BIOGRAPHICAL SKETCH

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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 Date MM/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 2010 MD 2012

A. Personal Statement

I am excited about this new R01 application that determines if extracellular vesicles can be targeted therapeutically to improve outcomes in burn patients. Burn patients are among the sickest patients in the hospital. My experience as a General Surgery resident made me intimately aware of this reality. I was stunned to discover that long-lasting immune dysfunction was the major cause of death in these critically ill patients. However, to date there are no effective immune therapeutic strategies. Driven by these experiences we have sought to find underlying drivers of immune dysfunction after burn injury. This led to studying burn-induced immune dysfunction being a key portion of my K08 award, where we investigated the role of EV signaling as drivers of immune pathology. Our recent manuscripts have found that EVs released early after burn recapitulate the immune dysfunction seen early after burn. This has led to the development of this proposal, where we use various translational approaches that target EV signaling to restore immune function. The work proposed in this R01 is an outgrowth of my K08 and involves collaborations that were formed from that ongoing project. Rob Maile (co-PI and close collaborator), Bruce Cairns (co-investigator and co-mentor on my K08), and I are excited to build on our recent reports to move towards these new therapeutic approaches. The work in my group also focuses on novel mechanisms of immune induction in brain and the periphery. Our recent work implicates CNS-peripheral neuro-immune crosstalk in burn immune dysfunction. This is a new concept which could have significant implications across a range of immune disorders.

My scientific goal is to identify novel therapeutic targets for inflammatory diseases. Regarding my motivation to perform translational research, I have witnessed first-hand the merciless effects critical illness can 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 to not only making discoveries but helping to produce scientists who make discoveries. I am funded by NIH to study cellular and molecular mechanisms that contribute to both central and peripheral inflammatory processes. Other projects include an R01 studying the contribution of alcohol abuse to Alzheimer's pathology and an R21 studying the effect of alcohol on anti-PD1 cancer immunotherapy efficacy. I am experienced in studying pharmacology and immune biology using a broad array of technical approaches including: EV assays, animal models, immunohistochemistry, cell culture, molecular biochemical assays (e.g. RT-PCR, ELISA, and Western Blot), immunological assays (e.g. flow cytometry, nanostring), electron microscopy, and MRI. 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).

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) 05/10/21 – 08/30/23 1.2 Calendar
NIAAA
Ethanol Inhibition of anti-PD-1 Immunotherapy via T-cell Dysfunction and Intestinal Dysbiosis.

Pending:

P60 AA011605-21: (PI: Kash) 12/1/22-11/30/26 1.2 Calendar
NIAAA (co-I: Coleman)
Molecular and Cellular Pathogenesis in Alcoholism

U54 AA019767-07 (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)

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

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 - 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
2010 Best 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 (920 citations):
https://www.ncbi.nlm.nih.gov/myncbi/leon.coleman.1/bibliography/public/

1. ***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.
   a. 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
   b. 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.
   c. 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
   d. **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.

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.
   a. 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.
   b. **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.
   c. 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

d. **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

e. **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. ***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.
   a. 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.
   b. 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*
   c. **Coleman,** Zou and Crews. Microglial depletion and repopulation in brain slice culture normalizes sensitized proinflammatory signaling. *J Neuroinflammation.* 2020 Jan 18;17(1):272019
   d. 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.

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.
   a. **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*.
   b. **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
   c. **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
   d. **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.