OMB No. 0925-0001 and 0925-0002 (Rev. 12/2020 Approved Through 02/28/2023)

 BIOGRAPHICAL SKETCH

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

NAME: Coleman Jr, Leon Garland

eRA COMMONS USER NAME (credential, e.g., agency login): leoncoleman

POSITION TITLE: Assistant Professor of Pharmacology, University of North Carolina School of Medicine

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

| INSTITUTION AND LOCATION | DEGREE(if applicable) | Completion DateMM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| University of Virginia, Charlottesville, VA | BS | 2003 | Chemical Engineering |
| University of North Carolina, Chapel Hill, NC | M.D./PhD | 5/2012 | PhD in Neurobiology 2010MD 2012 |

**A. Personal Statement**

My scientific goal is to identify novel therapeutic approaches for inflammatory diseases including addiction, Alzheimer’s disease, and cancer. I have witnessed first-hand the merciless effects these diseases have on individuals, families, and communities. Therefore, I am highly motivated to make impactful discoveries that could lead to new therapeutics. The quest to find new therapies involves a life-long commitment that is the priority of my mission. I am funded by NIAAA to study both the central and peripheral effects of ethanol on cellular biological processes that contribute to both addiction and alcohol-related diseases. I am a K08 awardee and have received an R01 studying the contribution of alcohol abuse to Alzheimer’s pathology and an R21 studying the effect of alcohol on anti-PD1 immunotherapy efficacy. Other ongoing projects include the role of neuroimmune signaling on ethanol-induced neurodegeneration, cognitive dysfunction, and mood dysfunction as well as novel immune mechanisms that promote poor outcomes in critically ill burn patients.

I began my independent research program in the UNC Department of Pharmacology in July of 2020. I am experienced in neuropharmacology and neuroimmune signaling using a broad array of technical approaches including: animal behavior, immunohistochemistry, cell culture, molecular biochemical assays (e.g. RT-PCR, ELISA, and Western Blot), immunological assays (e.g. flow cytometry, nanostring), microvesicle analyses, electron microscopy, and MRI analyses. I completed the MD/PhD program at the University of North Carolina at Chapel Hill. During that time, I received and completed an F30 Ruth L. Kirschstein NRSA award for MD/PhD students investigating the effects of alcohol on brain development during the third trimester and adolescence (F30AA018051-01). The findings from that award were impactful, resulting in (1) foundational data for the preparation and submission for an ongoing NIAAA-NADIA consortium grant (2) highly cited peer-reviewed first author publications in top alcohol research journals (3) National attention: research was selected as a “Hot Topic” by the Society for Neuroscience in 2009 (4) and media coverage on WRAL and UNC Healthcare News (5) Lectures to middle and high school students using our results to inform them about the risks of binge-drinking. These experiences demonstrate a history of making research discoveries that can have a significant impact. My clinical training and research experience have given me a holistic perspective on health and disease. Further, experiences with patients and families have given me a strong motivation to find solutions that directly impact people’s lives.

Ongoing and recently completed projects that I would like to highlight include:

**Ongoing:**

K08 AA024829: (PI: Coleman) 09/08/17 – 08/31/22 9 Calendar

NIAAA

**Ethanol modulates central and peripheral immune responses via HMGB1, IL-1β and other Immune Signaling Molecules (ISMs).**

R01AA028924: (PI/PD: Coleman) 09/20/20-05/31/25 3 Calendar

NIAAA

**Microglia Activation and TLR-induced Neurodegeneration by Alcohol Promotes Progression of Alzheimer’s Pathology.**

R21AA028599 (PI/PD: Coleman) 05/10/20 – 08/30/22 1.2 Calendar

NIAAA

**Ethanol Inhibition of anti-PD-1 Immunotherapy via T-cell Dysfunction and Intestinal Dysbiosis.**

**COMPLETED:**

K08 AA024829-S1: (Coleman) 09/03/19 – 08/31/20 3 Calendar

NIAAA

**Ethanol modulates central and peripheral immune responses via HMGB1, IL-1β and other Immune Signaling Molecules (ISMs) to enhance Alzheimer’s Pathology.**

AA020023-09S1 (Crews) 09/17/18 – 08/31/19 3 Calendar

NIAAA

**Neurobiology of Adolescent Drinking in Adulthood (NADIA) NADIA Supplement for Alzheimer’s Research.**

F30 AA018051 (Coleman) 09/09/08 – 09/8/12 12 Calendar

NIAAA

**Ruth Kirschstein NRSA F30 award for MD/PhD students.**

**B. Positions, Scientific Appointments, and Honors**

**Positions and Employment**

2004 - 2005 Data Collection and Analysis Specialist, UNC-Hospitals Continuous Quality Improvement

