1) **Protocol Title**

Addressing Tobacco Health Disparities via Group Intervention

2) **Objectives***

Purposes and aims: (1) Examine the effects of CBT for smoking cessation on perceived stress and depressive symptoms in a racially/ethnically diverse sample; (2) test the efficacy of CBT for eliminating smoking cessation disparities; and (3) Examine physiological distress as an underlying mechanism for the effects of CBT on racial/ethnic minority smokers (exploratory).

3) **Background***

Significance: Tobacco smoking is robustly associated with significant morbidity and mortality, from conditions such as cancer, diabetes, cardiovascular disease, and hypertension. Pervasive smoking-related health disparities exist across racial/ethnic and socioeconomic status (SES) groups. The most established disparities are observed in comparisons of African Americans and Whites, though evidence demonstrates disparities across populations of smokers.

The importance of reducing tobacco-associated health disparities between cannot be understated. Racial/ethnic minority smokers are less likely to quit successfully, even in the context of treatment. Perceived stress and depressive symptoms are known barriers to smoking cessation, yet have virtually been ignored in the disparities literature. Racial/ethnic minority smokers tend to have elevated distress levels, which may contribute to disparities in cessation and health. Cognitive behavioral therapy (CBT) for cessation addresses these concerns and has the potential to reduce or eliminate disparities. Our preliminary studies, conducted in our established research clinic, found race/ethnic differences in baseline perceived stress and depressive symptoms. Following CBT, these differences were no longer present. Moreover, the lack of disparity in cessation appeared to be driven by the positive change in stress and depressive symptoms. This study will be the first RCT to test the impact of CBT on smoking cessation disparities.

4) **Inclusion and Exclusion Criteria***

Inclusion criteria for this study include: (1) self-identify as African American/Black, Hispanic (any race), or White non-Hispanic; (2) smoke at least 5 cigarettes/day or CO reading of at least 8 ppm; (3) be over age 18; and (4) speak/read English and/or Spanish.

Exclusion criteria include: (1) contraindications for transdermal nicotine patch therapy (TNP); (2) cognitive or mental health impairment that inhibits group treatment; (3) currently being treated for smoking cessation, alcoholism, or illicit drug use; (4) unable to attend sessions; (5) indications that participant is not appropriate for the study (e.g., aggressive, intoxicated, disruptive, visibly ill); (6) does not self-identify as African American, Hispanic, or White (non-Hispanic).

Withdrawal of Subjects
The following are reasons for withdrawal of subjects from the study:

- A subject does not meet the eligibility criteria, (the subject will be considered a screen failure).
- A subject withdraws informed consent.
- A subject dies during protocol participation or
- A study investigator decides the subject should be withdrawn from the study (e.g. subject non-compliance)

Regardless of reason for withdrawal, once a subject has been randomized to a study arm, an intention to treat analysis will be performed.

Procedures Involved

This behavioral intervention study includes a baseline assessment, randomization to one of two conditions, and 4 subsequent assessments. Screening may occur in person or over the telephone. Eligible participants may be scheduled for an appointment to attend orientation/baseline assessment. Time permitting prior to the appointment, we may attempt to mail a confirmation letter and/or complete reminder contacts (telephone calls, text messages, email) leading up to the appointments.

Assessments. At the baseline visit, eligible participants will provide written informed consent, and complete some or all of the baseline measures (described below). They may also be asked to complete intra-treatment assessments during the 8 sessions. Follow-up assessments (called "reunions") may occur at the end-of-therapy (EOT), and 3, 6, and 12-month follow-ups. The full assessment (at baseline) may require approximately 90 minutes to complete. Intra-treatment assessments may require 5 minutes, and follow-ups may require 60 minutes. The questionnaires may be completed (fully or in part) electronically using iPads/computers or on paper. Skip patterns may be built into the measures to decrease participant burden. All items are voluntary, thus participants may select an answer for each item before moving forward, and will have the option of selecting 'I would rather not say' on the electronic version or skipping items as desired. Surveys in either electronic or paper format will use identification numbers rather than identifying information.

Participants may complete some or all of the following measures:
Questionnaires: A standard demographic questionnaire assessing race, ethnicity, nativity, age, education, employment status, health insurance, marital status, and number of children. Measures may also include current medications, medical history (e.g., diabetes, hypertension, chronic back pain, arthritis, emphysema, and asthma), height, weight, smoking history, nicotine dependence, readiness to quit smoking, perceived stress, depressive symptoms, alcohol use, ethnic discrimination, nicotine withdrawal and urges to smoke, social support, daily hassles, e-cigarette use, sleep quality, intervention evaluations, group cohesion, smoking pattern, history of substance dependence and treatment, and use of other tobacco products and pharmacotherapies.

