PI Name: Stephen Wilson Phone Number: 814-865-6219
College/ Dept: College of Liberal Arts / Department of Psychology

1. Title of Proposal: Blood nicotine absorption, subjective and neurocognitive effects of different types of electronic nicotine delivery devices (ENDDs) in current daily users.

2. Descriptive keywords: blood, nicotine, fMRI, cognition, withdrawal, reinforcement

3. Lay Abstract:

Smoking is the leading cause of premature death from diseases such as lung cancer and chronic respiratory disease. Seventy percent of smokers want to quit, but they find it difficult because they are addicted to the psychological effects of the spikes of nicotine they receive from inhaling tobacco smoke. In addition to nicotine, cigarette smoke contains thousands of chemicals, including over 60 carcinogens. Medicinal nicotine replacement products help smokers to quit, but compliance is poor and they are perceived as unsatisfying, partly because of their low or slow nicotine delivery. In 2007 electronic nicotine delivery devices (ENDDs) were launched in the US as "electronic cigarettes." Recently, these devices have become quite popular. ENDDs use rechargeable battery power to create a vapor of propylene glycol (the same substance in theatre mist and some medicines). Preliminary studies confirm that they do not deliver smoke, and they also deliver very little nicotine. However, more recent studies suggest that, while many ENDDS deliver only minimal nicotine in their propylene glycol vapor, some (with higher battery power) are capable of delivering cigarette-like spikes of nicotine. The present study aims to compare the blood nicotine concentrations obtained by current users of these two types of ENDDs, as well as to compare the subjective and neural effects of these two ENDDs variants using functional magnetic resonance imagery (fMRI). Ten regular users of high battery power ENDDs and ten regular users of low battery power ENDDs will abstain overnight from all nicotine containing substances and then will attend the laboratory to have their subjective experiences, cognitive performance, blood nicotine and brain activity measured before and after puffing on their usual brand of ENDDs. This study will attempt to clarify which types of ENDDs deliver nicotine like a cigarette and consequently have the greatest potential to help smokers quit.

4. Specific Aims and Objectives:

A large number of different types of ENDDs are available on the market, and these vary along a number of parameters (e.g. size, battery power/voltage etc). Our preliminary study, based on interviews with experienced users (Foulds et al, 2011), and other studies (Etter, 2011; Vansickel, 2010; Vansickel 2011), suggest that one important variable (other than the concentration of nicotine in the liquid) distinguishing ENDDs that deliver minimal nicotine and those capable of delivering cigarette-like levels of nicotine is the power delivered by the battery (the wattage being determined by the battery voltage and the atomizer resistance). The most widely sold types of END are small cigarette-sized devices that typically have a single 3.6v battery combined with a medium to high resistance atomizer, resulting in insufficient power to deliver nicotine vapor that the user can absorb. These will be referred to as standard battery power ENDDs (StENDDs). However, some ENDDs have (generally larger) batteries with a higher voltage (e.g. 5v) and a lower resistance atomizer. These models appear to be able to deliver nicotine in their vapor like a cigarette, and will be referred to as high battery power ENDDs (HiENDDs).

The primary objectives of this pilot study are (a) to compare the nicotine delivery efficiency of StENDDs and HiENDDs (b) to measure the nicotine absorption and resulting psychological, physiological and brain effects associated with the use of StENDDs versus HiENDDs. Our main hypotheses are as follows:

1. ENDD users of models with higher battery power (HiENDD) will obtain higher blood nicotine levels than ENDD users of the "cigarette-sized" models with a standard 3.6v battery (StENDD).
2. HiENDD users will experience stronger subjective effects following acute use than StENDD users.
3. HiENDD users will exhibit larger pre-post improvements in cognitive performance after acute use than StENDD users.
4. HiENDD users will exhibit cue-elicited changes in neural activity after acute use similar to those previously found following acute cigarette use, whereas StENDD users will not.

This will be the first study to directly compare blood nicotine delivery from two different types of ENDDs in existing ENDD users, and the first to simultaneously assess the effects on cognitive performance and brain activation using fMRI. It will generate crucial preliminary data for a proposal to fund larger-scale studies of the use of ENDDs for smoking cessation.

5. Brief background, rationale, and description of methods:

Smoked tobacco products are the only legal products that kill half their consumers and some of those around them when used as intended. More than 17 billion cigarettes are smoked world-wide every day, and this number continues to increase (Shafey, 2009). People smoke for the psychoactive and addictive effects of nicotine, but are killed by other toxins in the smoke (Royal College of Physicians, 2007). The psychoactive effects of cigarettes are partly determined by the rapidity with which they deliver nicotine to the blood stream and to the brain. Our prior studies have shown that a single cigarette can result in an increase in venous blood nicotine levels of over 15 ng/ml within 4 minutes (Foulds et al, 1996), and cigarettes (or injected nicotine) reliably evoke changes in brain function, as measured by EEG or fMRI (e.g., Stein et al., 1998; Foulds et al., 1994. Medicinal nicotine replacement delivers nicotine much more slowly (e.g., 4 mg nicotine gum takes around 30 minutes to achieve venous nicotine concentration around 8 ng/ml) and it is believed that this limits its acceptance by addicted smokers. For many years the idea of a nicotine replacement device that delivered nicotine like a cigarette, but without thousands of toxic chemicals in the smoke, has been considered the "holy grail" of smoking cessation pharmacotherapy, but no satisfactory device was developed (partly because of perceived technical difficulties in delivering nicotine in an aerosol with small enough particle sizes for pulmonary absorption, without having excessive sensory harshness, and at a price comparable to cigarettes or other nicotine replacement products).

Early studies of ENDDs found that they delivered meager amounts of nicotine (Bullen et al, 2010; Vansickel, 2010). However, Etter & Bullen (2011) observed that they are being used as aids to smoking cessation much as people use nicotine replacement medications. Preliminary results from a study in which ENDDs users were allowed to use their own (customized) electronic cigarettes indicated that they achieved cigarette-like increases in blood nicotine concentration (>10 ng/ml in 5 min; Vansickel, 2011). These studies, along with our own survey of experienced ENDDs users, have led us to believe that some ENDDs can deliver nicotine with cigarette-like rapidity, and that one key characteristic of these devices is their battery power.

Method

Participants: Ten regular users (i.e., daily use for at least two months) of HiENDDs and ten regular users of StENDDs will be recruited to participate. In order to be eligible, participants must report that they have not have used any tobacco products in the previous two months (or more), and that they use "high" or "medium" nicotine e-liquid/cartridges. A number of

volunteers for our previous survey study volunteered to participate in future laboratory studies and provided their contact information. It is anticipated that some of these ENDD users will participate in this study, and that others will be recruited via online ENDD discussion forums.