2012 - 2014 General Surgery Resident, University of North Carolina Hospitals

2014 - 2016 Research Associate, Crews Lab, University of North Carolina School of Medicine

2017 - 2020 Research Assistant Professor of Pharmacology, University of North Carolina School of Medicine

2017 - Member, Bowles Center for Alcohol Studies

2020 - Assistant Professor of Pharmacology, University of North Carolina School of Medicine

**Other Pertinent Experience and Professional Memberships**

2004 UNC Medical School “Hidden Topics” Curriculum Committee to design a seminar for the medical school curriculum addressing health disparities and the role of race in medicine.

2004 Chancellor’s Diversity Task Force

2005 Graduate and Professional Student Federation Diversity Affairs, Committee co-chair

2005 UNC Medical School Advisory Panel for Cultural Competence

2008 Search committee for TIBBS Associate Director Position

2008 - Member, Research Society on Alcoholism

2008 - Member, Society for Neuroscience

2009 Summer student research host and advisor for the graduate school Training Initiative in Biomedical and Biological Sciences (TIBBS)

2015-2018 Chair, Minority Health Advisory Committee for the State of North Carolina

2019 Search committee member for Department of Psychiatry Research Assistant Professor Position

2019 - Search committee member for Department of Psychiatry Translational Medicine Position

2020 - Member, International Society for Extracellular Vesicles

2020 Search committee member for Department of Psychiatry Research Assistant Professor Position

2020 Cellular and Molecular Biology of Glia ad-hoc study section member, September 2020

2021 NIAAA Neuroscience study section, June 2021

## Honors and Awards

1999 - 2003 University Achievement Award, University of Virginia

1999 - 2003 Rodman Scholar, University of Virginia

2002 - 2003 Virginia Engineering Foundation Award, University of Virginia

2003 BS in Chemical Engineering with Distinction

2004 - John B. Graham Research Society

2008 - 2012 **National Institute on Alcohol Abuse and Alcoholism: Ruth Kirschstein NRSA F30 award for MD/PhD students (1F30A A018051)**

2009 Speaker, NIAAA Trainee Workshop Meeting Program, New Orleans LA

2009 Research selected as one of the *“Hot Topics”* and press release for the Society for

 Neuroscience 2009 annual meeting

2009 Local news coverage: <http://www.wral.com/lifestyles/healthteam/story/9385540/>

2009 University of North Carolina news coverage: <http://news.unchealthcare.org/news/2011/april>

2009 - 2012 Selected for the Neuroscience Scholars Program, the Society for Neuroscience

2010Best Graduate Student Presentation Award, UNC Radiology Research Day

2013 Eskelund Award for Excellence in Pediatric Surgery, UNC-Hospitals

2016 **ISBRA/ESBRA Junior Investigator Award**

2016 Speaker, ISBRA/ESBRA Junior Investigator Symposium, Berlin, Germany

2016 Speaker, Research Society on Alcoholism, Symposium, New Orleans LA

2016 Speaker, Duke University Neuroimmunogy and Glia Retreat Symposium

2017 - **National Institute on Alcohol Abuse and Alcoholism (NIAAA): K08 Mentored Clinical Scientist Research Career Development Award (AA024829)**

2017 **NIAAA/NIDA Early Career Investigator Showcase Travel Award**

2017 Speaker, NIDA/NIAAA Early Career Investigator Showcase

2017 Speaker, Research Society on Alcoholism, Symposium

2017 Speaker, NCCU/BBRI Spring Seminar Series Symposium, Durham, NC

2017 Speaker, UNC Bowles Center for Alcohol Studies Symposium

2018 Speaker, University of Chicago at Loyola

2018 Speaker, International Society for Biomedical Research on Alcoholism, in Kyoto Japan

2018 Speaker, Society for Neuroscience, Nano-symposium,

2018 Speaker, Research Society on Alcoholism, Symposium

2018 International Society of Biomedical Research on Alcoholism Travel Award

2018 Research Society on Alcoholism, Annual Meeting Program Committee

2019 **UNC Simmons Scholar Awardee,** a 5-year salary support institutional award