Bio-verification: Saliva cotinine levels may be assessed at baseline, and to confirm self-reported cessation at the 3, 6, and 12-month follow-ups. Research staff will be trained in the U.S. Centers for Disease Control (CDC) guidelines for transport of biological

specimens within the United States. The CBT intervention includes carbon monoxide (CO) testing at each treatment session to provide immediate feedback to participants regarding the benefits of cessation.

Salivary cortisol: At each assessment point, we may collect saliva samples for cortisol analyses. Participants who agree will be provided with the needed materials and trained in saliva collection procedures at orientation and prior to assessments. They may be asked to collect saliva up to 4 times throughout the day. Saliva samples will be stored in the lab freezers. At the time of collection, we will ask participants to record hours of sleep, food consumption, and exercise within the past hour.

Randomization. Participants may be randomly assigned to one of 2 conditions. In the first condition, *Group Cognitive Behavioral Therapy for Smoking Cessation (CBT)*, participants may receive 8 group sessions and eight weeks of TNP [21mg (4 weeks), 14mg (2 weeks), and 7mg (2 weeks)]. The four-week CBT protocol includes 4 sessions during week 1, 2 sessions during week 2, 1 session during week 3, and 1 session during week 4. We will request that participants attend every session; however, we recognize that this will not always be feasible. CBT is intended to guide participants through the cessation process and teach relapse prevention skills. Sessions may include a functional analysis of smoking patterns, environmental cues, and motivation for change, and cover nicotine addiction and withdrawal, health consequences, benefits of cessation, stress management, negative affect, alcohol use, triggers, coping responses, cognitive restructuring, social support, decision making, weight control, and physical activity. In the second condition, *General Health Education*, participants may receive sessions including didactic information on tobacco-associated morbidities, such as heart disease, diabetes, and hypertension. Content may include PowerPoint-delivered lectures on the prevalence, etiology, basic pathology, symptom patterns, and treatment of the conditions, and discussion questions designed to facilitate learning and interest. Smoking cessation specific topics will not be addressed, and coping skills will not be provided. Participants will be allowed to share feelings regarding smoking (if they mention them) and general questions will be answered, although no specific behavioral quitting advice will be provided (i.e., they will be encouraged to adhere to the TNP protocol). The groups in both conditions are expected to require 90-120 minutes, depending on group size. Sessions may be audio or video taped.

Participants will be paid for completing assessments, baseline ($20), EOT ($30), 3-month ($40.00), 6-month ($50.00), and12-month ($50.00), prorated by half for incomplete assessments. Funds permitting, participants may also receive reimbursement for transportation and light refreshments during visits. We anticipate that data collection may occur within a 4-year period, although this may vary depending on recruitment progress.

5) **Data and Specimen Banking***

N/A

6) **Data Management***
Statistical Analysis
Descriptive statistics such as frequencies, percentages, means, medians, standard deviations, and interquartile ranges may be tabulated to describe the study sample.

Associations between variables and intervention effects may be assessed with Wilcoxon/Kruskal-Wallis tests, Chi-squared/Fisher exact tests, analyses of variance, multiple regression, generalized linear mixed models, and logistic regression.

Data may be collected using the University of Miami Qualtrics survey program and stored on password-protected university servers. Surveys collected on paper will be entered by members of the research team into password protected data files. Access to the files containing the survey and survey responses is restricted and only study personnel will be given access to these files. Identifying information will not be collected with electronic or paper questionnaires. Data published from this survey will be presented in group form, so that individual participant data is not identifiable. Data may be stored for up to five years following publication of findings.

Guidelines for Adverse Events (AEs) and Smoking Cessation Rates
We anticipate few adverse events due to study participation. Abstinence from smoking may lead to withdrawal symptoms, including irritability, anxiety, restlessness, sadness, and difficulty concentrating. These symptoms are expected and manageable and most resolve in two to six weeks in abstinent smokers. Withdrawal can be attenuated by the use of nicotine replacement therapy (NRT). The NRT to be administered in this study is FDA-approved and has demonstrated adverse side effects in only a minority of users. To ensure the safety of subjects, any persons who report adverse side effects from NRT will be advised to discontinue use and encouraged to visit their private doctor or referred to the emergency room. Any persons who report problematic nicotine withdrawal (e.g., depression) will be assessed for severity by the Dr. Antoni, who is a clinical psychologist. If the participant's depression is greater than that expected due to typical nicotine withdrawal or is causing significant impairment in functioning, the subject will be referred for services at the Psychological Services Center—the Psychology Department's on-campus training clinic, or to a community mental health provider. In the case of serious adverse events (SAEs) or other untoward occurrence, the PI will notify the Data and Safety Monitoring Committee (DSMC), the Office of Research, and the IRB via telephone at the time of the incident, followed by a detailed written account of the nature and scope of the events and the reason(s) for their occurrence. The activities of the project will be suspended, pending a full IRB review. The IRB will follow-up with appropriate action and the research will proceed only with written IRB approval. In the event of serious adverse events (SAEs) or incidents, the Office of Research and DSMC will take the necessary steps to document the events in writing to our regulatory boards.