Procedures: Participants will be asked to abstain from all nicotine containing and caffeinated products from midnight the night before and to attend the lab at 10am. They will complete baseline ratings of nicotine withdrawal symptoms and urges to puff on their ENDDs (i.e., to "vape"), and a 5 minute computer test of cognitive performance (Rapid Visial Information Processing: RVIP). This test has proven sensitive to the effects of nicotine withdrawal and nicotine administration in our prior work (e.g. Foulds et al, 1996). They will then enter the fMRI scanner to complete a smoking cue exposure procedure adapted from our prior research (Wilson, Sayette, Delgado, & Fiez, 2005; Wilson, Sayette, & Fiez, in press). The cue exposure paradigm consists of the presentation of control and smoking-related auditory and visual stimuli that reliably elicit different subjective and neural responses in smokers (Wilson, Sayette, Delgado, & Fiez, 2005; Wilson, Sayette, & Fiez, in press; Williams et al, 2008), making it well-suited for examining neurocognitive functioning in ENDDs users. Ratings of urges to vape will be made before and after exposure to cues. Subjects then will be removed from the scanner and have an indwelling catheter inserted into their vein and a baseline blood sample drawn. Next, they will be instructed to puff on their own ENDS ad-lib for the next 10 minutes with the proviso that one puff is taken every 30 seconds. (Participants will be prompted to take a puff of their own ENDD every 30 seconds, but will be free to take additional puffs in between those time points). A blood sample will be drawn at 1,2,4,6,8,10,12 and 15 minutes after the first puff. Before the first puff, and at minutes 3, 7, 11 and 13, participants will rate how they are feeling on a 0-100 visual analog scale on measures of "high", liking", "rush" and "craving", and then once again complete a rating scale of nicotine withdrawal symptoms and the RVIP task. They will then enter the fMRI scanner for a second time to complete the aforementioned cue exposure procedure. As above, ratings of urges to vape will be made before and after exposure to cues.

A unique feature of the proposed research is that we propose to scan half of the sample using the 3T Siemens scanner installed in the SLEIC at University Park and half using the identical model 3T Siemens scanner installed at the CNMRR at Penn State Hershey College of Medicine. This cross-campus collaborative effort will allow us to collect key data regarding the feasibility of scanning across sites, which will be essential for pursuing such an approach in a larger grant proposal. If successful, this cross-campus effort will open up valuable opportunities for recruiting a sizeable and diverse sample of ENDD users from the communities surrounding State College and Hershey. More generally, this effort will facilitate future multi-site brain imaging collaborations between UP and Hershey campuses. Importantly, quality assurance testing is conducted routinely on both scanners with exactly this idea in mind. Specifically, to ensure that the SLEIC and CNMRR scanners are operating comparably and well within manufacturer specifications, quality insurance assessments scans are performed weekly or after any equipment service (these assessments indicate that the two scanners are effectively equivalent).

Statistical analyses and sample size justification: Based on effect sizes from the Eissenberg, 2010 and Vansickel 2011 studies, power to detect a difference in peak blood nicotine concentrations between HiENDD users and StENDD users using a two-sided, two-sample t-test will be 82% with 10 participants per group. Similarly, simulation-based power analyses for

fMRI research indicate that this sample size provides approximately 80% power to detect typical activations at conventional threshold levels (Desmond & Glover, 2002).

Behavioral data analysis. Two-sided, two-sample t-test will be used to test for a statistically significant difference in peak blood nicotine concentrations between groups. Descriptive statistics will be used to present the nicotine concentration profiles for the two user groups. Ratings of craving during cue exposure and subjective responses during ENDDs smoking ("high", "liking", "rush", and "craving") will be analyzed using mixed-model ANOVAs.

fMRI data analysis. Analysis of FMRI data will be conducted using BrainVoyager QX software (Brain Innovation, The Netherlands). Prior to statistical analysis, the following preprocessing steps will be applied to the data: a) motion correction, b) slice scan time correction, b) spatial smoothing using a three-dimensional Gaussian filter to account for small variations in signal due to movement and vascular effects, and c) voxel-wise linear detrending and high-pass filtering of frequencies to adjust for scanner drift between runs. Structural and functional data from each participant then will be transformed to standard stereotaxic space to facilitate group averaging of functional data. Statistical analysis of fMRI data will be conducted using a standard two-level random-effects general linear model approach.

6. Translational or Community Engagement Research Potential:

The research evidence showing that medicinal nicotine replacement helps smokers to quit is solid, but these products are less widely used than we would like, and compliance and quit rates in the community are poorer than in randomized clinical trials. This study aims to better characterize the psychopharmacological effects of a new nicotine delivery device that is already widely available within our community, but with very little data on its effects. Better understanding of the acute psychopharmacological effects of these products will bring us closer to being able to conduct controlled clinical smoking cessation trials of these products, and also to better able to properly educate the community about their effects.

7. Relevance to Cancer Control:

ENDDs have great potential as effective smoking cessation aids and so could play a major role in preventing serious diseases such as lung cancer and COPD.

8. Relevance to social/behavioral science or CTSA Community Engagement Core:

The study will recruit from the local communities in central PA as well as from the online community, and the results will be used to inform these communities about the effects of ENDDs. The study will contribute to our understanding of nicotine addiction and enable us to better inform nicotine users and help them to quit smoking.

9. Anticipated Outcomes:

We anticipate that this study will be completed by May, 2012 and we plan to submit an application to NIH for the next study (a larger study examining the use of ENDDs for short term smoking cessation) in June 2012.

10. External Funding Sources:

a) Investigators involved: All the investigators on this proposal, plus Dr. Thomas Eissenberg (Virginia Commonwealth University) as a consultant.
b) Title of proposal: Short term effects of an electronic nicotine delivery device on smoking cessation and nicotine withdrawal symptoms.
c) Time frame of proposal: To be submitted June, 2012

d) External funding sources to be targeted: NCI, which currently has an RFA on "Testing Tobacco Products to reduce Harm RO1" (PA-07-174) and is likely to announce another in 2012.

11. Timeline:

- Dec 2011: Finalize planned protocol
- Jan 2012: Apply for IRB approval.
- March, 2012: Initiate data collection
- May, 2012: Complete data collection, conduct data analysis, and write reports/grant.
- June, 2012: Submit grant application to NCI/NIH for follow-up study.

12. Personnel: Stephen Wilson, Jonathan Foulds, Gang Chen, and Arthur Berg

Stephen Wilson, assistant professor of psychology at PSU-UP, will help oversee all study procedures. In particular, he will be responsible for the design and implementation of fMRI procedures for the proposed research, as well as the analysis and interpretation of fMRI data collected during the study. He has authored conceptual reviews of human neuroimaging addiction research and published a series of empirical studies using functional magnetic resonance imaging (fMRI) to examine cue-reactivity and craving in hundreds of cigarette smokers, with several additional papers on these topics are currently under review.

Jonathan Foulds is a professor of public health sciences & psychiatry based at the Penn State College of Medicine in Hershey, PA. Dr. Foulds will play a central role in overseeing the design and implementation of the study. Among other things, he will have a primary role in the recruitment of ENDDs users and the design and implementation of cognitive and subjective assessments. He has published over 80 papers on tobacco and smoking cessation in peer reviewed journals, including randomized clinical trials of nicotine replacement products for smoking cessation and laboratory studies of the psychopharmacology of nicotine delivery products. He was recently an invited reviewer of the forthcoming Institute of Medicine report, "Scientific Standards for Studies on modified Risk Tobacco Products."

