its enhancement potentiates nicotine-facilitated hippocampal dependent learning and memory behavior. The results provide support for the development of pharmacological interventions directed at alpha2-containing nAChRs to influence hippocampal dependent learning and memory behavior in humans.

45-**Menthol Cigarette Smoking and Neuroinflammation: Initial Findings**

Arthur L. Brody, Robert Hubert, Kyoji Okita, Edythe D. London, Mark A. Mandelkern
Brentwood Biomedical Research Institute, Los Angeles

California has a large population of minority groups that have high rates of smoking menthol cigarettes. A central issue with these cigarettes is that smokers who use them have lower cessation rates in standardized treatment programs than smokers who use non-menthol cigarettes. Greater exposure to cigarette smoke (and its constituents) has been implicated in the greater severity of tobacco dependence in menthol cigarette smokers. For this Exploratory/Developmental study, we are examining the effects of menthol (and non-menthol) cigarette smoking on neuroinflammation in humans. Using PET scanning and a recently developed radiotracer ($[^{11}\text{C}]\text{DAA1106}$), we are determining if menthol (and non-menthol) cigarette smoking affects radiotracer binding (a marker for neuroinflammation). To do this, menthol and non-menthol cigarette smokers, as well as non-smoking controls, are undergoing PET scanning, with smokers scanned in the satiated state (smoking per their usual habit on the day of scanning and smoking to satiety immediately prior to scanning). Binding potential values are being determined for whole brain and regional volumes of interest for brain structures known to mediate cigarette-related behavior (e.g., prefrontal cortex and ventral striatum). Thus far, 10 participants have completed the study protocol during this first year of TRDRP funding. Preliminary brain imaging results from these participants will be presented.

***POSTER SESSION: Cornelius Hopper Diversity
Award Recipients***

(DAY-1: Tuesday, October 27, 5:35-6:30PM)

Abstract #46-52

46-**Third Hand Smoke Causes Oxidative Stress in the Liver Leading to Hepatic Steatosis**

Cristina Flores, Neema Adhami and Manuela Martins-Green

Department of Cell Biology and Neuroscience University of California Riverside,
Riverside, California 92521

Third-hand smoke (THS) is the accumulation of secondhand smoke on surfaces; it ages with time, becoming progressively more toxic. We have developed an in vivo THS exposure system using mice that mimics exposure to humans. Here we show that THS-exposed mice on normal diet have increase in oxidative stress, with higher levels of superoxide dismutase activity and H₂O₂. However, no change in activity of antioxidant enzymes catalase and glutathione peroxidase was found. THS-exposed mice also have a lower NADP⁺/NADPH ratio, indicating decrease in the ability of these mice to combat oxidative stress. This excess oxidative stress results in hepatic cellular damage with intracellular lipid accumulation, decrease in ATP production and AST function and molecular damage such as lipid peroxidation, protein nitrosylation and DNA damage. We determined whether these effects worsened by treating the mice with the liver-damaging drug N-acetyl-p-aminophenol (APAP/tylenol). Treatment with APAP results in higher oxidative stress and higher cellular/molecular damage. Also, feeding the THS-exposed mice with western diet, that is known to increase oxidative stress, increased the damage over THS-exposure alone. In order to determine whether oxidative stress is responsible for the cellular and molecular damage we observe, we treated the THS-exposed mice with antioxidants N-acetyl-cysteine and α -Tocopherol for 5 months. This treatment reversed the lipid accumulation and lipid and protein damage but not the DNA or functional damage. In summary, our results show that THS is a new risk factor contributing to development liver steatosis and highlight the danger of THS in general.

47-

Puffing Topography and Nicotine Intake of Electronic Cigarette Users

My Hua¹, Rachel Behar^{2*}, and Prue Talbot^{1,2} * = co-first author

¹Environmental Toxicology Graduate Program, ²Dept. of Cell Biology & Neuroscience, UC Riverside, Riverside, CA 92521

Topography data were analyzed for 20 prescreened electronic cigarette (EC) users (16 male; 4 female). Participants puffed Blu and V2 in two 10 min intervals separated by a 10-15 min break on 2 different days (within a 7 day period). Brand order was reversed on day 2. A handheld topography device (CRess Pocket) was validated and used to measure topography parameters. Puff counts ranged from 13-42 puffs/10 min. Most users took between 20-39 puffs/10 min (average = 32). From the combined data, average puff volume (51 ± 21 ml), average puff duration (2.65 ± 0.98 sec), and average inter-puff interval (17.9 ± 7.5 sec) were determined. The average flow rates for Blu and V2 were 21 ± 6 ml/sec and 18 ± 6 ml/sec, respectively. Nine patterns of use were identified. EC puffing topography was variable among participants in the study, but were often similar within an individual between brands or days. Puff duration, inter-puff interval, and puff volume varied from conventional cigarette standards. The combined average volumes/puff were 56 ± 22 ml/puff (Blu) and 45 ± 22 ml/puff (V2), and the combined average total volume was 1853 ± 786 (Blu) and 1304 ± 477 (V2). The average volumes for both brands exceed the ISO standard for conventional cigarettes (35 ml/puff over 2 sec/min). Data on total puff volume and nicotine intake suggest compensatory usage of EC. These data will be useful in EC smoking machine protocol development and will aid researchers in designing experiments involving EC.

48-

Interviews with On-Site Managers about Tobacco and Marihuana Smoking Policies in Multiunit Housing

Angelica Delgado Rendon, MS., Jennifer Unger, PhD., Tess Boley Cruz, Lourdes Baezconde Garbanati, Daniel Soto

University of Southern California, Keck School of Medicine, Preventive Medicine Department

This presentation aims to identify on-site managers' barriers and facilitators to tobacco and marihuana SHS exposure in multiunit housing in Los Angeles County. Multiunit housing buildings were randomly selected within predominantly Hispanic neighborhoods in Los Angeles County. Managers completed an interview in the properties (n = 20, 10 cities). All of the managers believe SHS from tobacco is harmful to their tenants' health. There are discrepancies on rules about the use of medicinal marihuana in the premises. Twelve of the buildings (60%) had smoking bans for outdoor and indoor common areas but the rules were not always followed. More than half of the managers favor a complete smoking ban on the property (85%). Managers reported having the following vulnerable groups: people with chronic health conditions, children, seniors, and Hispanics. Fifteen (75%) had received complaints from tenants about tobacco SHS exposure and 13 (65%) about marihuana exposure. Many of the managers are not aware of the smoking policies in multiunit housing in their respective cities and would like more assistance in preventing exposure to these carcinogens. Smoking policies need to be implemented at the City level and collaborations with stakeholders will be needed to maintain compliance. Fotonovela will be a useful resource to communicate with the tenants about their susceptibility to exposure and rights. The study assesses the barriers managers face in implementing smoking policies in areas with large vulnerable communities. The managers provided opinions on strategies to protect tenants.

49-**Adapting a Youth-based Outreach Cessation Program for a Community College Setting**

Sarah Hellesen, Kimberly Bankston-Lee, Carol Maytum, Susan Stewart, Elisa Tong
UC Davis, Breathe California of Sacramento-Emigrant Trails

Introduction: From 2006-2009, Breathe California of Sacramento-Emigrant Trails (BCSET) implemented a 'Street Team' program that had youth (ages 16-18) conduct cessation outreach at public events. Since 2013, BCSET and UC Davis adapted the Street Team model into the community college setting through their tobacco cessation study utilizing student-delivered interventions. **Methods:** The BCSET and UC Davis project team implemented the Street Team structure offering small incentives (\$5-50) based on participation. Inclusion criteria were 1) being a current college student 2) 18+ years old, and 3) commit to one semester. Exit surveys of discontinuing Street Team participants to evaluate their experience were offered. **Results:** While 11 students attended the initial training in Fall 2014, only 4 participated in the project with one remaining active through May 2015. Two more were trained in March 2015. The 3 participants who completed the exit survey all rated their experience highly. Individual discussion showed that demands on students' time prevented them from continuing. The BCSET team changed the small incentive structure for 15 members to a prorated stipend (\$200-300) for 3-4 members. The change was received favorably, and 2 who received monetary compensation committed to future participation in summer and fall 2015. **Conclusion:** The retention of community college students to conduct student-delivered cessation interventions was improved by changing the incentive structure to a prorated stipend. These lessons learned might apply to engaging college students for tobacco control work.

50-

Using a Partnered, Peer-Led Process to Develop the BREATHE Intervention: Key Lessons Learned from Our Participatory Approach

Denise Maratos, Ed.M.; Herman Corteza, M.S., M.S.W.; Elizabeth Bromley, M.D., Ph.D.

Pacifica Graduate Institute; Pacific Clinics; UCLA Department of Psychiatry and Biobehavioral Sciences

The peer-led intervention BREATHE (Bringing Resilience and Engaging Awareness of Tobacco Habits for Everyone) was developed by a Task Force of 17 mental health clients to encourage fellow clients to stop smoking and live a healthier life. By exploring our own experiences with addictions, we developed and delivered a pilot intervention in 8 sessions, in group and one-on-one formats. In order to identify and elaborate on the 8 topics we thought most important for mental health clients, we shared our experiences of addiction and mental health issues with each other while reviewing evidence-based interventions. We also completed training in peer-led smoking cessation with the New Jersey-based CHOICES program and in Motivational Interviewing. Throughout, we trusted and empowered each other to talk with openness and transparency. By having weekly group meetings and individual visits, we developed a comradery to value and draw from our diversity to refine existing interventions. We revised stigmatizing language, added perspectives on mental health treatment culture, made room for harm reduction approaches, and focused on health and resilience. Ultimately, we exceeded our expectations by becoming more confident of encouraging our peers to make healthy choices. In this presentation, we describe data from Task Force members on the impact of their participation including talking with family and friends about quitting smoking, advocating for non-smoking policies in living environments and mental health settings, and increasing self-efficacy and knowledge about tobacco use and health.

