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 |
| University of North Carolina Hospitals, Chapel Hill NC | Residency | 6/2014 | General Surgery |
| University of North Carolina at Chapel Hill, NC | Postdoc | 1/2018 | Neurobiology and Immunology |

**A. Personal Statement**

I am excited to participate as a Research Training Faculty member for this Translational T32 application. Mentoring is a key foundation of my laboratory and have mentored 10 students to date (8 undergraduate and 2 graduate) in the 2 years of leading an independent research program. Fifty percent of these students have been from under-represented ethnic minority groups. As an African American physician-scientist, I have benefitted greatly from both caring mentorship and targeted collaborations. I am co-Director of the Carolina Summer Fellows program in the Department of Pharmacology and am a leader on a U54 Collaborative Partnership renewal between UNC and North Carolina Central University, a local Historically Black University, where I serve as co-PI of the Student Mentoring Core. As an MD/PhD scientist, I believe I have a unique perspective and skill set to help train the next generation of diverse scientists that conduct ethically sound and rigorous scientific research. Further, we are devoted to ensuring the safety of all individuals in our group. We also recognize that students often pursue careers beyond academia, thus we support student participation in activities such as industry internships and mentor students such that they complete their Ph.D. in a timely fashion to facilitate their transition into the biomedical career of their choice.

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 completed a K08 award, have received an R01 studying the contribution of alcohol abuse to Alzheimer’s pathology, and an R21 studying determinants of response to cancer immunotherapy. My doctoral training in both medicine and biology have given me expertise across multiple organ systems; thus, I am able to mentor across multiple translational research focuses. I am experienced in 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), extracellular vesicle analyses, electron microscopy, and MRI analyses. My experience as a General Surgery resident made me intimately aware of the suffering of patients. Driven by these experiences we have sought to find underlying drivers of immune dysfunction across multiple disease. Ongoing and recently completed projects that I would like to highlight include:

**Ongoing:**

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.**

P60 AA011605-21: (PI: Kash) 12/1/22-11/30/26 1.2 Calendar

NIAAA (co-I: Coleman)

**Molecular and Cellular Pathogenesis in Alcoholism**

R21AA028599 (PI/PD: Coleman) 05/10/21 – 08/30/23 1.2 Calendar

NIAAA

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

U54AA030463 (PI: Crews) 10/1/2022-9/30/27 1.2 Calendar

NIAAA (co-I: Coleman)

**Partnerships to Enhance Alcohol Research Across NCCU and UNC (PEAR-NC)**

**Pending:**

R01GM149731: (PI: Coleman) 4/1/23-3/31/28 3 Calendar

NIGMS

**Extracellular Vesicles as Novel Therapeutic Targets for Burn Injury**

**Completed:**

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).**

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**

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

2017 - Member, Bowles Center for Alcohol Studies

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

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

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

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

**Other Pertinent Experience and Professional Memberships**

2022- Cellular and Molecular Biology of Glia study section member

2022- Society of Leukocyte Biology Editorial Board member

2022 - Research Society on Alcoholism Fundraising Committee

2021 - Co-Director, UNC Carolina Summer Fellows Program

2021 - Mentor, Neuroscience Scholars Program, Society for Neuroscience

2021 - UNC MD-PhD Advisory Committee

2021 NIAAA Neuroscience study section, June 2021

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

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

2020 - Member, International Society for Extracellular Vesicles

2019 Search committee member for Department of Psychiatry Translational Medicine Position

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

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

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

2008 - Member, Society for Neuroscience

2008 - Member, Research Society on Alcoholism

2008 Search committee for TIBBS Associate Director Position

2005 UNC Medical School Advisory Panel for Cultural Competence

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

2004 Chancellor’s Diversity Task Force

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.