Gang Chen is an assistant professor of public health sciences, Penn State College of Medicine. Dr. Chen will be responsible for performing nicotine assays on blood samples collected from participants. In prior work funded by NIH, he has developed effective measures of all major nicotine metabolites in biological samples (e.g., urine).

Arthur Berg, assistant professor of biostatistics and bioinformatics, is a collaborating investigator on the proposed study. He will play a central role in perform statistical calculations on data collected during the study. He has extensive experience in utilizing numerous software tools to perform diverse types of statistical analyses. Along with Dr. Foulds, he has participated in several projects involving tobacco cessation, including a recently published manuscript that presents survey results from a large group of e-cigarette users.

13. Budget and Justification:

Total cost = $40,260

- MRI scanning: $18,260 total (2 hr/sub * 10 subs each at Hershey [$445/hr] and UP [$468/hr])
- Nicotine assay of blood samples: $13500 total ($75/sample * 180 samples)
- Subject payment: $3000 total ($150/sub * 20 subs)
- Research nurse with physician supervision: $2400 total ($12/hr * 2hrs * $100 p/hr)
- Consumables (blood sampling kits/tubes, questionnaires, computer, software): $5500 total

Name and phone number of your department's budget coordinator: Dawn Corman, 814-865-1815

14. Investigator Information:

Lead Investigator:
Stephen J. Wilson, PhD
Assistant Professor
Department of Psychology
College of Liberal Arts, University Park
814 865 6219
sjw42@psu.edu
Tenure Track - Yes; Psychology

Collaborating Investigator:
Jonathan Foulds, PhD
Professor of Public Health Sciences & Psychiatry
Public Health Sciences/PSU Cancer Institute
Penn State Hershey College of Medicine
717 531 3504
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Tenure Track – Yes; Public Health Sciences.

Collaborating Investigator:
Gang Chen, PhD
Assistant Professor of Public Health Sciences
Public Health Sciences
Penn State Hershey College of Medicine
717 531 6581
gxc30@psu.edu
Tenure Track – No.

Collaborating Investigator:
Arthur Berg
Assistant Professor
Department of Public Health Sciences & Statistics/PSU Cancer Institute
Penn State Hershey College of Medicine
717 531 3039
berg@psu.edu
Tenure Track – Yes; Public Health Sciences

15. Letters of Support from All Collaborators
Attached

16. Please attach 4- page NIH biosketches for PI and key personnel.
Attached

References:

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Vansickel A. R., Cobb C. O.,Weaver M. F., Eissenberg T. E. A clinical laboratory model for evaluating the acute effects of electronic 'cigarettes': nicotine delivery profile and cardiovascular and subjective effects. *Cancer Epidemiol Biomarkers Prev* 2010; **19**: 1945–53.

Vansickel A. R., Blank M., Cobb C., Kilgalen B., Austin J., Weaver M. *et al*. Clinical laboratory model for evaluating the effects of electronic cigarettes'. February 2011; 17th AnnualMeeting of the Society for Research on Nicotine and Tobacco. Toronto, Canada, 2011.

Williams JM, Gandhi KK, Karavidas MK, Steinberg ML, Lu SE, Foulds J. Open-Label Study of Craving in Smokers With Schizophrenia Using Nicotine Nasal Spray Compared to Nicotine Patch. *J Dual Diagn*. 2008 Oct 1;4(4):355-376.

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Wilson, S. J., Sayette, M. A., & Fiez, J. A. (in press). Quitting-unmotivated and quitting-motivated cigarette smokers exhibit different patterns of cue-elicited brain activation when anticipating an opportunity to smoke. *Journal of Abnormal Psychology*.

November 2, 2011

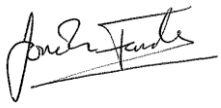
Stephen J. Wilson, Ph.D.
Assistant Professor
Department of Psychology
The Pennsylvania State University
438 Moore Building
University Park, PA 16802

Dear Stephen,

I am writing to offer my full support for our collaborative Cancer Control Seed Grant Application titled "**Blood nicotine absorption, subjective and cognitive effects of different types of electronic nicotine delivery devices (ENDDs) in current daily users**." I believe that this proposal will be the first to directly compare the nicotine delivery of different types of electronic nicotine delivery devices, and the first to measure changes in brain activity using fMRI in response to use of these products.

These products are already becoming popular, and are currently on sale in gas stations throughout Pennsylvania as well as on the internet. So there is an urgent need to better understand their effects so we can better inform our communities about their potential risks and benefits.
I believe that this line of work has strong potential for external funding, particularly as the Food and Drug Administration will likely attempt to exert regulatory authority over these products in the new year and will require a scientific basis for doing so. I am confident that this study will further the mission of the Penn State Hershey Cancer Institute of improving the quality of life for patients.

I am pleased to work with you and our other collaborators on this important project.
Sincerely,



Jonathan Foulds, Ph.D.
Professor of Public Health Sciences & Psychiatry
Penn State Hershey College of Medicine
jfoulds@psu.edu

November 2, 2011

Stephen J. Wilson, Ph.D.
Assistant Professor
Department of Psychology
The Pennsylvania State University
438 Moore Building
University Park, PA 16802

Dear Stephen,

Re: **Blood nicotine absorption, subjective and cognitive effects of different types of electronic nicotine delivery devices (ENDDs) in current daily users .**

Thank for inviting me to be co-investigator in this grant application. I study nicotine metabolism *in vitro* and *in vivo*. As indicated in my publications, I have expertise in utilizing UPLC-MS/MS to quantify nicotine and its metabolites in biological samples from smokers. One key component of the current proposal is to determined nicotine levels in blood from subjects using electronic nicotine delivery devices. The current proposal is aimed to develop new effective approach for smoking cessation, and may leading to ground breaking development in reducing of smoking. I am fully support this proposal and will dedicate ample effort.

Yours sincerely,

Gang Chen, PhD
Assistant Professor
Cancer Control Program, Penn State Cancer Institute
Department of Public Health Sciences
Penn State College of Medicine
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500 University Drive,
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Email: gxc30@psu.edu

November 3, 2011

Stephen J. Wilson, Ph.D.
Assistant Professor
Department of Psychology
The Pennsylvania State University
438 Moore Building
University Park, PA 16802
RE: Letter of collaboration for E-Cig Nicotine Delivery Study

Dear Stephen,
It is my sincere pleasure to confirm that I support your proposal to study nicotine delivery and effects of electronic nicotine delivery devices and look forward to working on the statistical aspects of this study should it be funded by the Cancer Control Seed Funding RFA.

Having been involved in the power calculations, I think this pilot study is well designed and promises to help us understand the effects of these new products and positions us to successfully apply for external funding in the near future.

I look forward to working with the team on this exciting study.

Sincerely,
Arthur Berg, Ph.D.

November 3, 2011

Stephen J. Wilson, Ph.D.
Assistant Professor
Department of Psychology
The Pennsylvania State University
University Park, PA 16802

Dear Steve:

It's my pleasure to write this letter supporting your application to Hershey Cancer Institute entitled "Blood nicotine absorption, subjective and cognitive effects of different types of electronic nicotine delivery devices (ENDDs) in current daily users."