51-**Lay Health Worker Processes Involved in Working with Vietnamese Smokers and their Families**

Phung K, Yu F, Nguyen I, Chuang LP, Le K, Wong C, McPhee SJ, Nguyen TT, Tsoh JY, Burke NJ

(1)University of California, San Francisco (2) Asian American Research Center on Health

We describe characteristics that made lay health workers (LHWs) effective in a family-based approach to health promotion among Vietnamese American smokers and their families. Participants were enrolled in a randomized controlled trial testing the efficacy of a family-based LHW outreach program to promote smoking cessation. Nine Vietnamese LHWs (44% males, mean age = 58.7 years) recruited 54 Vietnamese smoker-family member dyads (54.6% males, 68.5% spoke limited English). We observed 15 sessions of LHWs teaching about tobacco cessation (intervention) or nutrition/exercise (comparison) to 2-3 dyads per session. Observations were recorded in photographs and detailed field notes, including description of LHW and participant characteristics and interactions. Two research staff independently coded field notes using Atlas.ti. Team members reconciled coding differences and discussed emerging themes. We found five key characteristics that made LHWs effective in engaging smokers and family members in discussing tobacco cessation or nutrition/exercise: 1) being well-prepared; 2) having prior relationships with participants; 3) verbal and nonverbal communication skills; 4) ability to elicit and acknowledge questions; and 5) ability to cultivate a welcoming environment for sharing personal stories. In summary, characteristics of effective LHWs include advance preparation, prior relationship, and engaging communication styles. Further research should focus on which LHW characteristics are most important to promote smoking cessation and healthy lifestyle changes in Vietnamese Americans.

52-

Bioaccumulation of Cigarette Butt Toxicants in the Freshwater Fish, *Oncorhynchus mykiss*, & Saltwater Mussel, *Mytilus galloprovincialis*

Lenard Yabes, Eunha Hoh, Richard Gersberg, Violet Renick, Adrienne Cibor, Kayo Watanabe, Hung-Hsu Wei, Thomas Novotny

San Diego State University, Graduate School of Public Health, Division of Environmental Health, San Diego, CA; Nautilus Environmental, San Diego, CA

Cigarette butts (CBs) comprise the single most abundant litter form worldwide. An estimated 8 million CBs are littered per minute generating pervasive tons of toxic waste. Despite significant strides in smoking cessation, cigarette consumption & its concomitant waste is rising globally. Inevitably CBs travel downstream via erosion & rainfall into aquatic ecosystems. Their cellulose acetate filters are non-biodegradable & 4000+ identified chemicals may enter the environment. Studies report that CB chemicals form a toxic leachate that poses deleterious effects to aquatic life. However, human health exposures to these persistent & potentially bioaccumulative contaminants remain unknown. This innovative research looks to elucidate the bioaccumulation potential of CB leachate in the aquatic food chain. Machine-smoked CBs were used throughout the testing phase for consistency. Range-finding tests were performed to determine maximum tolerable CB leachate concentrations (0.5 CB/L of freshwater for the rainbow trout & 1 CB/L of saltwater for the mussel) whereby no mortality & behavioral changes occurred. Currently, 28-day definitive tests are underway whereby each species is exposed to selected dilutions to further assess bioaccumulation. Upon completion trout & mussel tissues will undergo extraction/analysis for any leachable chemicals. Non-targeted analysis using GC×GC/TOF-MS for chemical identification & ICP-MS for elemental determination will follow. This study's findings will be used in an ongoing effort to assess human exposures to the toxic chemicals associated with CB waste.

POSTER SESSION: How Tobacco Causes Disease

(DAY-2: Wednesday, October 28)

Abstract #53-62

53-

Chromatin remodelers Brg1 and Baf60c regulate transcription and switch subunits during cardiac differentiation

Swetansu K. Hota,¹ Jeffrey R. Johnson,^{1, 2} Erik Verschuere, ^{1, 2} Nevan J. Krogan ^{1, 2} and Benoit G. Bruneau¹

¹Gladstone Institute of Cardiovascular Disease, 1650 Owens Street, San Francisco, CA 94158 ²Department of Cellular and Molecular Biology, University of California at San Francisco

Prolonged tobacco usage leads to cardiac hypertrophy in adults and is implicated in abnormal heart development in the fetus. Both adult and fetal heart diseases are caused by abnormal transcriptional regulation of key genes. Chromatin regulatory proteins Brg1 and Baf60c are necessary for cardiac homeostasis and normal cardiac development. We investigated transcriptional changes caused by the loss of Brg1 or Baf60c by measuring gene expression using RNASeq from stem cell-derived cardiomyocytes. In absence of Baf60c, genes encoding developmental signaling and transcription machinery were altered in mutant cardiac precursors and beating cardiomyocytes. In contrast, we found that Brg1 was required for mesoderm specification and regulation of several important cardiac precursor specific genes. Proteomic analysis of the Brg1 associated factor (BAF) complex revealed cell-type specific enrichment of Brg1 subunits, which switched during cardiomyocyte differentiation. Further, BAF complexes were found to auto-regulate their biochemical activity. Cardiomyocyte specific BAF complexes showed reduced ability to hydrolyze ATP and to mobilize nucleosomes, compared to the ES cell-BAF complex. Together, these results indicate that Brg1 associated factors form cell-type specific complexes to regulate transcriptional programs during cardiac lineage specification. These findings form a basis to study tobacco induced transcriptional changes during heart development and may lead to identification of genes responsible for altering transcriptional programs leading to cardiac diseases.

54-

The critical role of mast cells in a mouse model of asthma in which airway hyperreactivity and inflammation are exacerbated by epicutaneous exposure to a component of thirdhand smoke

Mang Yu¹, Mindy Tsai¹, and Stephen J. Galli^{1,2}

¹Department of Pathology and ²Department of Microbiology and Immunology, Stanford University School of Medicine

Asthma is one of the most prevalent chronic disorders of children and adults. Extensive studies have evaluated the adverse effects of cigarette smoking and exposure to second hand smoke in asthmatics, however, very little is known about the influence of exposure to thirdhand smoke (THS) on the development and severity of asthma.

Approximately 43% of children are at high risk of exposure to THS and exposure to cockroach allergen (CRA) has been identified as the most important risk factor for asthma in inner-city households. We developed an asthma model in mice in which the animals are sensitized to CRA via intranasal challenge and used this model to investigate the influence of epicutaneous exposure to a major component of THS, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), on the development of asthma phenotypes. Using state-of-the-art genetic and cell transfer approaches, we found that epicutaneous NNK exposure significantly exacerbated airway hyperreactivity (AHR) and recruitment of neutrophils and lymphocytes into the lung air spaces in this model by activating $\alpha 7$ nicotinic acetylcholine receptors ($\alpha 7$ nAChRs). We also showed that expression of $\alpha 7$ nAChRs by mast cells significantly contributed to such effects of epicutaneous exposure to NNK. We conclude that epicutaneous exposure to THS can exacerbate airway hyperreactivity and inflammation in a mouse model of asthma induced by CRA, and that mast cells importantly contribute to the pathophysiological changes induced by NNK and CRA.

This study advances our knowledge of the potential adverse health effect of exposure to THS and would provide support for public policies to reduce exposure to THS.

55-**Imaging Inhaled Nicotine Using 3-Dimensional Liquid Extraction Sample Analysis**

Christopher Wallis, Anthony Wexler

Air Quality Research Center, University of California, Davis

The health effects of environmental tobacco smoke (ETS) depend on where smoke particles and gases deposit in the airways. The ability to perform 3D molecular imaging will enable examination of local damage. Here we present a method and preliminary results for imaging the 3D distribution of nicotine and other ETS-related compounds while simultaneously acquiring a high resolution 3D optical image set. Liquid Extraction Sample Analysis (LESA) has been used with success in 2D molecular sampling at room temperature. We have adapted this technique to 3D at frozen temperatures, where traditional LESA does not work, by integrating a custom LESA probe to an Imaging Cryomicrotome (ICM). The ICM serially slices through a frozen sample block, exposing a new plane of the sample after each slice and imaging the exposed surface optically. LESA samples molecules off each slice to acquire a 2D molecular image of that slice. By combining a stack of slices, we achieve a 3D optical and molecular image. Optical image resolution can be as small as 10 μm while molecular image resolution is about 1 mm. Our results include verification of the method in 2D and experimental 3D analysis in tissue. This method will allow us to map inhaled cigarette smoke deposition patterns within a lung in 3 dimensions by analyzing LESA solvent samples for nicotine. Additionally, the same method will allow imaging of foreign particle, chemical and biochemical (e.g., cytokines) distribution within a tissue sample.

56-**Cardiotoxicity Study of Tobacco Smoking Using hiPSC-CMs**

Yingxin LI

Stanford University

The effect of tobacco smoking on abnormal rhythms of the heart is less clearly defined. Nicotine is the main constituent of tobacco smoking which is responsible for the elevated risk of the heart and vascular disease and sudden cardiac death. The effect of nicotine on heart with cardiac diseases may increase the tobacco-related heart diseases. The disparate predispositions of heart cells with variant disease backgrounds to tobacco-induced cardiotoxicities and the mechanisms are less clearly defined. A powerful novel cellular platform to study the human cardiac toxicity is generated. The human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) from the normal population and patients with long QT syndrome are generated. The cells recapitulate key phenotypic features of the cardiac cells with heart disease. We have verified that hiPSC-CMs could model the increased susceptibility of genetic cardiac disorders to drug-induced heart adverse effects. Normal hiPSC-CMs have been treated with a range of doses (10 nmol/L-1 mmol/L) of nicotine, and the cardiotoxic responses were evaluated by multielectrode array. Nicotine was observed to induce a dose-dependent field potential duration prolongation and beating rate decreases. I plan to further examine tobacco-induced cardiotoxicities of LQT hiPSC-CMs. The study will elucidate whether tobacco smoking can increase the incidence of the abnormal rhythms of the heart. It will also shed light on the mechanism by which nicotine is associated with abnormal rhythms of the heart in patients with preexisting heart diseases.