2019 Speaker, Society for Leukocyte Biology, Alcohol and Immunology Research Interest Group

2019 Speaker, Society for Neuroscience Nanosymposium on AUD and Alzheimer’s Pathology

2019 Speaker, Society for Neuroscience Nanosymposium on Microvesicles in Neuroinflammation

2019 Speaker, European Society for Biomedical Research on Alcoholism in Lille, France

2019 Speaker, Research Society on Alcoholism Symposium

2020 International Society for Extracellular Vesicles, Member

2021 Invited Speaker, University of North Carolina Bowles Center for Alcohol Studies

2021 Invited Speaker, University of North Carolina Department of Behavioral Psychology

2021 Invited Speaker, Louisiana State University Health Sciences Department of Physiology

**C. Contributions to Science (Maximum 4 Selected Publications per topic)**

1. ***Microvesicle-mediated signaling in burn injury and alcohol use disorder involves Toll-like Receptor (TLR) Signaling and DAMP/cytokine heterocomplexes***. Immune signaling contributes to the pathologies of several disorders such as alcohol use disorder and burn injury. Though immune dysfunction is involved in these pathologies, the mediators underlying this dysfunction and therapeutic targets are unknown. Microvesicles (MVs) have emerged as mediators of innate immune dysfunction. The high comorbidity of alcohol abuse and burn injury, and the worse outcomes in patients with alcohol use disorder led to the development of this project. We found that MVs in response to ethanol and/or burn injury are enriched in DAMPs such as HMGB1 and miRNA let-7b. These DAMPs are endogenous agonists for endosomal immune TLRs (HMGB1-TLR4, let-7b-TLR7). Further, we found MVs are a reservoir for the cytokine IL-1β after burn injury, and that HMGB1 formed complexes IL-1β and let-7b in MVs to enhance their efficacy. These findings identify MVs as key drivers for innate immune signaling and reservoirs of immune mediators. Thus, MVs may represent novel therapeutic targets. In conjunction with my mentors and collaborators, I developed the hypotheses and planned the experiments. I analyzed data and wrote the manuscripts.
	1. Willis ML, Mahung C, Wallet SM, Barnett A, Cairns BA, **Coleman LG Jr**\*, Maile R\*. Plasma extracellular vesicles released after severe burn injury modulate macrophage phenotype and function. Journal of Leukocyte Biology 2021. doi: 10.1002/JLB.3MIA0321-150RR.
	2. Crews, Zou, and **Coleman.** Extracellular microvesicles promote microglia-mediated pro-inflammatory responses to ethanol. Journal of Neuroscience Research 2021. doi:10.1002/jnr.24813. PMID: 33611821
	3. **Coleman LG Jr**, Maile R, Jones SW, Cairns BA, Crews FT. HMGB1/IL-1β complexes in plasma microvesicles modulate immune responses to burn injury. PLoS One. 2018 Mar 30;13(3):e0195335.
	4. **Coleman LG Jr**, Zou J, Qin L, Crews FT. HMGB1/IL-1β complexes regulate neuroimmune responses in alcoholism. Brain Behavior and Immunity. 2018 Aug;72:61-77
2. ***Microglial and Toll-like Receptor Signaling in the Neuropathology of Alcohol Use Disorder.*** Neuroimmune activation is emerging as playing a key role in the pathology of alcohol use disorder. Sterile inflammation via activation of Toll-like Receptors (TLRs) and cytokine signaling might regulate neuronal dysfunction, neuronal cell death, and neuronal circuits to contribute to the formation of alcohol-associated behavioral phenotypes. We found that alcohol causes induction of innate immune signaling in brain that contributes to pathologic features such as neurodegeneration. We find that microglia play a key role, with microglial depletion and repopulation restoring aspects of alcohol-induced pathology. This implicates neuroimmune signaling as a key and causative feature of alcohol-induced pathology. These findings have indicated that neuroimmune signaling contributes to pathologic features of alcohol use disorder, which may be targeted therapeutically. In conjunction with my mentors and collaborators, I developed the hypotheses and planned the experiments. I analyzed data and wrote the manuscripts.
	1. Qin L, Zou J, Barnett AM, Vetreno RP, Crews FT, and **Coleman LG.** TRAIL Mediates Neuronal Death in AUD: A Link Between Neuroinflammation and Neurodegeneration. *Int. J. Mol. Sci. 2021, 22(5), 2547; https://doi.org/10.3390/ijms22052547*
	2. Barnett AM, Crews FT, and **Coleman LG.** Microglial depletion and repopulation: a new era of regenerative medicine? *Neural Regeneration Research* 2021. June; 16(6):1204-1205. Doi: 10.4103/1673-5374.300439
	3. **Coleman,** Zou and Crews. Microglial depletion and repopulation in brain slice culture normalizes sensitized proinflammatory signaling. *J Neuroinflammation.* 2020 Jan 18;17(1):272019
	4. **Coleman LG Jr,** Zou J, and Crews FT. Microglial-derived miRNA let-7 and HMGB1 contribute to ethanol-induced neurotoxicity via TLR7. *Journal of Neuroinflammation*  January *2017*; 14(1):22.
3. ***Effect of Alcohol on Brain Development During Adolescence, Young Adulthood and the Late Pregnancy*.** Alcohol abuse during the adolescent period in particular is associated with and increased risk of developing alcoholism in adulthood. The early postnatal period is associated with heightened vulnerability to ethanol toxicity. Little was known, however, on the effects of ethanol exposure during the third trimester. Adolescent binge ethanol treatment reduces adult neurotransmitter gene expression, particularly cholinergic genes, reduces basal forebrain and olfactory bulb volumes, and causes a reduction in the density of basal forebrain acetylcholine neurons. Adolescent binge ethanol also caused persistent anxiety like behavior in reversal learning deficits into adulthood. These behaviors are thought to be involved in perseveration and the maintenance of addiction. Adolescent binge ethanol also resulted in permanent changes in the brain extracellular matrix, which might contribute cognitive inflexibility. In summary, adolescent binge causes permanent alterations in brain structure and behavior. These findings have informed the public regarding the dangers of underage drinking. In addition, these studies were the basis of a subsequently funded NIAAA-NADIA consortium. I performed the experiments, analyzed the tissues and the data.