As you know, Penn State's University Park campus has embarked on a significant expansion in hu- man neuroscience, including the acquisition of a Siemens Trio 3T MRI scanner dedicated to research use. The scanner is part of the newly formed Social, Life, & Engineering Sciences Imaging Center (SLEIC). In addition to visual and auditory display and manual response (button box, two-button grip, and joystick) equipment, the 3T portion of the SLEIC also has a scanner simulator located in a room dedicated to paradigm testing and development, as well as dedicated participant waiting and debrief- ing rooms. The SLEIC maintains a Unix-based file server with more than 4.8 TB of disk capacity dedicated to temporary image storage. The SLEIC works with Penn State's High Performance Com- puting Center (HPC). The HPC has both interactive and batch nodes with more than 66 TB of stor- age capacity, and supports a wide range of imaging analysis software packages, including MATLAB, SPM, FSL, AFNI, and FSL. The SLEIC also has three full-time staff dedicated to supporting 3T imaging research: an MR technologist, an MR physicist, and a managing director. As a member of the Penn State research community, you have full access to the Center's resources and expertise as you design and implement your research project.

In this case of your particular project, I am happy to say that SLEIC is able to support your request for 20 scan hours (10 participants, 2 scan hours/participant) over the project period. Should you have other needs, do not hesitate to contact me or Anna Engels.

We look forward to working with you on what promises to be an exciting effort.

Sincerely yours,

Rick O. Gilmore
Associate Professor of Psychology
Director of Human Imaging, Social, Life, & Engineering Sciences Imaging Center (SLEIC)

November 4, 2011

Stephen J. Wilson, Ph.D.
Assistant Professor
Department of Psychology
The Pennsylvania State University
University Park, PA 16802

Dear Steve:

It is a pleasure to write this letter supporting your application for seed funding from Penn State Hershey Cancer Institute to support your project, "Blood nicotine absorption, subjective and cognitive effects of different types of electronic nicotine delivery devices (ENDDs) in current daily users."

As you know, the MRI Core facility of the Center for NMR Research at Penn State College of Medicine is equipped with has three MRI systems dedicated for research, including a 3.0T Siemens Tim Trio that is identical to the system installed at the University Park Campus. These identical systems (which are subject to regular quality assurance testing to ensure their comparability) allow for the kind of innovative cross-campus collaboration that you and your colleagues have proposed. As a member of the Penn State research community, you have full access to the Center's resources and expertise as you design and implement your research project. We look forward to supporting your intriguing study.

Sincerely,

Qing Yang, PhD
Professor of Radiology and Neurosurgery
Center for NMR Research
Penn State Hershey College of Medicine

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Stephen J. Wilson, Ph.D.	Assistant Professor
eRA COMMONS USER NAME SJWILSON	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Univ. of Pittsburgh-Johnstown, Johnstown, PA	B.S.	1999	Psychology
Univ. of Pittsburgh, Pittsburgh, PA	M.S.	2004	Clinical Psychology
Univ. of Pittsburgh, Pittsburgh, PA	Ph.D.	2008	Clinical Psychology

A. Personal Statement

My primary area of research interest is addictive behavior, with a specific focus on cigarette smoking. The overarching goal of my research program is to advance our understanding of the self-regulatory failures characteristic of drug addiction. I utilize an interdisciplinary approach that integrates theory and methods from traditional behavioral addiction research with those derived from the affective, cognitive and social neurosciences. I have used this mulitmethod approach to investigate cue-reactivity in regular cigarette sokers. I have authored a conceptual review of human neuroimaging addiction research focusing on the context-dependent nature of responses to drug cues. I also have published results from a series of empirical studies using functional magnetic resonance imaging (fMRI) to examine the effects of cigarette cue exposure on affect, motivation, and cognition in active and quitting cigarette smokers. Several additional papers on these topics are currently under review. I am currently the principal investigator on an NIH funded study using fMRI to examine the effects of cigarette availability on reward-related processing in active (i.e., non-quitting) cigarette smokers (R03 DA029675-01). Given my research background and expertise, as well as the support provided by the broader investigative team and research environment, I am well-suited to oversee the proposed research.

B. Positions and Honors

Positions

1998-1999	Research Assistant, Dept. of Psychology, U. Pittsburgh-Johnstown, Johnstown, PA
2000-2001	Research Assistant, Dept. of Psychology, U. of Pittsburgh, Pittsburgh, PA
2001-2008	Graduate Student Researcher, Dept. of Psychology, U. of Pittsburgh, Pittsburgh, PA
2007-2008	Clinical Psychology Intern, VA Pittsburgh Healthcare System, Pittsburgh, PA
2008-2009	Research Associate, Dept. of Psychology, Penn State U., University Park, PA
2009-	Assistant Professor, Dept. of Psychology, Penn State U.

Honors

1995	Senior Thesis Excellence Award, U. of Pittsburgh-Johnstown
1995-1996	Rhea Louise Smith Scholarship, U. of Pittsburgh-Johnstown
2000	Natural Sciences Division Travel Grant, U. of Pittsburgh-Johnstown
2000	College Scholar Award in Psychology, U. of Pittsburgh-Johnstown
2000	Outstanding Student Award in Psychology, U. of Pittsburgh-Johnstown
2001	Honorable Mention, American Psychological Association Minority Fellowship Program
2001	Ford Foundation Predoctoral Fellowship for Minorities
2002	K. Leroy Irvis Fellowship, U. of Pittsburgh
2002-2003	African American Summer Graduate Research Award, U. of Pittsburgh
2004	National Institute on Drug Abuse Frontiers in Addiction Research Travel Award
2004-2007	Bassell Student Publication Award, U. of Pittsburgh
2007	Bassell Award for Excellence in the Clinical Psychology Program, U. of Pittsburgh

2009-2011 National Institutes of Health Clinical Research Loan Repayment Program
2010 SRNT Tobacco-Related Health Disparities Travel Award

C. Selected peer-reviewed publications (in chronological order)

Stern, S.E., Mullennix, J.W., Dyson, C., & Wilson, S.J. (1999). The persuasiveness of synthetic speech versus human speech. *Human Factors*, *41*, 588-595.

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Wilson, S.J., Sayette, M.A., Fiez, J.A., & Brough, E. (2007). Carry-over effects of smoking cue exposure on working memory performance. *Nicotine & Tobacco Research*, *9*, 613-619. PMID: 17454718. PMID: 17454718.

Wilson, S.J., Sayette, M.A., Fiez, J.A., & Delgado, M.R. (2008). Effects of smoking opportunity on responses to monetary gain and loss in the caudate nucleus. *Journal of Abnormal Psychology, 117*, 428-434. PMID: 18489219. PMID: 18489219.

Wilson, S.J., Sayette, M.A., & Fiez, J.A. (in press). Quitting-unmotivated and quitting-motivated cigarette smokers exhibit different patterns of cue-elicited brain activation when anticipating an opportunity to smoke. *Journal of Abnormal Psychology*. PMID: 21859165.