57-**Telomere Length and Lung Cancer Risk: Does Timing of DNA Collection Matter?**

L. Sakoda, K. Thai, L. Shen, C. Quesenberry Jr, E. Jorgenson, C. Iribarren, M. Kvale, N. Risch, C. Schaefer, L. Habel

Division of Research, Kaiser Permanente Northern California; Institute for Human Genetics, UC San Francisco

Telomeres are the repetitive DNA sequences capping ends of chromosomes. Altered maintenance of telomere length (TL) may lead to cancer. Shorter TL has been associated with smoking (also seen in our data), but inconsistently with lung cancer risk. We investigated whether inconsistent findings may be explained by whether lung cancer is diagnosed before vs. after DNA collection among participants of the Kaiser Permanente Research Program on Genes, Environment and Health providing saliva samples. Cohort and case-control analyses were conducted to estimate lung cancer risk associated with tertiles of TL, adjusted for age, sex, race/ethnicity, and smoking pack-years. Among 61,083 cancer-free participants at saliva collection (median follow-up=4.3 years), including 285 diagnosed later with lung cancer, longer TL was suggestively associated with increased lung cancer risk in never smokers [tertile 3 (longest) vs.1 (shortest): hazard ratio (HR)=1.68, 95% confidence interval (CI): 0.88-3.21], but with decreased lung cancer risk in ever smokers [tertile 3 vs. 1: HR=0.89, 95% CI: 0.64-1.23]. Comparing 243 cases diagnosed before saliva collection to the 61,083 controls, this pattern was more pronounced [tertile 3 vs. 1: odds ratio (OR)=1.83, 95% CI: 0.97-3.44 in never smokers; OR=0.65, 95% CI: 0.44-0.96 in ever smokers]. However, the number of cases in our analyses was small, and some results may be due to chance. Results from this study suggest that lung cancer risk associated with TL differs by smoking status and that timing of DNA collection relative to diagnosis may be influential.

58-**Genetic and Epigenetic Profiling reveal Key Regulators of Small Cell Lung Cancer Progression and Metastasis**

Dian Yang, Sarah Denny, Julien Sage, William Greenleaf and Monte Winslow

Cancer Biology Program, Stanford University

Small cell lung cancer (SCLC) is a prevalent and fatal malignancy. Several factors contribute to the poor outcome of SCLC patients, especially the ability of cancer cells to leave the primary tumors and establish inoperable metastases. How SCLC cells gain the ability to spread to distant organs is a poorly understood question of immense clinical importance. We purified SCLC cells by FACS from primary tumors and metastases that developed in a genetically-engineered mouse model of SCLC, *Rb1^{fl/fl}*, *p53^{fl/fl}*, *p130^{fl/fl}*, *R26^{mTmG}*. We used ATAC-Seq to identify changes in chromatin accessibility and RNA-Seq to identify key gene expression alterations that define different stages of SCLC progression. In advanced SCLC cells, we observed a massive increase of chromatin accessibility which correlated with gene expression changes. Motif analysis of the newly accessible regions showed enrichment for the NFI transcription factor binding motif. Nf1b, an important member of the NFI transcription factor family, is frequently amplified and functions as an oncogene in SCLC. Functional studies suggest Nf1b may play key roles in proliferation, cell death and anchorage-independent cell growth. Preliminary functional *in vivo* data suggest Nf1b and its downstream genes regulate SCLC metastatic ability. Current studies are focused on understanding how Nf1b drives chromatin structure changes and how this regulation networks influence SCLC aggressiveness, which may greatly benefit patients' survival.

59-**Sustained MARCKS Phosphorylation Promotes Stem Cell-Like Properties in Tobacco Smoke-Mediated Lung Cancer Progression**

Ching-Hsien Chen¹, Muhammad Arif¹, Phoebe Yam¹, Kent E. Pinkerton², Reen Wu^{1*}

¹Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine and Center for Comparative Respirator

Phosphorylation of MARCKS at Ser159/163 (phospho-MARCKS) has been reported to confer malignant potential of neoplastic disease, but little is known regarding how phospho-MARCKS is up-regulated in lung cancer. Herein, we aimed to determine if elevation of phospho-MARCKS results from exposure to smoke and plays a key role in smoke-related lung cancer. In a screen of 122 patients with lung cancer, high phospho-MARCKS levels in primary tumors were found to be significantly associated with shorter disease-free survival in smokers. Further studies showed that MARCKS becomes activated in airway epithelium and lung cancer in response to tobacco smoke, both in vitro and in vivo. Through the use of genetic and pharmacological approaches, we demonstrated that up-regulation of phospho-MARCKS acted in parallel with increased messages of inflammatory mediators and stemness genes in smoke-treated cells. Conversely, down-regulation of smoke-induced genes including TNF-alpha, IL-8, MMP9, Oct-4, and CD133, as well as suppression of smoke-enhanced clonogenic activity, invasiveness, and migratory capability of lung cancer cells were achieved by knocking down MARCKS expression or by using MPS peptide to target MARCKS phosphorylation. Our data suggest that phospho-MARCKS functions in smoke-mediated lung cancer progression and serves as a potential biomarker for predicting prognosis in smoke-related lung cancer.

60-

Ultra Low Dose Lung Cancer Screening using CT

Michael McNitt-Gray, Stefano Young, Frederic Noo, Pechin Lo, John Hoffman, Grace Kim and Matthew Brown

David Geffen School of Medicine at UCLA and the University of Utah

Objective: While CT scans used for Lung Cancer Screening are performed at low radiation dose levels, the objective of this study was to investigate the effect of further reducing dose on the ability to detect suspicious lung nodules. **Methods:** Using a previously published technique that uses physical principles to simulate reduced radiation dose CT scans, a set of simulated-reduced dose cases were created at 50% and 25% of the original dose. This technique was applied to 50 CT scans performed during the National Lung Screening Trial (NLST). To evaluate detection performance at each dose level, a computer-aided detection (CAD) algorithm was run on each dataset and its results were compared to nodule locations identified by radiologists. **Results:** The CAD algorithm's nodule detection performance was similar across all dose levels. The CAD algorithm identified about the same number of false positives at original and 50% dose level but this increased substantially at the 25% dose level due to the increase in image noise. **Conclusion:** Detection performance was similar for the CAD algorithm at all dose levels. However, the false-positive rate at 25% dose rose substantially, which indicates some noise reduction methods need to be developed if dose levels are to go that low. **Broader Relevance:** CT scans for Lung Cancer Screening may be performed at further reduced radiation doses, limiting the radiation exposure to the screening population.

61-**Childhood Secondhand and Prenatal Smoke Exposure in Relation to Timing of Puberty in Girls**

G.C. Windham¹, R. Lum², R.W. Voss¹, M.S. Wolff³, S.M. Pinney⁴, F. Biro⁴, S.L. Teitelbaum³, R. Hiatt⁵, M. Galvez³, L. Kushi

¹CA Dept. of Public Health, Richmond, CA; ²Impact Assessment Inc., La Jolla, CA; ³Mt Sinai School of Medicine, NY, NY; ⁴

Tobacco smoke contains hormonally active chemicals, which may affect puberty. Only a few studies (including our TRDRP-funded project) have examined prenatal or secondhand smoking (SHS) and age at menarche, with inconsistent results. We use data from a longitudinal study in CA, NY and OH to examine earlier markers of puberty. An ethnically diverse cohort of 1,237 girls, starting at ages 6-8, participated in annual exams to assess growth and Tanner breast (B) and pubic hair (PH) stages. Current and prenatal tobacco smoke exposures, and demographics, were obtained from parent report. Using statistical models, time ratios (TRs) were calculated to compare age at pubertal onset by level of smoke exposure, adjusting for child race and BMI, caregiver income, and site. About 40% of girls had SHS exposure; those with highest exposures developed PH younger (TR=0.95; 95% CI 0.92, 0.98). Daughters whose mothers smoked in pregnancy also had earlier PH development; for ~5 cigarettes/day vs. none, the TR was 0.91 (95% CI 0.86, 0.97), or about 11 months younger. Including both smoke exposures in one model revealed similar patterns. In conclusion, both prenatal and peri-pubertal smoke exposure was associated with earlier onset of puberty in girls. These findings have implications for guiding future research of the effects of smoke exposure on childhood growth and reproductive development, which in turn may impact long-term health outcomes, as well as for policies limiting childhood SHS.