## Honors and Awards

2022 Invited Speaker, Gordon Research Seminar on Alcohol-induced tissue injury

2022 Invited Speaker, Gordon Research Conference on Alcohol-induced tissue injury

2022 Symposium, Winter Brain Research Conference

2021 Invited Speaker, Neurobiology of Addiction Seminar, www.world-wide.org

2021 Invited Speaker, NIAAA-wide T32 Symposium

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

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

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

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

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

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

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

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

2010Best Graduate Student Presentation Award, UNC Radiology Research Day

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

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

2004 - John B. Graham Research Society

2003 BS in Chemical Engineering with Distinction

2002 - 2003 Virginia Engineering Foundation Award, University of Virginia

1999 - 2003 University Achievement Award, University of Virginia

1999 - 2003 Rodman Scholar, University of Virginia

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

**Complete List of Published Work in NCBI MyBibliography (>1,000 citations):**

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

1. ***Microglial and Toll-like Receptor Signaling in Alcohol-Related Neurodegeneration and Alzheimer’s disease.*** 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 also find that alcohol promotes Alzheimer’s pathology, which involves microglial activation. Microglia depletion and repopulation is promising intervention, restoring aspects of alcohol-induced neuroinflammation. Together, these findings have indicated that neuroimmune signaling contributes to pathologic features of alcohol use disorder, which may be targeted therapeutically.
	1. Barnett AM, David E, Rohlman A, Nikolova VD, Moy SS, Vetreno RP, and **Coleman LG Jr**. Adolescent Binge Alcohol Enhances Early Alzheimer's Disease Pathology in Adulthood Through Proinflammatory Neuroimmune Activation. *Frontiers in Pharmacology.* 2022;13:884170. doi: 10.3389/fphar.2022.884170.
	2. 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*
	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. Crews FT, Lawrimore CJ, Walter TJ, **Coleman LG Jr**. The role of neuroimmune signaling in alcoholism. Neuropharmacology. 2017 Aug 1;122:56-73. doi: 10.1016/j.neuropharm.2017.01.031. Epub 2017 Feb 1. Review. PubMed PMID: 28159648; PubMed Central PMCID: PMC5493978.
2. ***Extracellular vesicles mediate immune signaling in alcohol use disorder***. Immune signaling contributes to the pathology of alcohol use disorder. Though immune dysfunction is involved in these pathologies, the mediators underlying this dysfunction and therapeutic targets are unknown. Extracellular vesicles (EVs) have emerged as mediators of innate immune dysfunction. We found that EVs released in response to ethanol are enriched in damage-associated molecular pattern molecules (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 that HMGB1 formed complexes IL-1β and let-7b in EVs to enhance their activity. Recently, we found that EVs are critical mediators of alcohol-induced neuroinflammation, with blockade of their secretion preventing immune responses. Thus, EVs may represent novel therapeutic targets for neuroinflammation. In conjunction with my collaborators, I developed the hypotheses and planned the experiments. I analyzed data and wrote the manuscripts.
	1. Zou J, Walter TJ, Barnett AM, Rohlman A, Crews FT, **Coleman LG Jr.** Ethanol Induces Secretion of Proinflammatory Extracellular Vesicles that Inhibit Adult Hippocampal Neurogenesis Through G9a/GLP-Epigenetic Signaling. *Frontiers in Immunology.* 2022; 13. doi: 10.3389/fimmu.2022.866073.
	2. **Coleman LG**. The emerging world of subcellular biological medicine: extracellular vesicles as novel biomarkers, targets, and therapeutics. Neural Regen Res. 2022 May;17(5):1020-1022. doi: 10.4103/1673-5374.324846. PMID: 34558528.
	3. 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
	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
	5. **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. ***Extracellular vesicles promote immune dysfunction after burn injury and pancreatitis***. Immune dysfunction is key in the morbidity and mortality after trauma and infection. Druggable mediators that underlying this dysfunction and therapeutic targets are unknown. We recently found that EVs released in response to burn injury promote immune dysfunction after burn injury and their contents (protein and miRNA) may be used as biomarkers. These findings identify EVs as key drivers for innate immune signaling and reservoirs of immune mediators. We are continuing to investigate the predictive value of EV contents in identifying at risk patients and the utility of blocking EVs therapeutically. In conjunction with my collaborators, I developed the hypotheses, planned the experiments, 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. \*denotes co-senior author
	2. Maile R, Willis ML, Herring LE, Prevatte A, Mahung C, Cairns B, Wallet S, **Coleman LG Jr**. Burn Injury Induces Proinflammatory Plasma Extracellular Vesicles That Associate with Length of Hospital Stay in Women: CRP and SAA1 as Potential Prognostic Indicators. Int. J. Mol. Sci. 2021, 22(18), 10083; doi: 10.3390/ijms221810083.
	3. Desai CS, Khan A, Bellio MA, Willis ML, Mahung C, Ma X, Baldwin X, Williams BM, Baron TH, **Coleman LG**, Wallet SM, Maile R. Characterization of extracellular vesicle miRNA identified in peripheral blood of chronic pancreatitis patients. Mol Cell Biochem. 2021 Aug 27. doi: 10.1007/s11010-021-04248-5. PMID: 34448998
	4. **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. ***Persistent effects of Alcohol on Brain Development During Adolescence and Late Pregnancy*.** Alcohol abuse during adolescence is associated with increased risk of developing alcohol use disorder. The early postnatal period is associated with heightened vulnerability to ethanol toxicity. 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 caused persistent anxiety like behavior and reversal learning deficits in 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. These findings have informed the public regarding underage drinking and were the basis of an ongoing NIAAA-NADIA consortium. We further 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. 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,** 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
	3. **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
	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.