D. Research Support

Pending Research Support

R21 DA034160-01 Wilson (PI) 07/01/2012-06/30/2014
Neural and naturalistic effects of cigarette availability on reward processing
The study will use a novel integration of brain imaging (i.e., functional magnetic resonance imaging) and ecological momentary assessment methods to address the following specific aims: 1) To examine the effects of a laboratory-based cigarette availability manipulation on neural responses to non-drug rewards immediately prior to a quit attempt; 2) To examine the effects of naturally varying cigarette availability on reward-contingent cognitive performance under real-world conditions over the course of a cessation attempt; and 3) To examine the relationship between the effects of cigarette availability on reward-related behavior in the laboratory and under naturalistic conditions.
Role: PI

Ongoing Research Support

R03 DA029675-01 Wilson (PI) 09/01/2010-08/31/2012
Effects of smoking expectancy on neural response to reward in human smokers
The goal of this grant is to examine the nature and implications of individual differences in the effects of drug availability on neural responses to non-drug rewards in adult cigarette smokers. The specific aims of the proposed research are: 1) To examine the effects of a novel within-subjects cigarette availability manipulation on neural responses to non-drug (i.e., monetary) rewards in human smokers, and 2) To

examine how individual differences in the effects of cigarette availability on neural responses to non-drug rewards relate to the ability to resist smoking in order to obtain an incentive.
Role: PI

Social Science Research Institute, Pennsylvania State Univ. 01/01/2011-05/31/2012
Validation of saliva sample compliance in self-reported smokers and non-smokers
The goal of this pilot work evaluate tobacco abstinence compliance in a small daily diary study
.Role: Co-I

Completed Research Support

Social Science Research Institute, Pennsylvania State Univ. 06/01/2009-05/31/2010
Somatosensory Stimulation for the Alleviation of Craving to Smoke: A Pilot Study
The goal of this work was to investigate a novel procedure for alleviating craving to smoke in tobacco dependent individuals. Specifically, the study examined the utility of somatosensory stimulation as an intervention for preventing/reducing craving in cigarette smokers.
Role: PI

Penn State Institute of the Neurosciences, Pennsylvania State Univ. 06/01/2010-06/01/2011
Alcohol links to brain and behavior: A short-term longitudinal study in Penn State freshman
The goal of this project was to examine how cognitive processing, brain function, and brain structure change with extensive alcohol use during late adolescence.
Role: Co-PI

Penn State Institute of the Neurosciences, Pennsylvania State Univ. 06/01/2010-06/01/2011
The role of olfactory cues in addictive behavior
The goal of this project was to examine the role that olfactory smoking-related and food-related cues play in cigarette addiction and binge eating pathology, respectively, using a novel MRI-compatible olfactory stimulus delivery device.
Role: Co-PI

Social Science Research Institute, Pennsylvania State Univ. 09/01/2010-04/01/2011
Understanding divergent progressions of risk among children with early-starting externalizing problems
The goal of this project was to examine the role of executive dyscontrol in two aspects of divergent progressions of risk: 1) the developmental course of inattention and related aspects of cognitive functioning, and 2) the emergence of substance use, including smoking and alcohol/drug use, as well as associated risky behaviors.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Foulds, Jonathan	Professor, Public Health Sciences & Psychiatry
eRA COMMONS USER NAME (credential, e.g., agency login) Foulds	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Aberdeen	M.A.	06/87	Psychology
University of Glasgow	M.App.Sci.	08/89	Clinical Psychology
University of London	Ph.D.	06/97	Psychology

A. Personal Statement

This grant aims to compare the nicotine delivery and acute subjective and neural effects of two types of electronic nicotine delivery devices. I trained as a clinical psychologist in the United Kingdom and received my initial training in nicotine psychopharmacology with the leading research group in the world in that field in the late 1980's, led by professor Michael Russell. I have now focused my career on clinical, policy and research aspects of tobacco addiction for the past 20 years. While at UMDNJ I directed a multidisciplinary team that provided smoking cessation services and training for the state of New Jersey. During that time the team published over 90 papers in peer-reviewed journals. Since my recent arrival at Penn State College of Medicine my role is to develop behavioral research focusing on nicotine addiction and smoking cessation. This will involve expanding on my previous clinical research on smoking cessation, and laboratory research on nicotine psychopharmacology (involving over 80 publications in peer-reviewed journals). I have previously been a PI or investigator in four randomized trials of smoking cessation interventions, including one of the largest trials ever carried out in pregnant women. I was director of research for the smoking cessation charity, QUIT (UK) which at that time ran the largest telephone tobacco quitline in the world. I was an advisor to the Livestrong Foundation on the development of their smoking cessation application for the Iphone: "Myquit Coach", and have developed a telephone counseling protocol for a major health insurance company.

B. Positions and Honors

Positions and Employment

1989-1994	Research Clinical Psychologist, Institute of Psychiatry, London UK
1994-1997	Lecturer in Addictive Behaviour, St George's Hospital Medical School, London, UK
1997-2000	Senior Lecturer in Clinical Psychology, University of Surrey, Guildford, UK
2000	Director of Research, Quit (UK Charity, running UK Quitline)
2003-2010	Clinical Associate Professor, Department of Psychiatry, UMDNJ-RWJ Medical School
2000-2007	Associate Professor, University of Medicine and Dentistry of New Jersey, and Director of the Tobacco Dependence Program, UMDNJ- School Of Public Health
2007-2010	Professor, Department of Health Ed./Behavioral Science, UMDNJ-School of Public Health
2010-present	Professor, Department of Public Health Sciences, Penn State College of Medicine

Other Experience and Professional Memberships

1995-1997	Management Group Member, Population-Based Anti-Smoking Program, Hungary
1999-2000	Technical Leader/Consultant, World Health Organization European Partnership Project on the Regulation of Tobacco Dependence Treatment Products.
2001-2010	New Jersey Governor's Advisory Committee on Tobacco Dependence Treatment.
2003-2006	Vice President: Association for the Treatment of Tobacco Use and Dependence

2003-2006 Products and Communications Workgroup Chair: Association for the Treatment of Tobacco Use and Dependence
2008 National Committee for Quality Assurance, Smoking Cessation Advisory Board.
2008 Member, National Committee on Quality Assurance, Smoking Cessation Measurement Workgroup.
2008-11 Smoking Cessation Advisory Boards for GSK, Pfizer, Novartis, Cypress Bioscience.
2008-ongoing Member, Editorial Board and Efficacy Section, www.treatobacco.net
2009-ongoing Editorial Board: International Journal of Clinical Practice
2011-ongoing Associate Editor: BMC Public Health

Honors

2007 Recipient of UMDNJ-SPH "Community-Campus Partnership Award".
2009 Recipient of New Jersey GASP award for smoking cessation work.