62-**SMYD3 Links Methylation of MAP3K2 to Ras-driven Tumors**

Pawel K. Mazur, Nicolas Reynoird, Or Gozani and Julien Sage

Stanford University, Departments of Genetics and Pediatrics

Lysine methyltransferase (KMT) expression is frequently deregulated in human cancers, but the contributions of KMTs to oncogenic signaling pathways are not well understood. In an effort to determine whether deregulated KMT activity contributes to RAS-driven cancers, I evaluated KMT expression in lung adenocarcinoma, which is usually initiated by oncogenic RAS signaling, and observed increased expression of the KMT gene SMYD3. The largely cytoplasmic KMT SMYD3 is overexpressed in numerous human tumors. However, the molecular mechanism by which SMYD3 regulates cancer pathways and its relationship to tumorigenesis in vivo are largely unknown. Here I show that methylation of MAP3K2 by SMYD3 increases MAP Kinase signaling and promotes the formation of Ras-driven carcinomas. Using mouse models for lung adenocarcinoma, I found that abrogating SMYD3 catalytic activity inhibits tumor development in response to oncogenic Ras. I employed protein array technology to identify the MAP3K2 kinase as a target of SMYD3. In cancer cell lines, SMYD3-mediated methylation of MAP3K2 at lysine 260 potentiates activation of the Ras/Raf/MEK/ERK signaling module. Finally, the PP2A phosphatase complex, a key negative regulator of the MAP Kinase pathway, binds to MAP3K2 and this interaction is blocked by methylation. Together, obtained results elucidate a new role for lysine methylation in integrating cytoplasmic kinase-signaling cascades and establish a pivotal role for SMYD3 in lung cancer.

POSTER SESSION:

***Bridging the Gap between Discovery and Policy
by Research***

(DAY-2: Wednesday, October 28)

Abstract #63-71

63-**Tobacco Wastecare: Model Legislation to Mitigate Butt Waste**

Novotny TE, Curtis C.

Cigarette Butt Pollution Project (CBPP)

Model legislation can require tobacco producers to implement programs to collect, transport, process, and dispose of tobacco product waste (TPW). Other hazardous materials are taken back, recycled, or disposed of as post-consumer waste through extended producer responsibility and product stewardship policies (EPR/PS). We reviewed existing EPR/PS legislation involving paint, electronics, appliances, batteries, and other hazardous materials. We drafted legislation to address TPW, which was reviewed by ChangeLab Solutions, the Product Stewardship Institute, and the Public Health Law Center. This legislation, based on EPR/PS, establishes a Tobacco WasteCare program which would require tobacco producers to reduce environmental impacts associated with tobacco use. Other stakeholders, especially suppliers, retailers and governments, would also be encouraged to take complementary actions throughout the TPW life cycle as an effective joint producer responsibility and product stewardship program. This would involve record keeping, tracking, and documentation of TPW within the State; special attention to handling this waste; and adequate liability coverage for contractors working for the program. Tobacco WasteCare offers an important legislative approach to hold the tobacco industry responsible for TPW prevention, mitigation and reduction. If enacted, cleanup costs for TPW will shift from communities and taxpayers to the tobacco industry, while increasing the cost of tobacco products.

64-

Assessing Toxicity of Tobacco Product Waste to Humans

E Hoh, R Gersberg, D Schlenk, S Schick, V Renick, A Cibor, L Yabes, H Wei, T Novotny

San Diego State University, UC Riverside, Nautilus Environmental

Discarded cigarette butts are the most prevalent litter found in ocean beaches and inland waterways. Cigarette tobacco and smoke contain numerous toxic chemicals. Cigarette filters trap particulate matter and less volatile chemicals present in the main stream cigarette smoke. Therefore, we hypothesize that cigarette butts contain harmful chemicals due to the trapped chemicals in filters and chemicals in unburned tobacco. Thus, identification of the leachable chemicals and assessment of their environmental occurrence and toxicity is critically important for characterizing the human health risk associated with cigarette butts. Therefore, we are currently conducting three experiments: 1) identification of leachable chemicals in cigarette butts; 2) bioaccumulation of chemicals from cigarette butt leachate in freshwater fish (trout) and saltwater mussels; and 3) cell-based toxicological tests. For consistency, machine smoked cigarette butts have been used. The chemical identification is conducted by nontargeted analysis using GC×GC/TOF-MS. For the bioaccumulation test, preliminary tests were conducted to determine cigarette butt leachate concentrations at maximum without causing death and behavioral changes. After bioaccumulation tests are complete, both fish and mussel tissues will be analyzed for the leachable chemicals. For evaluation of possible human toxicity, cell-based assays will be conducted including aryl hydrocarbon receptor (AhR) activity, the UMU assay for genotoxicity, and Estrogen Receptor activity. Prior to these tests, MTT assays were tested for cytotoxicity.

65-**The Use of Twitter during An Election: Media Campaign Lessons from California's Proposition 29**

Miao Feng, Glen Szczyпка, John Pierce*, and Sherry Emery

University of Illinois at Chicago, *Moore's UCSD Cancer Center

California's Prop 29, the Tobacco Tax for Cancer Research Act, aimed to increase the tax on cigarettes \$1.00/pack for cancer and tobacco-related research and programs. Initially, there was solid popular support but it eroded and Prop 29 was defeated on June 12, 2012. We investigated Twitter content for this issue. Using 10 keywords, 115,619 tweets related to Prop 29 were collected from Twitter between January to June 2012. 17,100 tweets with a high relevance score were used for analyses. We conducted a network analysis of the users involved in Prop 29 debates; we conducted content analysis to study how users interpreted the debate. In the 9 weeks before the vote, the oppositional campaign vastly outspent the tobacco control campaign, which concentrated spending only in the final 3 weeks. Throughout the 9 weeks, tweet content was much more likely to be supportive (62%) than oppositional (12%) to Prop 29. Supportive tweets emphasized celebrities, health and stand up to big tobacco. Oppositional tweets emphasized tax hikes, bureaucracy and these successful framed the messages put out by neutral tweets. Oppositional tweets appeared to mobilize and circulate among densely connected users against Prop 29 whereas supportive tweets lacked a clear network structure. Oppositional campaign to Prop 29 significantly out-maneuvered the supportive campaign with help of a vastly superior traditional media presence. Supportive campaign activated many more tweets, but not helpful to the campaign.

66-**Exposure to secondhand and thirdhand tobacco smoke among Hispanic residents of multiunit housing**

Jennifer B. Unger, Ph.D., Tess Cruz, Ph.D., Daniel W. Soto, MPH, Angelica Delgado Rendon, MA

University of Southern California

Although smoking is banned in most California public spaces, many residents of multiunit housing, especially low-income and Hispanic residents--are exposed to tobacco smoke from neighboring apartments. In our evaluation of a bilingual fotonovela about secondhand smoke in multiunit housing, we conducted a survey of 403 Hispanic apartment residents (71% female, 69% foreign-born). Although only 9% were smokers, 22% reported that someone in the household smoked; 8% reported that someone smoked inside their apartment unit. Most respondents reported that smoke entered their homes at least once a month (65%) and that they were bothered by smoke in their home (73%). Although most respondents (62%) favored a complete smoking ban in and around the building, only 23% reported that their building had a complete smoking ban and enforcement was inconsistent. Barriers to avoiding smoke included inability to control other people's actions (85%), reluctance to make trouble (68%), discomfort about telling others not to smoke (61%), and reluctance to anger smokers (57%). Only 30% had asked someone not to smoke in the past 6 months; even fewer intended to talk with their neighbors (26%) or landlords (30%) about smoke in the next 6 months. Interventions are needed to help apartment residents advocate for smokefree living conditions. After this survey, we randomly assigned these residents to receive our new fotonovela or a pamphlet about secondhand smoke. Follow-up data collection is underway.

67-

Sexual identity disparities in smoking and secondhand smoke in California: 2003-2013

Wendy Max, Brad Stark, Hai-Yen Sung, Naphtali Offen

University of California, San Francisco

Introduction: This study determined smoking prevalence, smoking behavior patterns, and secondhand smoke (SHS) exposure of lesbian, gay, and bisexual-identified Californians; compared these with heterosexuals; and analyzed changes in these behaviors over the last decade. **Methods:** We analyzed the 2003-2013 California Health Interview Surveys, using multivariate logistic regression models to analyze the impact of sexual identity on smoking behaviors, and conducted time trend analyses for each smoking-related outcome measure. **Results.** Lesbian and bisexual women smoke at significantly higher rates than heterosexual women, and female bisexual smokers were less likely to be light smokers than heterosexuals. Among men, smoking prevalence was higher among gays and bisexuals than among heterosexuals; and gay smokers were more likely to be light smokers than heterosexuals. Sexual minority men and women were more likely to be exposed to SHS at home than heterosexuals. Current smoking prevalence and SHS exposure have fallen among sexual minorities. **Conclusion:** Disparities in tobacco use and exposure by sexual orientation exist in California; bisexual women and men are particularly at risk. **Relevance:** While smoking and secondhand exposure have fallen for most California populations, some groups still smoke and are exposed to SHS at relatively high rates, including lesbian, gay, and bisexual men and women. Interventions should consider the unique needs of the sexual minority community.

68-

Responsiveness of smoking and quitting behaviors to cigarette prices among African Americans

Hai-Yen Sung, Courtney Keeler, Tingting Yao, Michael Ong, Valerie Yerger, Wendy Max

University of California, San Francisco

Introduction: This study evaluates the impact of tobacco tax and price policy on smoking prevalence, smoking intensity, and quitting in African Americans (AAs). **Methods:** We analyzed all non-Hispanic AAs aged 18+ (N=28,131) from the 2006-2007 and 2010-2011 Tobacco Use Supplement to the Current Population Survey data, that were merged with state-specific cigarette retail price database. A two-part econometric model was used to examine the impact of cigarette prices on the decision to smoke and cigarettes per day by smokers. Multivariate logistic regression analysis was conducted to examine the impact of cigarette prices on having any quit attempt in the past 12 months and on successful cessation for at least 6 months among recent active smokers. **Results:** Cigarette prices were negatively associated with smoking participation and smoking intensity with the price elasticity at -0.27 and -0.18 , respectively. The sum of these two elasticities gives the overall price elasticity of cigarette demand at -0.45 . Cigarette prices were positively associated with quit attempt (price elasticity at 0.36) but not with successful cessation. **Conclusion:** Non-Hispanic AAs are responsive to price increases in reducing smoking prevalence and intensity, and in increasing quit attempt. **Relevance:** Non-Hispanic AAs smoke at the highest rate among all racial/ethnic groups in California. This study provides evidence that raising tobacco taxes is an effective policy to reduce cigarette smoking for AAs.