We found that ethanol treatment during the analog of the human third trimester causes persistent reductions in adult brain volume, frontal cortical neuron number and adult neurogenesis. This may proceed through the NMDA antagonism effect of ethanol. These findings show that the third trimester of pregnancy is also a ‘danger period’ for alcohol use. This informs debate regarding alcohol consumption during pregnancy. This may proceed through the NMDA antagonism effect of ethanol.

 Both local and national media covered the findings from these projects. The manuscripts prepared from this work have been cited approximately 188 times. I prepared first author manuscripts and presentations under the supervision of my mentor.

* 1. **Coleman LG, Jr,** Liu W, Oguz I, Styner M, Crews FT. Adolescent binge ethanol treatment alters adult brain regional volumes, cortical extracellular matrix protein and behavioral flexibility. *Pharmacology, Biochemistry and Behavior 2013*.
	2. **Coleman LG Jr,** He J, Lee J, Styner M, Crews FT. Adolescent binge drinking alters adult brain neurotransmitter gene expression, behavior, brain regional volumes and neurochemistry in mice. Alcoholism: Clinical and Experimental Research April 2011; 35(4):671-88
	3. **Coleman LG Jr,** Oguz I, Styner M, and Fulton T. Crews. Persistent effects of P7 ethanol treatment on adult mouse brain: reduced brain volume, frontal cortical neuron reductions and altered adult hippocampal neurogenesis. *Alcohol* September 2012; 46(6):603-12
	4. **Coleman LG Jr**, Jarskog LF, Moy SS, Crews FT. Deficits in adult prefrontal cortex neurons and behavior following early post-natal NMDA antagonist treatment. *Pharmacology, Biochemistry and Behavior* 2009; 93(3):322-30.
1. ***Oxidized low density lipoprotein activates blood platelets.*** Elevated plasma levels of low-density lipoprotein are a well-recognized risk factor for stroke, heart attack, and atherosclerosis. This relationship has been linked to increased amounts of oxidized low-density lipoprotein (ox-LDL) present in atherosclerotic plaques. Oxidized-LDL is highly effective at inducing platelet activation, causing stable aggregation and alpha-granule secretion dependent on p38 MAPK activation. In conjunction with my mentor and collaborators, I developed the hypotheses and planned the experiments. I performed the experiments and analyzed the data. I prepared a first author manuscript under the supervision of my mentor. This data supported the hypothesis that ox-LDL stimulates platelets and is involved in the pathogenesis of stroke and heart attack. Further, it identified the p38 MAPK pathway as critical for this activation, identifying a potential drug target for platelet protection.
	1. **Coleman LG Jr**, Polanowska-Grabowska RK, Marcinkiewicz M, and Gear AR: LDL oxidized by hypochlorous acid causes irreversible platelet aggregation when combined with low levels of ADP, thrombin, epinephrine, or macrophage-derived chemokine (CCL22). *Blood*. 2004; 104(2):380-9.

**Complete List of Published Work in NCBI MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/leon.coleman.1/bibliography/public/>