SAEs: The DSMC will engage in expedited reviews for any occurrences meeting the FDA definition of SAEs – i.e., any fatal event, acute life-threatening event, permanently or substantially disabling event, event requiring participant hospitalization, or any congenital anomaly. These reviews will determine whether the event poses a significant hazard, side effects, or requires precaution. Any SAE will be required to be reported to the DSMC, irrespective of its perceived relatedness to the study. Reports will include a description of the event and its outcome, related medications, the participant's medical history and current conditions, and all relevant clinical data. Notification by e-mail, and FAX transmittal of SAE's and all related documents will be sent to the DSMC within 2 days of the occurrence.

Smoking cessation rates are assessed via Qualtrics at end of counseling (EOC) and follow-up time points.

7) **Risks to Subjects***

The risks to subjects, immediate and long range, are considered minimal. Study participants will be asked to complete relatively benign questionnaires and before and after receiving behavioral treatment plus nicotine replacement for smoking cessation. It is possible that subjects might become psychologically distressed while completing questionnaires or be dissatisfied with the intervention. They will be provided with transdermal nicotine patches that are available over-the-counter and required to indicate whether they have any health conditions that may negatively interact with the patches.

To minimize the risk of psychological distress due to questionnaire completion, the measures do not contain private or potentially embarrassing items, and are limited to 90 minutes completion time per assessment. To minimize the risk of dissatisfaction with the intervention, we will use an established intervention that has high efficacy. To minimize risks associated with the nicotine patches, subjects will be provided with thorough education of the indications for the nicotine patch, possible side effects, and known health conditions that preclude patch use. The patches are available over the counter; thus, they do not pose a significant health risk to most people. They contain minimal amounts of nicotine (which are much less than they get from smoking), and are absent the remaining 7,000 toxins contained in cigarettes. In addition, we will refer patients with a questionable medical history to their family physician or to Jackson Memorial Hospital or Tampa General (which accept uninsured patients) for consultation.

8) **Potential Benefits to Subjects***

9) Individual subjects can potentially benefit from participating in the study because they may be exposed to one of two established smoking cessation treatments plus transdermal nicotine patch therapy. Thus, all participants will have the opportunity to make a quit attempt and the possibility of long-term smoking cessation.
This is associated with a number of additional benefits including improved health, economic savings, the confidence and happiness associated with becoming an ex-smoker, and eliminating the second-hand smoke exposure to others.

10) **Vulnerable Populations***

This research study does not include vulnerable populations.

11) **Setting**

The primary study site is the University of Miami Clinical Research Building, with offices on the Miller School of Medicine campus, and in the Flipse building on the Coral Gables campus. The Miami site will also recruit participants in Broward County and conduct groups at several Broward locations for participant convenience. The second study site is the Tobacco, Research, and Intervention Program (TRIP) at the H. Lee Moffitt Cancer

Center and Research Institute in Tampa, FL. Participants may also be recruited and screened at community events and may be scheduled to come to the lab at a later date. Community-based recruitment is intended to diversify the sample, and will reduce barriers to on-campus participation.

12) **Resources Available**

Principal Investigator, David Lee, Ph.D.: Dr. Lee is a tenured Professor in the University of Miami Miller School of Medicine, Department of Public Health Sciences. Dr. Lee will contribute his expertise as a chronic disease epidemiologist with research interests in tobacco control, SHS exposure, and special populations. Dr. Lee has worked with Hispanics, African-American, and low-income youth and adult populations, both nationally and in Florida. Dr. Lee also is a member of the SCCC and Cancer Control Program. He also serves as the Principal Director of the Florida Cancer Data System Cancer Registry, leading to the recent publication of a comprehensive monograph on the cancer experience of Florida Hispanics, including major tobacco associated cancers. He has been involved in tobacco research for over 19 years and has directed studies employing both cross-sectional and longitudinal cohort designs. Dr. Lee has been the Principal Investigator in six NIH-supported studies and on three grants examining the health effects of SHS awarded by the Flight Attendant Medical Research Institute (FAMRI), the primary funding organization for SHS in the United States. His most recent FAMRI supported grant is examining associations of self-reported telephone survey data with biologically confirmed SHS exposure and health outcomes in a diverse sample of Florida adults. Dr. Lee was a Co-Investigator for the Hispanic Community Health Study where tobacco was one of the primary outcome variables. Dr. Lee served as Project Director for the Team Science Program working to "Reduce the Burden of Tobacco-Associated Cancers in Florida." Dr. Lee's publications have appeared in highly rated peer reviewed journals, such as *Tobacco Control*, the *American Journal of Public Health*, and *Nicotine and Tobacco Research*. Dr. Lee's publication, "Respiratory Effects of SHS Exposure Among Young Adults Residing in a 'Clean' Indoor Air State" was distributed worldwide to tobacco control experts via GLOBALink.