69-**'R3Crew' Peer-Delivered Interventions for Community College Student Smokers about Tobacco Cessation: Baseline Demographics from the STAND Trial**

Kimberly Bankston-Lee, Carol Maytum, Susan Stewart, Sarah Hellesen, Elisa Tong

Breathe California of Sacramento-Emigrant Trails and University of California, Davis

INTRO: Community colleges have more students with lower socioeconomic status and higher smoking rates than universities. The Sacramento Taking Action Against Nicotine Dependence (STAND) project is conducting a randomized controlled trial with two peer-delivered intervention arms (brief motivational interviewing; direct referral to the California Smokers' Helpline), compared to usual care (student clinic referral). **METHODS:** An academic-community partnership of UC Davis and Breathe California of Sacramento-Emigrant Trails (BCSET) conducts the study at Sacramento City College. BCSET's young adult "Street Team" program was adapted to the "R3Crew" student program. BCSET staff trained the R3Crew (n=13, 1-4 active/semester) on the study protocol, and supervised the R3Crew delivering the interventions. **RESULTS:** Among 113 smokers screened to date, 104 completed the baseline survey. Participants are diverse in age (18-70 years, median 32.5), sex (59% women), and race/ethnicity (38% white, 32% African American, 16% mixed, 5% Latino). Among those who provided data on household income (n=74), 73% reported <\$20,000 annually. Most were daily smokers (84%). Cigarettes were most commonly used (96%), followed by electronic smoking devices (16%), hookah (13%) and little cigars/cigarillos (9%). Many intended to quit in the next 30 days (42%) and in the next 6 months (18%). **CONCLUSION:** The R3Crew model is a promising method for recruiting and intervening with community college student smokers.

70-**Measuring Particulates in Tribally-Owned Casinos: Feedback for Smoke-Free Policy Improvements**

Roland S. Moore, Ph.D., Neil Klepeis, Ph.D., Narinder Dhaliwal, M.A., Francisco Buchting, Ph.D., Juliet P. Lee, Ph.D.

PIRE, Stanford University, ETR Associates, Buchting Consulting

Smoke-free indoor space policies reduce health risks. However, SHS protection is still limited in California Indian-owned casinos, because of tribal sovereignty. After gaining permission of tribal council members and casino management, we performed air quality monitoring at four California casinos on two consecutive days per location. We used Sidepak AM510 Personal Aerosol Monitors (TSI, Inc.) to record realtime fine particle concentrations (PM_{2.5}) every 10 seconds in different casino areas using a predetermined schedule. Sidepaks were also placed at fixed locations. Patrons' PM_{2.5} exposures, reflecting levels occurring in different casino rooms, had medians of up to 55 micrograms per meter cubed in the main slot areas of each casino. Exposure levels in nonsmoking poker and player's club areas were generally much lower, like typical outdoor levels, but the median level of one part of a nonsmoking area at one casino was higher than on the main smoking floor at 65 micrograms per meter cubed. High PM_{2.5} levels (median levels up to ~20 times above outdoor levels in casino smoking areas) represent substantial exposures for both casino staff and patrons. In one casino, levels in labeled nonsmoking gaming and lower level recreation areas were also high, apparently due to the free flow of air from the main smoking areas. To encourage the expansion of tribal smoke-free policies to reduce PM_{2.5} exposure, monitoring results are shared with tribal casino management and tribal leadership.

71-

Producer Responsibility and Product Stewardship for Tobacco Control: An Environmental Approach

Novotny TE, Curtis C, Collins S, Cunningham S, Stigler-Granados P.

Cigarette Butt Pollution Project (CBPP)

Introduction: Tobacco Product Waste (TPW) is a toxic environmental hazard and the most ubiquitous waste item collected throughout the world. The tobacco industry has avoided any responsibility for cleanup, prevention, mitigation, or reduction of TPW. The Cigarette Butt Pollution Project joined with tobacco control and environmental groups to raise public attention to TPW using the environmental principles of Extended Producer Responsibility and Product Stewardship to stimulate advocacy, implement new research, and formulate novel policies to benefit both the environment and tobacco control. Using paid and social media, cleanup campaigns, toxicology research, economic modeling, and policy advocacy, new approaches to TPW that will benefit tobacco control have been developed. Most prominent are proposed legislation to ban sale of filtered cigarettes, prohibit smoking in outdoor public spaces, and engage hazardous waste laws to address TPW. Conclusion: Environmental principles applied to TPW are able to stimulate new alliances among environmental and tobacco control advocates. Existing environmental legislation can be used to reduce tobacco use as well as hazardous TPW deposition in the environment. Conclusion: The environmental approach to TPW may prove to be an innovative channel for global tobacco control efforts aimed at shifting responsibility for TPW cleanup, take-back, recycling, product changes, and financing back to the tobacco industry and to other businesses.

POSTER SESSION:

Tobacco Addiction and Cessation Research

(DAY-2: Wednesday, October 28)

Abstract #72-79

72-**The BREATHE Team: A Pilot Study of a Peer-Led Approach to Tobacco Cessation for Specialty Mental Health Clinic Settings**

Elizabeth Bromley and Herman Corteza

UCLA Department of Psychiatry and Biobehavioral Sciences; Pacifica Graduate Institute; Pacific Clinics

Given persistent disparities in rates of tobacco dependence among individuals with serious mental illnesses (SMI; psychotic disorders, severe mood disorders) there is a need for effective, tailored, and sustainable interventions for tobacco cessation for use in mental health clinic settings. Such interventions are not only effective but can heighten attention to issues of health generally and tobacco use specifically in sites where individuals with SMI receive the majority of their care. Peer-led approaches to encouraging tobacco cessation have advantages because they draw on peers' salient experience and motivation to support one another. To develop a novel, peer-led psychosocial intervention for tobacco cessation for SMI, we used a partnered participatory process that included the following phases: peer engagement, agenda & vision-setting, evidence review & rating, intervention refinement, and training. Our Task Force of 17 peers and Peer Providers developed and trained to deliver an 8-session intervention called BREATHE (Bringing Resilience and Engaging Awareness of Tobacco Habits for Everyone). In a pilot feasibility study, Task Force members delivered BREATHE to study participants receiving care at a public mental health clinic. We describe enrollment and participation, fidelity, acceptability, and impact on tobacco use (expired CO, self-report). We report results for potential mechanisms of change (i.e., illness severity, motivation, self-efficacy, hope, recovery, group environment) and next steps to refine and examine effectiveness of the intervention.

73-**Correlates of Cessation Activities among Transit Workers**

Carol B. Cunradi, M.P.H., Ph.D.*, Roland S. Moore, Ph.D., Robynn S. Battle, Ed.D.

HBSA, A Supporting Organization of Pacific Institute for Research and Evaluation

Introduction: Gaining insight into factors associated with participation in cessation activities can aid worksite efforts to promote cessation and reduce tobacco-related disparities. This study describes correlates of past-year cessation activities among transit workers who are current smokers (n=190). **Methods:** In cooperation with transit agency management and the transit workers union, data were obtained from a cross-sectional survey on tobacco use conducted among 1,572 eligible employees at an Oakland-based public transit agency. Surveys were completed by 935 workers (59% participation rate). Adjusted odds ratios were calculated to identify factors associated with past-year cessation activity. **Results:** Approximately 54% of smokers (n=101) stopped smoking for one day or longer during the past year in order to quit. The most common cessation activity was use of nicotine replacement therapy (19.9%), followed by 'cold turkey' (14.5%). Few reported using group cessation programs, quitlines, or other pharmacotherapy. Workers in the contemplation/precontemplation stage for intention to quit were less likely to have engaged in cessation activities than those in the action/preparation stage. Frequency of coworker encouragement for quitting was positively associated with past-year cessation activities. **Conclusion:** Most transit workers who smoke try to quit. Coworker encouragement for quitting can be leveraged in the worksite to promote participation in cessation activities.

74-

Does 30 day exposure to cigarette pack graphic warnings affect smoking behavior?

Joseph Guydish, Catherine Henderson, Barbara Tajima, Shilpa Dutta

Institute for Health Policy Studies, University of California San Francisco

This study investigates effects of exposure to FDA-approved Cigarette Graphic Warning Labels (GWLs) on smokers in addiction treatment. GWLs are now used in 45 countries, and were mandated for use in the U.S. under provision of the 2009 Tobacco Control Act (TCA). *R.J. Reynolds v. FDA* stopped use of GWLs in the U.S., concluding that GWLs would infringe tobacco company first amendment rights without achieving the government's objective to reduce smoking. The court's view was that there was insufficient data to show that GWLs reduced smoking behavior. The current study applied an experimental design with sequential cohorts of persons enrolled in residential addiction treatment assigned to receive either GWLs or control stickers placed on their cigarette packs over a period of 30 days. The primary outcome is the proportion of participants who enroll in a smoking cessation service following the labeling period, and the hypothesis is that use of cessation services will be higher in the GWL condition compared to control. To date, 400 participants have completed the labeling process and about 25% subsequently used the cessation service. Differences by condition will not be explored until study completion in August 2015. At that time, with an estimated 500 participants, we will assess differences by condition for the primary outcome and for secondary smoking behavior measures (cigarettes per day, quit attempts, use of cessation medications). Although findings are not available at the time of this writing, findings will be reported at the time of the TRDRP conference in October.