C. Selected Peer-reviewed Publications (Selected from 87 peer-reviewed publications)

Most relevant to the current application:

1. **Foulds J**, McSorley K, Sneddon J, Feyerabend C., Jarvis MJ, Russell MAH. Effect of subcutaneous nicotine injections on EEG alpha frequency in non-smokers: a placebo-controlled pilot study. Psychopharmacology 1994; 115: 163-166.
2. **Foulds J**, Stapleton J, Swettenham J, Bell N, McSorley K, Russell MAH. Cognitive performance effects of subcutaneous nicotine in smokers and never-smokers. Psychopharmacology 1996;127: 31-8.
3. Williams J, Gandhi KK, Lu SE, Kumar S, Shen J, **Foulds J**, Kipen H, Benowitz NL.Higher nicotine levels in schizophrenia compared with controls after smoking a single cigarette. Nicotine and Tobacco Research 2010 Aug; 12(8): 855-9
4. **Foulds J**, Parth J, Bover-Manderski M. Blood glucose levels produced by glucose tablets in abstaining smokers. Psychopharmacology 2010; 209:283-284.
5. **Foulds J**, Veldheer S & Berg A. Electronic cigarettes: views of aficionados and clinical/public health perspective. Int J Clinical Practice 2011 Oct;65(10):1037-42.

Additional publications of importance to the field (in chronological order):

6. **Foulds J**, Stapleton J, Hayward M, Russell MAH, Feyerabend C, Fleming T, Costello J. Transdermal nicotine patches with low- intensity support to aid smoking cessation in outpatients in a general hospital: a placebo-controlled trial. Arch Fam Med 1993;2:417-23.
7. Hajek P, West R, **Foulds J**, Nilsson F, Burrows S, Meadow A. Randomised comparative trial of nicotine polacrylex, transdermal patch, nasal spray and inhaler. Arch Int Med 1999;159:2033-8.
8. Hajek P, West R, Lee A, **Foulds J**, Eiser JR, Main N. Randomized controlled trial of a midwife-delivered brief smoking cessation intervention in pregnancy. Addiction 2001; 96: 485-494.
9. **Foulds J**, Ramstrom L, Burke M, Fagerstrom K. Effect of smokeless tobacco (snus) on smoking and public health in Sweden. Tobacco Control 2003;12(4):349-59.
10. Steinberg M, Delnevo C, **Foulds J**, Pevzner E. Characteristics of smoking and cessation among high school students in New Jersey. Journal of Adolescent Health 2004; 35: 231-133.
11. **Foulds J**, Gandhi KK, Steinberg MB, Richardson D, Williams J, Burke M, Rhoads GG. Factors associated with quitting smoking at a tobacco dependence treatment clinic. Am J Health Behav 2006; 30:400-412.
12. Gandhi KK, **Foulds J**, Steinberg MB, Lu SE, Williams J. Lower quit rates among menthol cigarette smokers at a tobacco treatment clinic. International Journal of Clinical Practice 2009 Mar;63(3):360
13. Steinberg MB, Greenhaus S, Schmelzer AC, Bover M, **Foulds J**, Hoover DR, Carson JL Randomized trial of triple combination extended duration pharmacotherapy versus standard duration nicotine patch alone for smokers with medical illness. Annals of Internal Medicine 2009 150(7): 447-454

14. **Foulds J**, Pletcher M, Hooper M, Okuyemi K. Do smokers of menthol cigarettes find it harder to quit smoking? Nicotine and Tobacco Research 2010 Dec; 12(Supplement 2): S102-S109.
15. Oredein T & **Foulds J**. Causes of the decline in cigarette smoking among African-American youths from the 1970s to the 1990. Am J Public Health 2011 Oct;101(10):e4-e14. Epub

Completed Research Support

RWJF-59930-07 (Foulds) 12/1/2006-3/31/2009
Robert Wood Johnson Foundation /SRNT
Literature Review of Barriers to Consumer Use of FDA Approved medications for Smoking Cessation
This project aims to review the literature on barriers to use of FDA approved medicines for smoking cessation and recommend policy changes to address these barriers.
Role: PI

08-1997-TOB-E-0 (Foulds) 7/1/2006-6/30/2010
NJ Department of Health
Tobacco Dependence Program, Tobacco Dependence Clinic, Middlesex Partnership against Tobacco, REBEL Youth Tobacco Prevention
These projects aim to provide and evaluate state of the art tobacco dependence treatment for adults and adolescents, and training on treatment for health professionals.
Role: PI

RWJF-053452-06 (Foulds) 7/1/2005-3/31/2008
Robert Wood Johnson Foundation
Developing Culturally Competent Hispanic Smoking Cessation Outreach for New Jersey
This project aimed to develop and evaluate smoking cessation services for Latino smokers.
Role: PI

No Number Assigned (Foulds) 12/1/2004-6/30/2008
Cancer Institute of New Jersey
Evaluating New Treatments for Tobacco Dependence
This grant aimed to assess the effects of oral glucose on cigarette craving and nicotine withdrawal during short-term tobacco abstinence and evaluate the factors affecting outcomes of smokers in treatment.
Role: PI

RCHF-TDP-08 (Foulds) 7/1/2008-6/30/2010
Rutgers Community Health Foundation
Smoking Cessation Outreach to People of Color in New Brunswick
This project aims to develop and evaluate culturally competent smoking cessation outreach to people of color in New Brunswick, NJ.
Role: PI

No Number Assigned (Foulds) 7/1/2009-6/30/2010
Wellpoint Inc.
Development and training for a new tobacco quitline curriculum.
This project aimed to develop a new tobacco use assessment and intervention protocol for use by a health insurance company.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Chen, Gang	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) GACHEN	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Jilin University, Changchun, China	B.S.	09/82-04/86	Chemistry
CalPoly State U, Pomona, CA		01/94-08/96	Biochemistry
Wayne State U., Detroit, MI	Ph.D.	08/96-12/02	Cancer Biology
Fred Hutchinson Cancer Research Center, Seattle, WA	(Post-doc)	08/02-08/04	DNA Repair

A. Personal Statement

I have the expertise necessary to successfully collaborate on the proposed project. I have a broad background in cancer biology and molecular epidemiology, with specific training and expertise in key research areas for this application, including breast cancer and lung cancer. As an assistant professor at Penn State College of Medicine, I carried out research on tobacco related cancer risk and prevention. Particularly, I am interested in studying genetic variants that may be associated with altered metabolism of nicotine and tobacco-related carcinogens, and further may be associated with risk of cancer. As PI or co-Investigator on several previous university- and NIH-funded grants, I developed effective measures of all major nicotine metabolites in urine sample, identified novel functional polymorphism in gene involve in nicotine metabolism pathway, and demonstrate for the first time the important role of UGT2B10 and UGT2B17 in nicotine metabolism pathway. In addition, I successfully collaborated with other researchers, and produced several peer-reviewed publications from each project. In summary, I have a demonstrated record of successful and productive research projects in an area of molecular epidemiology, and my expertise and experience have prepared me to collaborate well on the proposed project.