13) **Prior Approvals**

This survey does not require additional approvals prior to commencing the research.

14) **Recruitment Methods**

Participant recruitment may occur using several methods, including radio and newspaper stories and advertisements, community events (e.g., health fairs), neighborhood canvassing, email, online social-media and advertising sites, and flyers and post-cards distributed throughout the community (e.g., churches, Laundromats, businesses, physicians' offices, health centers/clinics). Recruitment may also take place at other medical sites (e.g., Broward Health organization, and UHealth regional sites) through patient referrals, community outreach, or direct referrals to the Research staff. After calling the telephone

number provided in the advertisements or being identified in person, RAs may explain the study to participants (paraphrasing from a script) and conduct screening for eligibility.

Participants may be given small tokens of appreciation, such as water bottles, wallets, or bags.

15) **Local Number of Subjects**

We anticipate screening up to 1000 subjects and enrolling up to 500 to complete the study. Moffitt Cancer Center will enroll 150 subjects. Moffitt's enrollment numbers are not included in this protocol, being as it is stated in their own IRB protocol.

16) **Confidentiality**

Contact information for participants scheduling appointments to participate on site may be recorded over the telephone and stored in a password encrypted database. Following study completion, contact information may be deleted from the database. Only the PI and study personnel may have access to the database. Survey data may be collected and stored on University of Miami and H. Lee Moffitt Cancer Center password protected servers using electronic survey software. Assessment responses will not include identifying information. Only select study personnel may have administrative access to the survey data. Personnel with access must log onto the system with a username and password. Data may be maintained for five years post study publication.

17) **Provisions to Protect the Privacy Interests of Subjects**

Study participation is completely voluntary and confidential, which is explained during the informed consent process. Several RAs will recruit, schedule, and collect information from participants. They may elect to interact with (or not) any of the study staff. The questionnaires may be self-administered; however staff will be available to assist participants as needed. If desired and space-permitting, participants may be allowed to complete the assessment in private.

18) **Consent Process**

Participants will undergo screening for enrollment into the study. We are requesting a waiver of documentation of consent for this portion only as it is done via phone or in person; however, this is minimal risk and consent is not required outside of the research setting to ask the screening questions.

Informed consent may be obtained prior to confirming eligibility to participate in the study during the baseline visit. Consent will be obtained by the PI or key personnel (trained Research Associates and clinical psychology graduate students).

19) **Process to Document Consent in Writing**

Participants will be given an informed consent form. Study staff will be available to explain the assessments to participants and answer any questions they have about participation. Participants will be provided with copies of the consent document**.**

20) **Data & Safety Monitoring Committee Oversight**

The Sylvester Comprehensive Cancer Center (SCCC) Data and Safety Monitoring Committee (DSMC) will monitor this clinical trial according to the Cancer Center's Data and Safety Monitoring Plan (DSMP). In its oversight capacity, the DSMC bears responsibility for suspending or terminating this study.

DSMC oversight of the conduct of this trial includes ongoing review of adverse event data, and periodic review of self-reported smoking cessation rates. The guidelines appearing in Section #6 are offered for DSMC consideration in assessing adverse events and self-reported smoking cessation rates. In addition, the DSMC will review reports from all audits, site visits, or study reviews pertaining to this clinical trial and take appropriate action.

21) **Monitoring, Auditing, and Inspecting**

The investigator will permit trial-related monitoring, quality audits, and inspections by, government regulatory authorities, of all trial-related documents (e.g., source documents, regulatory documents, data collection instruments, case report forms). The investigator will ensure the capability for inspections of applicable trial-related facilities. The investigator will ensure that the trial monitor or any other compliance or QA reviewer is given access to all trial-related documents and trial-related facilities.
Participation as an investigator in this trial implies the acceptance of potential inspection by government regulatory authorities.

22) **Quality Assurance and Quality Control**

In addition to the Clinical Monitoring component of this protocol, Quality Assurance (QA) will be implemented to assess compliance with GCP and applicable regulatory requirements. Data or documentation audited shall be assessed for compliance to the protocol, accuracy in relation to source documents and compliance to applicable regulations.

23) **Financing and Insurance**

Not applicable.

24) **Publications and Data Sharing**

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study will be made available upon written request 30 days after the publication acceptance of primary study findings. De-identified requests will be honored for a period of 3 years of anniversary date by contacting principal investigator, David J. Lee.