75-

Views from Job-Seeking Unemployed Tobacco Users in the Bay Area: A Photovoice Adaptation Project

Anne Michalek, BS, SH4A Fellow 2015, Cati Brown-Johnson, PhD, Judith J. Prochaska, PhD, MPH

Stanford Prevention Research Center, Department of Medicine, Stanford University, Stanford, CA

This project aimed to: 1) pilot participant-led photovoice data collection methods with chronically unemployed job-seeking tobacco users and 2) gather data on participant perspectives for a cessation study aimed at this population. Smokers were recruited from the San Francisco Employment Development Department. Participants consented to take 27 photographs related to their use of tobacco and job-seeking over one week using a study-provided disposable camera or their own smartphone. Prompts related to job-seeking and tobacco were provided. In a follow-up session with study staff, participants reviewed the photos, provided audio-recorded narratives, and were paid \$10. Nine male participants ages 34-63 were enrolled 5/3/15-6/17/15. Three participants were veterans, only 2 had stable housing, and 4 had a criminal history. To date, 6 participants returned cameras with 97 photos total; 60 photos were of or discussed tobacco including: littered cigarette butts and packs (n=21), ?no smoking? signs (n=17), and pictures of people smoking cigarettes (n=9). Eleven photos were of jobsites. Emergent narrative themes cover job-related motivations and challenges with respect to quitting tobacco, restrictions on smoking, smoking in their social network, and tobacco litter in the streets. Participants were enthusiastic and open about sharing their experiences through photos and personal narratives. The findings are being incorporated into a job-seekers' tailored quit smoking intervention to be tested in a new TRDRP Research Project Award.

76-**Preliminary Outcomes of an Effectiveness Trial with Psychiatric Smokers**

Mark Myers, Timothy Chen, Erick Idy

VA San Diego Healthcare System, University of California San Diego

The primary aim of this study was to evaluate treatment outcomes of a specialty cessation clinic for smokers with psychiatric illness compared with telephone counseling. Participants were military veterans with psychiatric disorders randomized to participate in one of the two clinics. Participants were followed for 6-months following their target quit date (TQD) and self-reported abstinence was biochemically verified. 31 participants were included in the present analyses. The sample included 97% men, on average 55.9 years old, 48% African American, 6% Hispanic/Latino, and 39% White. 32% were diagnosed with PTSD, 29% Schizophrenia, and 29% with a Mood Disorder. Examination of treatment attendance indicated that those assigned to the group condition attended more sessions (2.6 versus 5.2, $p = .064$). Intent to treat analyses (ITT; $n=31$) indicated no differences in point abstinence at 1 or 6 months following TQD. At 3 months after TQD participants in the group condition were more likely to be quit (43.8% vs 15.4%, $p=.01$). ITT analyses of quit attempts (24+ hours) indicated no differences, all p 's $> .18$. When examining change in cigarettes per day, participants in the telephone clinic tended to report greater reductions from baseline at all time-points (p 's range .085 to .13). Findings from this study indicate that few outcome differences emerged across conditions. However almost 1/3rd of participants reported abstinence at 6 month follow-up.

77-**Promoting Patient-Provider Discussion of Tobacco Use in Korean And Vietnamese Smoking Patients Using an Interactive Mobile Doctor (Imd): A Pilot Study**

Janice Tsoh, Thu Quach, Thomas B. Duong, Emily Sa Nan Park, Ching Wong, Hy Lam, Susan Huang, & Tung Nguyen
Asian Health Services; University of California San Francisco; Asian American Research Center on Health

Low proportions of Asian-American smokers report discussing tobacco use with their healthcare providers. Using a community-based participatory research approach, we created an interactive 'Mobile Doctor' intervention (iMD) that delivers tailored in-language video messages to address patients' tobacco use via a mobile tablet to Korean and Vietnamese male smokers right before their clinic visit. iMD also generates a bilingual tailored printout to empower patients and remind providers to discuss tobacco use. Participants were 40 Korean- and Vietnamese-speaking male patients receiving primary care at a federally-qualified health center. Their mean age was 57 (SD=9.1, range: 30 to 71), 47% had < high school graduation, mean cigarettes smoked/day was 9.3 (SD=4.5); 55% had no intention to quit smoking within 6 months. iMD took an average of 13.3 minutes (range: 10-25 minutes) to complete. All patients reported discussing their smoking with their providers during the visit after receiving iMD. Many (>85%) perceived iMD was helpful in enhancing their communication with their providers. Medical record documentation of providers' assisting participants in reducing or quitting tobacco use increased remarkably from 10.3% at one visit prior to iMD to 59.0% at the visit right after iMD.

78-

Reducing Smoking among Homeless Youth

Joan Tucker, William Shadel, Daniela Golinelli, Brett Ewing, and Leslie Mullins

RAND Corporation

Approximately 70% of unaccompanied homeless youth are smokers, yet there has been little effort to understand and reduce smoking in this population. We will present findings on smoking behaviors, cessation services currently available, and barriers to reducing smoking among homeless youth in Los Angeles County. A survey of 292 homeless youth smokers found that 66% quit for at least 24 hours in the past year, 43% were motivated to quit, and 59% were interested in formal cessation treatment. Interviews with service providers from 23 shelters and drop-in centers found that nearly all were interested in offering cessation services, but 70% thought it would be difficult to do so (often citing limited resources or smoking cessation being a lower priority). When asked about the feasibility of offering specific types of cessation programs, those that required fewer resources were perceived as more feasible, but there was concern that the lowest intensity option (Quitline referral) would be insufficient. Focus groups with homeless youth highlighted important issues to consider in program development, such as coping and affective benefits of smoking, wariness of pharmacotherapy, and challenges of engaging youth in treatment. In sum, many homeless youth are interested in quitting and most service providers are interested in helping them quit. However, strategies to reduce smoking will need to address the organization- and individual-level barriers identified in this study.

79-

Electronic Cigarette Prevention within Middle and High Schools

Bonnie Halpern-Felsher, Ira Sachnoff, Malena Ramos, Stephen Smuin, Emily Justice and Cherrie Boyer

Stanford University, Contra Costa County Office of Education, and University of California at San Francisco

Most school-based tobacco prevention programs have focused on conventional cigarette smoking. While some schools have been informally developing electronic cigarette (e-cig) prevention curricula for their specific schools, no formal prevention program focusing on electronic cigarettes has been developed, tested, or widely disseminated throughout California. Given current use of e-cigs, co-use with other tobacco products, and extensive marketing, we have been developing an e-cig prevention module for use with middle and high school students. The goals of this program are to: (a) increase adolescents' understanding of basic information about e-cigs and the harm they cause from both short-term and long-term use; (b) increase adolescents' awareness of strategies e-cig manufacturers use to increase appeal and use among adolescents through deceptive and creative marketing strategies; and (c) provide students with skills to refuse experimentation and use of e-cigs. This prevention curricular contains the latest information and activities countering common myths and misperceptions about e-cigarettes, as well as information on the anatomy of the various e-cig products, advertising and marketing schemes to entice new and/or young users, ingredients including nicotine and flavors, and the harms linked to e-cigs. Each section and activity contains hyperlinks to additional information, graphics, handouts, and PDFs that educators, parents and youth will find easy to access and utilize.

POSTER SESSION:

Tobacco-Related Health Disparities

(DAY-2: Wednesday, October 28)

Abstract #80-87

80-

Perceptions of tobacco denormalization and tobacco-related stigma among young Black women in California

Tamar M.J. Antin, Sharon Lipperman-Kreda, and Rachelle Annechino

Prevention Research Center

Smoking risk for Black women is among the highest in California, and these women experience among the greatest risk for tobacco-related diseases. Though the denormalization of tobacco in California has been associated with reductions in smoking at the population-level, questions remain about how tobacco denormalization strategies may affect specific segments of the population, like Black women, whose prevalence of smoking remains high. This poster will present results from a qualitative study that investigated perceptions of tobacco denormalization approaches and experiences with tobacco-related stigma among Black young people in the San Francisco Bay Area. Interview narratives suggest that tobacco-related stigma may intensify the 'social isolation and marginalization' that women already experience as a result of their stigmatized gender and ethnic identities. This may result in increasing inequity and continued smoking for some Black women. The implications of this study for tobacco denormalization strategies and prevention for Black women will be presented.

81-

Associations among Adolescent Social Networks, Loneliness, and Smoking

Stephanie R. Dyal, B.S. & Thomas W. Valente, Ph.D.

University of Southern California, Keck School of Medicine

This study explores loneliness and social environment concurrently as predictors of adolescent smoking. Cross-sectional data from 949 12th graders attending 5 high schools in Southern California were collected using surveys completed during classroom sessions. Social network data were collected by asking the students to name their seven best friends in 12th grade who attend their school. Social network indicators were calculated for each participant. These include number of friends named, proportion of friends named who reciprocated the friendship, and the density of one's personal friendship network (a measure of the proportion of an adolescent's friends who are friends with each other). The network variables were included in a mixed effects multiple regression model along with variables assessing loneliness, negative affect, and demographics such as age, gender, socioeconomic status, and ethnicity as predictors of a categorical smoking variable which ranges from non-susceptible to daily smoker. Results indicate that friendship network density is protective against smoking. This suggests that students in close-knit friendship groups may be less likely to smoke. Loneliness, negative affect, and other network measures were not associated with smoking. However, the model was additionally computed separately for each school and it was noted that there is heterogeneity in the results. Youth prevention programs may be developed with the awareness that adolescents who are friends with students who are not friends with each other may have increased need for prevention efforts.

