Center for the Study of Diversity
Graduate Student Research Grant Program Progress Report

Full name: **Kelly A. Duran, M.A., Rachel Amey, and Chad E. Forbes, Ph.D.**
Department: Department of Brain and Psychological Sciences
Title of project: **The Impact of Interleukin 1 Beta Polymorphisms on Vulnerability to Threat Effects and Subsequent Health.**

II. Proposal

A. Title. The Impact of Interleukin 1 Beta Polymorphisms on Vulnerability to Threat Effects and Subsequent Health.

B. Project Overview.

There is a large gender gap within STEM fields where women are awarded approximately 30% of Ph.D.'s and occupy 25% of all positions in STEM fields[1]. For those few women who do manage to obtain a Master's or Ph.D. degree in a STEM field, they are still more likely to report job dissatisfaction and, in turn, are more likely to leave STEM faculty positions or careers compared to their male counterparts[2-4]. Though there are many factors likely contributing to women leaving STEM fields one factor largely unexplored is that of stereotype threat (ST). ST is a situational threat that targets of negative stereotypes experience when they fear their actions will inadvertently confirm a negative stereotype about a group to which they belong[5,6]. The stress produced by this response may have detrimental effects on high stakes performance tests (e.g. math portions of the SAT and GRE) or on an individual's mood[7-9], conscious and implicit anxiety as physiological arousal in general (e.g., skin conductance[10] and elevated blood pressure[11]). Given that ST can be triggered by factors such as being outnumbered by men in a STEM class[12], or having a male instructor[13], women in STEM classes could find themselves in stereotype threatening contexts on a daily basis.

All of the aforementioned threat responses can be considered stressors. As such, it's possible these individuals find themselves in situations of chronic stress. Psychosocial stress can directly provoke proinflammatory cytokine production in the absence of infection or injury[14]. Typically local inflammation is a vital aspect of immune function; in response to bodily insults proinflammatory cytokines attract immune cells to sites of infection or injury. However,

chronic inflammation has long been associated with negative health outcomes ranging from immune system dysregulation[15], cardiac disease[16,17] and mental health issues[18] to shorter life expectancy[17]. Exposure to chronically stressful situations associated with being negatively stereotyped in STEM fields may actually be bad for women's health. The proposed study seeks to examine this by investigating how vulnerability to stereotype threat may vary as a function of variation in the genetic marker il-1 β, which codes for the inflammatory cytokine interleukin 1 Beta, and how these variations may contribute to health outcomes.

Past research suggests that ST situations may engender cytokine responses among stigmatized individuals[19-22]. Mendonza-Denton and colleagues found that when individuals were placed in stereotype threatening situations they exhibited higher levels of interleukin 6 (il-6) compared to non-threatened minorities[19]. Further, follow-up analysis revealed that these effects were moderated by SES status, were individuals who had lower SES status showed the greatest il-6 increases[20]. Thus, there is at least initial evidence for cytokine responsiveness to psychosocial stressors such as ST. But these findings represent the tip of the iceberg so-to-speak. For instance, little is known about the role other potentially more serious cytokines, or genetic polymorphisms that alter the integrity of these cytokines, may play in ST contexts. Even less is known about how these cytokines may affect downstream processes like information processing or general well-being. One such cytokine, interleukin 1 Beta (il-1 β; a member of the same cytokine family as il-6), is known to have particularly potent inflammatory effects on the body, but this effect is modulated by the gene that codes for proteins comprising il-1 β[23]. Specifically, single nucleotide polymorphisms (SNPs; which alter the integrity and composition of the proteins they code for) in the promoter region of the il-1 β gene has been associated with dysfunctional systematic inflammatory responses[24]. For instance, when either one or both cytosine molecules are replaced with thymine (C/T and T/T respectively) people are more prone to elevated inflammatory responses[24], diabetes[25], rheumatoid arthritis[26], gastric diseases[27] and various cancers[28-33].Conversely, people who have the C/C polymorphism appear more resilient to negative effects associated with cancer treatment such as fatigue[31,34], and have better prognosis for disease course[35]. To date, no one has investigated how vulnerability to situational or chronic threats may vary as a function of different interleukin genetic SNPs.

The proposed research extends theory in ST by exploring genetic factors that may contribute to susceptibility to the negative consequences of ST and related health outcomes. We reason that individuals with genetic profiles that promote over-expression of il-1 β (C/T or T/T) will be more susceptible to the negative psychostressors associated with ST and be at greater risk for chronic illness. Conversely, those individuals with genetic profiles that promote less expression of il-1 β (C/C) will be less susceptible to stereotype threat-based stressors and will have more robust health.

See appendix A for study materials

Study1: *Participants/Methods*: As part of a larger, nationally funded study, students (125 male, 125 female) will either be told they are taking a test diagnostic of their math intelligence (DMT) or taking part in a study examining the different methods people use to solve problems (PST). Continuous EEG activity will be collected throughout the study. Participants will perform several different tasks in the study including math tasks, a memory task and measures of anxiety and domain identification. DNA samples will be collected to examine SNPs in a priori genes of interest (funded as part of the original grant). The current proposal would fund the isolation of the genetic marker for il-1 β from already extracted DNA samples. Health outcomes will be measured via questionnaire and include questions such as "How many colds have you had in the last 6 months?" and "Do you have any chronic health conditions?" *Outcomes*: Women with il-1 β T/T polymorphisms will show heightened threat responses as measured by EEG activity, math performance outcomes and memory for negative feedback to the extent that

they are identified with the domain. Further, they will have more incidents of being sick in the past 6 months and/or higher rates of chronic illness.

C. Impact Statement.

Identifying genetic markers that may provide insight in to which women may be more susceptible to ST and disengagement from STEM domains would be beneficial for the development of targeted interventions. Further, if these women are not only more vulnerable to ST effects and more likely to leave STEM fields but also at greater risk for negative health outcomes, it becomes even more important to develop appropriate interventions. This project will bring to light an important but over-looked aspect of ST threat research: Exposure to chronically stressful situations associated with being negatively stereotyped in STEM fields may actually be bad for women's health. Though some progress has been made in trying to engage more women in the STEM domains, the numbers are still abysmal. Developing a better understanding of the potential negative health outcomes engendered by chronic ST-induced stress effects experienced by women in the STEM domains may contribute to increased efforts in correcting the issue.

D. Completed Aspects and Projected Timeline.

Winter, 2015: Obtain IRB approval.-**completed**
February 20-May 20 (twelve weeks): **Data collection- because this grant data is being collected in conjunction with another grant the data collection has extended into the fall semester. As of now we have collected 235 samples and intend on collecting an additional 58 samples.**
May 21 – July 21(eight weeks): DNA processing- **as of now we have 180 samples that have been returned from CORE and are waiting for the results from an additional 55 samples at which time we can begin initial data analysis. Complete data analysis will be done when all samples have been collected and analyzed by the end of the fall 2015 semester.**
July 22 – August 12 (three weeks): Study data analysis and write-up manuscript for peer-reviewed journal submission. **This will now be done over the winter and into the spring semester because of extended data collection.**
Fall, 2015: Present findings at the CSD brown bag series and a social psychology brown bag meeting. **We will present findings during the Spring 2016 CDS brown bag series.**
Spring, 2016: Present findings at a national conference. **This will most likely take place not only in the spring but also during the summer and fall of 2016.**

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