B. Positions and Honors

Positions and Employment

1986-1993 Faculty, Department of Chemistry, Dalian Medical College, Dalian, China
2004-2006 Research Associate, Department of Public Health Sciences, Penn State College of Medicine
2006-Present Assistant Professor, Department of Public Health Sciences, Penn State College of Medicine

C. Selected Peer-reviewed Publications (Selected from a total of 29)

1. **Chen, G**. and Djuric, Z., Carotenoids are oxidized but do not protect lipids from peroxidation in unilamellar liposomes. *FEBS Letters*, 505:151-154, 2001.
2. **Chen, G**. and Djuric, Z., Detection of 2,6-cyclolycopene-1,5-diol in breast nipple aspirate fluids and plasma: a potential marker of oxidative stress, *Cancer Epidemiology, Biomarkers and Prevention*, 11, 1592-1596, 2002.
3. **Chen G**, Heilbrun LK, Venkatramanamoorthy R, Maranci V, Redd JN, Klurfeld DM, Djuric Z., Effects of low-fat and/or high-fruit-and-vegetable diets on plasma levels of 8-isoprostane-F2alpha in the Nutrition and Breast Health study. *Nutr Cancer*. 2004;50(2):155-60.
4. Zora Djuric, **Gang Chen**, Raghu Venkatramanamoorthy, Chandice Y. Covington, Omer Kucuk, Lance K. Heilbrun, Effects of high fruit-vegetable and/or low-fat intervention on breast nipple aspirate fluid micronutrient levels, *Cancer Epidemiol Biomarkers Prev* 2007 16(7): 1393-1399
5. Dellinger, R. W., **Chen, G**., Blevins-Primeau, A. S., Krzeminski, J., Amin, S., and Lazarus, P. Glucuronidation of PhIP and N-OH-PhIP by UDP-glucuronosyltransferase 1A10. Carcinogenesis, *28:* 2412-2418, 2007.

6. **Chen, G**., Blevins-Primeau, A. S., Dellinger, R. W., Muscat, J. E., and Lazarus, P. Glucuronidation of nicotine and cotinine by UGT2B10: loss of function by the UGT2B10 Codon 67 (Asp>Tyr) polymorphism. Cancer Res, *67:* 9024-9029, 2007.
7. **Chen, G**., Dellinger, R. W., Gallagher, C. J., Sun, D., and Lazarus, P. Identification of a prevalent functional missense polymorphism in the UGT2B10 gene and its association with UGT2B10 inactivation against tobacco-specific nitrosamines. *Pharmacogenet Genomics*, *18:* 181-191, 2008.
8. **Chen, G.**, Dellinger, R. W., Sun, D., Spratt, T. E., and Lazarus, P. Glucuronidation of tobacco-specific nitrosamines by UGT2B10. *Drug Metab Dispos*, *36:* 824-830, 2008. PMCID: PMC2714266
9. Muscat, J. E., **Chen, G.**, Knipe, A., Stellman, S. D., Lazarus, P., and Richie, J. P., Jr. Effects of Menthol on Tobacco Smoke Exposure, Nicotine Dependence, and NNAL Glucuronidation. *Cancer Epidemiol Biomarkers Prev*, *18:* 35-41, 2009. PMCID: PMC2676921
10. Blevins-Primeau, A. S., Sun, D., **Chen, G**., Sharma, A. K., Gallagher, C. J., Amin, S., and Lazarus, P. Functional significance of UDP-glucuronosyltransferase variants in the metabolism of active tamoxifen metabolites. *Cancer Research*, *69:* 1892-1900, 2009. PMCID: PMC2683344
11. Balliet RM, **Chen G**, Gallagher CJ, Dellinger RW, Sun D, Lazarus P. Characterization of UGTs active against SAHA and association between SAHA glucuronidation activity phenotype with UGT genotype. Cancer Res. 2009 Apr 1;69(7):2981-9. PMCID: PMC2694132
12. **Gang Chen**, Nino E. Giambrone Jr., Douglas F. Dluzen, Carla J. Gallagher and Philip Lazarus, Glucuronidation genotypes and nicotine metabolic phenotypes: Importance of UGT2B10 and UGT2B17 knock-out polymorphisms. Cancer Res 2010; 70*:* 7543-52.
13. Dongxiao Sun, **Gang Chen**, Ryan W. Dellinger, Arun K. Sharma and Philip Lazarus. Characterization of 17-dihydroexemestane glucuronidation. Potential role of UGT2B17 deletion in exemestane pharmacogenetics. *Pharmacogenet Genomics*, 2010; 20*:* 575-85.
14. Bushey RT, **Chen G**, Blevins-Primeau AS, Krzeminski J, Amin S, Lazarus P. Characterization of UDP-glucuronosyltransferase 2A1 (UGT2A1) variants and their potential role in tobacco carcinogenesis. Pharmacogenet Genomics 2011; 21*:* 55-65.
15. Olson KC, Sun D, **Chen G**, et al. Characterization of Dibenzo[a,l]pyrene-trans-11,12-diol (Dibenzo[def,p]chrysene) Glucuronidation by UDP-Glucuronosyltransferases. Chem Res Toxicol, 2011 Aug 5.

D. Research Support

Ongoing Research Support

R01 DE013158-07A2 (Lazarus) 5/1/2007-4/30/2012
NIH/NIDCR
UDP-Glucuronosyltransferase Genotype & Cancer Risk
The major goal of this program project is to examine the role of UGTs in genetic susceptibility to cancer.
Role: Co-Investigator

MD003352 (Chorney) 9/1/2008-8/31/2013
NIH
Development of a Quantitative and Sensitive Liquid Chromatographic/Mass Spectrometric Method to Correlate the Metabolic Profile of African American Smokers with Smoking Cessation Rate
The goal of this study is to investigate the relationship between nicotine metabolic profile and smoking cessation rate in African Americans.
Role: Mentor

Completed Research Support

SAP#4100038715 (Lazarus) 6/1/2007-5/31/2011
PA Department of Health
Gene-Environment Interactions for Colorectal Cancer in Northeast PA
The specific aims of this project are to determine the interactive effects of diet and metabolic genes on the risk of colorectal cancer in northeast Pennsylvania.

Role: Collaborator

No Number Assigned (Chen) 7/1/2008-6/30/2010
Penn State
Nicotine Metabolites in Urine as Potential Markers for Pathway Association Study of Lung Cancer Risk
The goal of this grant is to develop a reliable and sensitive UPLC-MS-MS method for analysis of nicotine metabolites in smokers' urine.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Berg, Arthur	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) ASBERG	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Southern California, Los Angeles	BS	08/02	Mathematics
University of Southern California, Los Angeles	MA	08/02	Mathematics
University of California, San Diego	MS	06/05	Statistics
University of California, San Diego	PhD	06/07	Mathematics

A. Personal Statement

As an Assistant Professor of Biostatistics & Bioinformatics, I have participated in several successful collaborations with projects requiring biostatistics expertise. I have experience in utilizing numerous software tools to perform diverse types of statistical analyses. Many of the computational tools that I have developed are made publicly available through a website portal (e.g. statgen.psu.edu) or through the Comprehensive R Archive Network (CRAN). In addition to my computational strengths, I have also written a number of methodological papers in biostatistics, and I have also participated in several collaborative projects from which several new methodological papers have stemmed. I have worked closely with the collaborative investigator Dr. Foulds on several projects involving tobacco cessation including a recently published manuscript that presents survey results from a group of e-cigarrette aficionados with insightful perspectives on public health. I will work all of the collaborators on this project to perform statistical calculations and work with them to secure more extensive support from the NIH. In summary, my extensive experience biostatistics has prepared me to successfully collaborate on the proposed project.