82-

Tobacco Prevention Works: LGB residing in California may be less likely to smoke cigarettes

Kristen Emory, PhD; Lisa Vera; Sherry Emery
University of California, San Diego; University of Illinois at Chicago

Purpose: Lesbian, gay, and bisexual (LGB) populations smoke cigarettes at extremely high rates nationwide. There is a need for research comparing LGB tobacco use in states with strong anti-tobacco programs, such as California, with the rest of the US. **Methods:** This study reports results from LGB respondents (N=924) to a 2013 nationally representative cross-sectional online survey of US adults (N=17,087). Transgender (N=168) tobacco use was also assessed; yet, too few resided in California (N=23) to make comparisons. Unweighted results are presented. **Findings:** Over half of LGB participants reported past 30-day cigarette use (N=498, 53.9%). LGB residing in California (N=118) reported significantly lower rates of past 30-day tobacco use (N=56, 44%) compared to LGB living outside of California (N=806, n=323, 55.3%, $P<0.05$). Past 30-day use of other tobacco products (E-cigarettes, as well as regular, medium and small cigars) was suggestive of a protective effect for California, but lacked power to detect significance. **Conclusions:** Although California's anti-tobacco program appears successful in reducing LGB populations' tobacco use; tobacco use remains unacceptably high across the US, including California. **Relevance:** While LGB populations may observe some benefit from generalized state- anti-tobacco campaigns, the benefit has less impact than that experienced by the general population. LGB targeted statewide anti-tobacco campaigns may help reduce tobacco health disparities.

83-

Comparing smoking consumption trends of Hispanic/Latino nationality groups in California and the United States between the 1990s and 2000s

Felicitas JQ, Sakuma KK, Blanco L, Fagan P, Perez-Stable EJ, Bostean G, Trinidad DR

Claremont Graduate University, UC San Francisco, University of Hawaii, Chapman University

We examined smoking behaviors and associated sociodemographic factors among Mexicans, Puerto Ricans, Cubans, and Central/South Americans in California and the remaining United States (US) between the 1990s and 2000s. We utilized 1992-2011 data from the Current Population Survey-Tobacco Use Supplements. Descriptive statistics were calculated to determine the prevalence of various cigarette consumption levels among Hispanic/Latino (H/L) groups across decades by state residence (California vs. US). Weighted logistic regression was conducted to explore the relationship between heavy smoking, state residence, and race/ethnicity across decades, after controlling for age, education, gender, and language of interview. Compared to the US, greater decreases in current smoking between decades occurred among H/L groups in California. Between decades, there was a 51% decrease in Puerto Rican heavy smokers in California. In the US, there was a 28% increase in Cuban light and intermittent smokers. Across decades, those who self-identified into a H/L group were less likely to be heavy smokers compared to non-Hispanic Whites. Those in California were less likely to engage in heavy smoking compared to those in the rest of the US.

84-

Acculturation and the Tobacco Retail Environment: A Multi-level Study in Hispanic Americans

S. Mills¹ ; S. Bohan²; R. S. Fox¹; E. A. Klonoff³; G. R. Sadler²; G. A. Talavera³; S. F. Castañeda³; L. Gallo³, V. L. Malcarne³

¹SDSU/UCSD Joint Doctoral Program in Clinical Psychology; ²UC San Diego Moores Cancer Center; ³San Diego State University.

Tobacco use is a harmful, cancer-risk health behavior in need of intervention for the Hispanic-American population. Lung cancer is the leading cause of cancer death among Hispanic-American men and the second leading cause of cancer death among Hispanic-American women. Cigarette smoking is the leading risk factor for lung cancer, and is estimated to be linked to approximately 90% of all lung cancers in the United States. Tobacco use among Hispanic Americans may be related to numerous factors at both the individual and environmental level. In an effort to understand how these diverse factors relate to tobacco use among Hispanic Americans, this study examines the relationships among individual-level acculturation variables, the tobacco retail environment, and tobacco use and health-related quality of life (HRQOL) in this population. Multi-level modeling is used to explore correlates of tobacco use and HRQOL in two community samples of Hispanic Americans. Neighborhoods are defined using census tracts. Study results are forthcoming. In sum, this project identifies which Hispanic Americans are at risk for tobacco use and poor HRQOL, and importantly, under what tobacco retail environment conditions. Uncovering moderated relationships allows for tobacco-related interventions to be designed and policies to be written that will more specifically target and resolve the root sources of cancer-related behaviors that contribute to cancer incidence and mortality among Hispanic Americans.

85-

Sex differences in nicotine intake and carcinogen exposure among African American light smokers

Gideon St.Helen PhD¹, Neal L. Benowitz MD¹, Jasjit S. Ahluwalia², Lisa Sanderson Cox³

¹Div of Clinical Pharmacology, UCSF; ²Rutgers Univ School of Public Health; ³Univ of Kansas School of Medicine

Objective: To assess sex differences in nicotine and carcinogen exposure and nicotine metabolic pathways among black light smokers. **Methods:** Baseline behavioral measures, plasma cotinine, and urine biomarkers of nicotine (urine total nicotine equivalents, TNE) and tobacco-specific nitrosamine exposure [urine total 4-(methylnitrosamino)-1-(3)pyridyl-1-butanonol (NNAL)] were obtained from 426 black light smokers (67% females) enrolled in Kick It at Swope III, a clinical trial of bupropion for black light smokers. Sex differences were examined using ANOVA. **Results:** Cigarette consumption and dependence measures were not significantly different by sex. Compared to males, females had significantly higher levels of TNE.

86-**Smoking Behavior Trends across Racial/Ethnic Groups in California compared to the U.S., 1992-2010**

Sakuma KK, Felicitas JQ, Fagan P, Blanco L, Perez-Stable EJ, Pulvers K, Romero D, Trinidad DR

Claremont Graduate University, Oregon State U., UC San Francisco, U. of Hawaii, Cal State San Marcos

California's progress in reducing smoking health disparities relative to the US is unclear. This study examines trends in smoking behaviors among non-Hispanic white (NHW), black (B), Hispanic/Latino (H/L), and Asian/Pacific Islander (API) groups in CA compared to the rest of the US using Tobacco Use Supplement to the Current Population Survey. We analyzed data from 1992 to 2010, combined into 1990, 2000, and 2010 decades. Ever smokers were categorized into heavy daily (20+ cigs/day), moderate daily (6-19 cigs/day), light and intermittent smokers (LITS; 0-5 cigs/day or non-daily smokers), and former smokers. NHW in CA showed an increase of 17.7% for LITS compared to increases among NHW(12.7%), B(16.6%) and H/L(18.3%) in the rest of the US. Only NHW in the US showed an increase in moderate smoking (32.8%). There were larger decreases in heavy smoking among NHW(55.6%), B(76.6%), H/L(60.7%) and API(63.0%) in CA compared to NHW(37.7%), B(37.7%), H/L(60.7%) and API(39.6%) in the US. Increases in former smoking for CA NHW (11.4%), B (18.8%) and H/L (13.7%) were observed compared to only 8.3% for NHW in the US. Stratified by race/ethnicity, CA had significantly fewer heavy smokers than US after controlling for age, education, and gender for all groups except API($p < .05$). Similar results predicting former smoking were found. Despite much work still remaining in reducing disparities, CA's progress in reducing smoking among race/ethnic groups may be applicable to the rest of the US.

87-

Virtual Intervention for Lung Cancer Stigma

Janine K. Cataldo RN, PhD

University of California at San Francisco (UCSF)

mHealthTLC is an interactive, immersive 3-D iPad health game that allows lung cancer patients to experience ethnic and culturally sensitive first person virtual visits with clinicians. mHealth TLC provides coached patient-provider communication techniques, symptom assessment, and patient-specific health information. Game features include: three levels of complexity; information provision by the virtual coach through virtual interactions and information brochures; smoking cessation treatment as needed; symptom assessment and treatment plans; and opportunities to receive information about finances, prognosis, and supportive/palliative care options. A usability test was conducted to observe players and conduct semi-structured interviews to assess: game scenario believability, impact of technical issues, transparency of game goals, and potential of mHealth TLC to provide intended game outcomes. Twelve users confirmed mHealth TLC to be: believable, engaging, fun but not silly; clinic-appropriate; helpful in promotion of informed healthcare consumers and in building self-confidence in ability to communicate with providers. Conclusion: Although the dialogue and interactions addressed emotionally charged issues, users were able to engage, learn, and benefit from role-play in a culturally sensitive virtual world. Health games have the potential to improve patient-clinician communication, improve symptom assessment, decrease lung cancer stigma, and promote optimal self-management.

Additional Abstracts:

Abstract #88-94

88-

Tobacco Treatment for Employable Californians: Total IMPACT Project

Judith J. Prochaska, PhD, MPH¹, Anne Michalek, BS¹, Cati Brown-Johnson, PhD¹, Amy Rogers, OTR/L², Timothy McClain³

¹Stanford University; ²San Francisco VAMC, ³Marin Employment Connection;
⁴Buckelew Programs

Our research program aims to mitigate tobacco-related health and economic disparities among California's job-seeking unemployed. Our analysis of 2012 California data indicated 21% of jobseekers smoked vs 15% of the employed. In a 12-month observational study of jobseekers, we tested associations between smoking, chronicity of unemployment, and successful re-employment. Recruited from Bay Area unemployment centers were job-seeking daily smokers and nonsmokers. The sample N=252 (52% smokers) was 66% male, 92% single, 22% unhoused, 69% with income <\$20,000/year, mean age 45 (SD=11); 38% White, 36% Black, 26% other; 29% reported prior alcohol/drug treatment; 20% had a criminal history; and 28% lacked reliable transportation. Smokers averaged 13 cigarettes/day (SD=11). In an ordinal regression model, controlling for age, race/ethnicity, marital status, education, county, transportation, criminal history, drug/alcohol treatment, and homelessness, only current smoking (p=.01) and older age (p<.01) predicted longer duration unemployed, full model p<.01, R²=0.12, median days unemployed was 360 for smokers vs. 180 for nonsmokers. Among smokers, smoking within 30 min of waking vs. longer was associated with being out of work for 6+ months (71% vs. 47%), p=.034; desire to quit did not differ by chronicity of unemployment. At 12-months (83% retention), 59% of nonsmokers vs. 30% of smokers were re-employed (OR=3.4, p<.001). Current smoking was a significant determinant of unemployment chronicity and lower re-employment. Our TRDRP Research Project award will test effects in an RCT.

89-**The Effects of Varenicline, Low Dose Naltrexone, and Their Combination in Heavy-Drinking Smokers**

L.A. Ray, D.J.O. Roche, K.E. Courtney, D.G. Ghahremani, S Bujarski, K Miotto, A Brody, and E.D. London

University of California Los Angeles

Heavy-drinking smokers represent a hard-to-treat subgroup of smokers for whom tailored smoking cessation therapies are unavailable. The present study employed a double-blind, randomized, 2x2 medication design, testing the effects of varenicline alone (VAR; 1 mg twice daily), low dose naltrexone alone (NTX; 25 mg once daily), VAR + NTX combined, and placebo on cigarette and alcohol craving, subjective response to alcohol and cigarettes, and smoking topography in a sample (n=130) of heavy-drinking daily smokers. After a nine-day medication titration period, participants completed an experimental session in which they consumed an alcoholic beverage and then smoked their first cigarette of the day using a smoking topography device. Subsequently, a subset of the participants (n = 40) underwent a functional neuroimaging session to examine medication effects on brain responses to visual smoking-related (vs. neutral) cues. The combination of VAR+NTX was superior to placebo, and at times to monotherapy, in attenuating cigarette craving, cigarette and alcohol 'high,' smoking intensity, and consumption of both cigarettes and alcohol during the nine-day titration period. Furthermore, analysis of brain responses to cigarette vs. neutral cues indicated that VAR+NTX reduced activation of the anterior cingulate cortex more than placebo and NTX alone. These findings indicate that clinical trials of the combination of VAR+NTX for heavy-drinkers attempting to quit smoking are warranted and may ultimately improve clinical care for this sizeable and treatment-resistant subgroup.

90-

Second- and third-hand smoke constituents alter the fundamental biology and turnover of specific membrane proteins predisposing to cell lipid transport abnormalities and disease

John K. Bielicki, Peter J. Walian, and Bo Hang

Lawrence Berkeley National Laboratory, Donner Laboratory

Cells lining lung airways are readily exposed to chemicals from tobacco smoke (TS). The impact of these chemicals on the cell-surface plasma membrane is largely not known. This represents an important area for study, since the plasma membrane coordinates many biological processes necessary for life. We have found that brief exposure of tissue macrophages to TS disrupts membrane lipid trafficking, and greatly extends the residence time of specific proteins at the cell surface. Consequently, these proteins are more susceptible to chemical inactivation by TS. One protein exquisitely sensitive to TS is ABCA1, which plays a critical role in lipid homeostasis, immune function and apoptosis. Treatment (48 h) and ~50% reduction in ABCA1 lipid efflux activity. A similar inhibition was seen with HOCl and, to a lesser extent, nitrosamines from third-hand smoke, but not with 4-hydroxynonenal. The scavenger receptor B1 was largely unaffected by TS. These data indicate that TS alters the turnover of specific membrane proteins to increase their residence time at the cell surface. We speculate this may reflect an initial adaptive response to maintain critical homeostatic mechanisms under conditions of oxidative stress. Prolonged exposures, however, renders these systems vulnerable to oxidative damage, predisposing to chronic inflammation and disease, such as cancer and COPD. Identification of the proteins involved may serve as a basis for early disease diagnosis.

91-

Do vape shops cluster near college campuses?

Erin Crew, Nina C. Schleicher, Trent Johnson, Isra Ahmad, Dianne Barker*, Lindsey Winn, David Hall, Lisa Henriksen

Stanford Prevention Research Center; Public Health Institute*

ENDS use is prevalent among young adults, particularly college students. An estimated 7.8%-9.3% of US adults (ages 18-24) have tried ENDS, but ever use among college students ranges from 4.9% to 29.9%. This study assessed whether vape shops cluster near college campuses in CA. After comparing search results from Yelp.com with other online sources, we used a Python script to systematically retrieve vape shops from Yelp for all CA zip codes. We linked these geocoded addresses (n=1,333) with addresses for 2- and 4-year colleges (n=457) obtained from the California Postsecondary Education Commission. We computed roadway distance between each campus and the nearest vape shop, and used intercensal estimates to compare neighborhood characteristics for vape shops with those for a random sample of licensed tobacco retailers (n=579). Approximately 82% of 2-year and 89% of 4-year colleges were located within 3 miles of at least one vape shop. Compared to observed tobacco retailer neighborhoods, the average vape shop neighborhood contained slightly more young adults (11.7% vs. 10.4%), more Asian (14.4% vs 11.4%), but fewer Hispanic (35.1% vs 38.3%) and African American residents (3.3% vs. 5.7%). Additional analyses will examine the degree to which vape shops are spatially clustered near colleges. In the absence of statewide licensing mechanisms for vape shops, results from this study provide a unique sampling frame for monitoring. The long-term research goal is to examine how availability and marketing of ENDS vary with the strength of tobacco-free policies at nearby college campuses.

92-

Does proximity to schools predict greater availability or cheaper prices of flavored tobacco products?

Trent Johnson, Nina C. Schleicher, Erin Crew, Lindsey Winn, Lisa Henriksen
Stanford Prevention Research Center

The proximity of tobacco retailers to schools is an important focus of local tobacco control, particularly to restrict availability and promotion of flavored products that are popular with adolescents. This research compared three measures of proximity to schools and examined whether proximity was associated with greater availability of flavored tobacco (menthol cigarettes, little cigars/cigarillos (LCCs), chewing tobacco, and e-cigarettes) and lower prices for these products. We created boundary shape files for CA public schools, and linked these data to addresses for all licensed tobacco retailers (n=37,004), as well as to observations in a random sample of these stores (n=579). The number of retailers within 1k feet of a school was 2,661 for the street address, 2,566 for the centroid, and 6,984 for boundaries. Among a random sample of observed retailers (n=579), 27% were within 1k feet of a school and 75% were within walking distance (1/2 mile). Menthol cigarettes were sold in 97% of stores, flavored LCCs in 83%, flavored snus or chewing tobacco in 33%, and e-cigarettes in 67%. Proximity to schools was not associated with greater availability of flavored tobacco products. Five prices were recorded in each store: the menthol variety of Newport, Blu, NJOY, Grizzly wintergreen, and any LCC for less than \$1.00). Only Newport cost less at stores within walking distance of schools. School boundary data are essential to predict how many and which retailers would be affected by regulation, and proximity to schools may be associated with lower prices for menthol cigarettes.

93-

Building tobacco cessation capacity in homeless shelters: A pilot study

Maya Vijayaraghavan and John P. Pierce
University of California, San Diego

We examined the feasibility of a capacity building intervention to improve homeless shelters' capacity to facilitate smoking cessation among homeless adults. The capacity building intervention, implemented in 2 transitional homeless shelters, consisted of training for staff to provide brief cessation counseling. Staff and clients were surveyed at pre-intervention, post-intervention (6 weeks), and at 12 weeks follow-up. Staff completed a questionnaire on tobacco-related knowledge, self-efficacy in providing cessation counseling, and beliefs and practices related to treating tobacco dependence. Clients completed a questionnaire on tobacco-related knowledge and exposure to tobacco cessation resources. From pre-intervention to 6-weeks post-intervention, staff efficacy with mean pre- and post-intervention scores.

94-

Healthy Retail in San Francisco: The potential for Health Promotion to reduce unhealthy influences and increase healthy influences while strengthening community

Susana Hennessey-Lavery, Jessica Estrada, Meredith Minkler
Tenderloin Healthy Corner Store Coalition, HealthyRetailSF Program, SF
Department of Public Health, UC Berkeley

This poster session will describe a proposed community-based participatory research (CBPR) study to evaluate healthy retail voluntary initiatives and legislation in San Francisco, with a particular focus on the city's Tenderloin, the neighborhood with the highest tobacco outlet density. We discuss contributions of a coalition (the Tenderloin Healthy Corner Store Coalition) of city agencies, store redesign experts, individual residents and university partners to the development and implementation of San Francisco's healthy retail program (www.HealthyRetailSF.org) as a strategy for reducing tobacco influences and increasing healthier food options. HealthyRetailSF (HRSF) as a tobacco control strategy will be a central focus of the poster session, as preliminary findings show that 1) store assessment scores/ratings are increasing since healthy retail efforts began in the Tenderloin neighborhood and 2) produce sales are increasing in HRSF participating stores, while tobacco sales are decreasing. The HealthyRetailSF "3 Legged Stool Model" model will be described, as it assists store owners in shifting their business model to increase healthy options while decreasing unhealthy products including tobacco, alcohol, and sugary beverages in three areas: improvement of business operations, improvement of the physical environment of the store, and community engagement/marketing to drive demand to the stores. Point of Sale (POS) data has also been collected from the HRSF participating stores. Implications for other food deserts, which also have high tobacco access and advertising,

-:-