B. Positions and Honors

Positions and Employment

2005-2006	Adjunct Instructor, Miramar College, San Diego, CA
2007 (Jan-Mar)	Associate-In Instructor, University of California, San Diego, CA
2007-2009	Assistant Professor of Statistics, University of Florida, Gainesville, FL
2009-present	Assistant Professor, Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA
2011-present	Director, Bioinformatics Core, Penn State College of Medicine, Hershey, PA
2011-present	Leader, CTSI Informatics Key Function, Penn State College of Medicine, Hershey, PA

Other Experience and Professional Memberships

2004-2007	Mathstorm Administrator and Consultant, UCSD Consulting Group
2008	Co-organizer of Statistical Genetics session, World Congress of Gene, Guangzhou, China
2009	Invited lecturer at the First Annual International Statistical Genetics Workshop, Beijing, China

C. Selected Peer-reviewed Publications (Selected from 45 peer-reviewed publications)

Most relevant to the current application

1. Foulds, J., S. Veldheer, **A. Berg** (2011) Electronic cigarettes (e-cigs): views of aficionados, and clinical/public health perspectives. *Journal of Clinical Practice* 65(10): 1037-1042.
2. Chen, G., N. Giambrone, D. Dluzen, J. Muscat, **A. Berg**, C. Gallagher, and P. Lazarus, (2010) Glucuronidation genotypes and nicotine metabolic phenotypes: Importance of UGT2B10 and UGT2B17 knock-out polymorphisms. *Cancer Research*. 70(20): 7543–7552.
3. Sharma, A.K., C.Kline, **A. Berg**, S. Amin, R. Irby. (2011) The Akt inhibitor ISC-4 activates Par-4 and reduces colon tumor growth in a nude mouse model. *Clinical Cancer Research*. 17(13): 4474-83. PMCID: PMC3131476
4. Avella DM, G. Li, T.D. Schell, D. Liu, S. Zhang, X. Lou, **A. Berg**, E.T. Kimchi, H.R. Tagaram, Q. Yang, S. Shereef, L.S. Garcia, M. Kester, H.C. Isom, B. Rountree, K.F. Staveley-O'Carroll. (in press) Regression of established hepatocellular carcinoma is induced by chemo-immunotherapy in an orthotopic murine model. *Hepatology* doi: 10.1002/hep.24652
5. **Berg, A.**, T. McMurry, and D. Politis, (2010) Subsampling p-values. *Statistics and Probability Letters*. 80: 1358-1364.

Additional recent publications of importance to the field (in chronological order)

6. Ramesh, G., **A. Berg**, C. Jayakumar. (2011) Plasma netrin-1 is a universal diagnostic biomarker of human cancer. *Biomarkers*. 16(2):172–180. PMCID: PMC3143477
7. Poritz, L., R. Sehgal, K. Hartnett, **A. Berg,** W. Koltun. (in press) Tumor volume and percent positive lymph nodes as a predictor of 5 year survival in colorectal cancer. *Surgery*
8. **Berg, A.**, Q. He, Y. Shen, Y. Chen, M. Huang, R. Wu. (2010) Multilocus Disequilibrium Analysis of Multiallelic Markers in Outcrossing Populations. *Statistical Application in Genetics and Molecular Biology*. 9(1), Article 16.
9. **Berg A.,** Politis D. (2009) CDF and survival function estimation with infinite-order kernels. *Electronic J Stat.* 2009;3,1436-1454. DOI: 10.1214/09-EJS396.
10. Drost, D., C. Benedict, **A. Berg**, E. Novaes, C. Novaes, Q. Yu, C. Dervinis, J. Maia, J. Yap, B. Miles, M. Kirst. (2010) Diversification in the genetic architecture of gene expression and transcriptional networks in organ differentiation of *Populus*. *Proceedings of the National Academy of Sciences*. 107(18): 8492-8497.
11. Anh, K, J. Luo, **A. Berg**, D. Keefe, and R. Wu. (2010) Functional mapping of drug response with pharmacodynamic-pharmcokinetic principles. *Trends in Pharmaceutical Science*. 31(7): 306–311.
12. He, Q.L., **A. Berg**, Y. Li, E. Vallejos, R. L. Wu, (2010) Mapping Genes for Plant Structure, Development and Evolution: Functional Mapping Meets Ontology. *Trends in Genetics*. **26**(1): 39-46.
13. Kim B.R., McMurry T., Zhao W., Wu R., **Berg A**. (2010) Wavelet-based functional clustering for patterns of high-dimensional dynamic gene expression. *J Comput Biol.* 17(8):1067–1080.
14. Kim B.R., Zhang L., **Berg A.**, Fan J., Wu R. (2008) A computational approach to the functional clustering of periodic gene-expression profiles. *Genetics.*;180:821-834. PMCID: PMC2567383
15. Brumback B., **Berg A.** (2008) On effect-measure modification: relations among changes in the relative risk, odds ratio, and risk difference. *Stat Med.* 27(18):3453-3465.

D. Research Support

Ongoing Research Support

1 UL1RR0330184-01 (Sinoway) 6/1/2011-2/29/2016
NIH
Title: The Penn State Clinical and Translational Science Institute
Project goal: The goal of Penn State CTSI is an engaged and responsive health science research and education enterprise that delivers on the promise of improved health.
Role: Head, Statistical Genetics

5 R01 AR054937-03 (Donahue) 4/1/2009 - 3/31/2014
NIH/NIAMS
Title: Biophysical Signals, Biomaterial Surface Characteristics and HMSC Differentiation
Project goal: to identify specific biomaterial surface characteristics and biophysical signals that interact synergistically in optimizing hMSC differentiation toward the osteoblastic lineage
Role: Co-Investigator

No Number Assigned (Aronoff-Berg) 6/1/2011-5/31/2012
Internal
Title: Using High Dimensional Models to Predict 30-day Readmission After Heart Failure
Role: Co-PI

Completed Research Support

No Number Assigned (Wu) 11/1/2009-10/31/2010
Penn State Hershey Cancer Institute
Title: Statistical Designs for Studying Genetic Mutations and Interactions in Breast Cancer
Project goal: The goal of this project is to develop a series of models and algorithms for identifying genes with complex interactions responsible for the formation and progression of breast cancer.
Role: Co-Investigator

1 K22 CA120092 (Wilson) 9/1/2008-8/31/2011
NIH
Title: Functional Vitamin D Receptor Gene Variants and Racial/Ethnic Cancer Disparities
Project goal: The goal of this project is to identify and characterize VDR binding polymorphisms and determine differences in level of VDR binding among healthy African American and Caucasian individuals.
Role: Co-Investigator

No Number Assigned (Sehgal) 9/1/2010-8/31/2011
ASCRS Research Foundation
Title: Correlation of Gene Haplotype with Complications after IPAA
Project goal: to attempt to identify specific gene mutations (SNPs) in UC patients who have undergone the IPAA that are associated with CD like complications, including severe or mild pouchitis.
Role: Co-Investigator