

**EAST TENNESSEE STATE UNIVERSITY
JAMES H. QUILLEN COLLEGE OF MEDICINE
SUMMARY OF SCHOLARLY ACTIVITIES
DEPARTMENT OF SURGERY**

July 1, 2019 through June 30, 2020

I. PUBLICATIONS

A. Journal Publications

Hernandez A, Patil NK, Stothers CL, Luan L, McBride MA, Owen AM, Burelbach KR, **Williams DL**, Sherwood ER, Bohannon JK. Immunobiology and application of toll-like receptor 4 agonists to augment host resistance to infection. *Pharmacol Res.* 2019 Dec; 150:104502. PMC6884699

Hoyer FF, Naxerova K, Schloss MJ, Hulsmans M, Nair AV, Dutta P, Calcagno DM, Herisson F, Anzai A, Sun Y, Wojtkiewicz G, Rohde D, Frodermann V, Vandoorne K, Courties G, Iwamoto Y, Garris CS, **Williams DL**, Breton S, Brown D, Whalen M, Libby P, Pittet MJ, King KR, Weissleder R, Swirski FK, Nahrendorf M. Tissue-Specific Macrophage Responses to Remote Injury Impact the Outcome of Subsequent Local Immune Challenge. *Immunity.* 2019 Nov 19; 51(5):889-914.e7. PMC6892583

Lajqi T, Lang GP, Haas F, **Williams DL**, Hudalla H, Bauer M, Groth M, Wetzker R, Bauer R. Memory-Like Inflammatory Responses of Microglia to Rising Doses of LPS: Key Role of PI3Ky. *Front Immunol.* 2019 Nov 8; 10:2492. PMC6856213

Tu F, Wang X, Zhang X, Ha T, Wang Y, Fan M, Yang K, Gill PS, Ozment TR, Dai Y, Liu L, Williams DL, Li C. Novel Role of Endothelial Derived Exosomal HSPA12B in Regulating Macrophage Inflammatory Responses in Polymicrobial Sepsis. *Front Immunol.* 2020;11:825. doi: 10.3389/fimmu.2020.00825. eCollection 2020. PubMed PMID: 32457753; PubMed Central PMCID: PMC7221167.

Bosteels C, Neyt K, Vanheerswynghe M, van Helden MJ, Sichien D, Debeuf N, De Prijck S, Bosteels V, Vandamme N, Martens L, Saeys Y, Louagie E, Lesage M, **Williams DL**, Tang SC, Mayer JU, Ronchese F, Scott CL, Hammad H, Guillemins M, Lambrecht BN. Inflammatory Type 2 cDCs Acquire Features of cDC1s and Macrophages to Orchestrate Immunity to Respiratory Virus Infection. *Immunity.* 2020 Jun 16;52(6):1039-1056.e9. doi: 10.1016/j.immuni.2020.04.005. Epub 2020 May 8. PubMed PMID: 32392463; PubMed Central PMCID: PMC7207120.

Zhang X, Wang X, Fan M, et al. Endothelial HSPA12B Exerts Protection Against Sepsis-Induced Severe Cardiomyopathy via Suppression of Adhesion Molecule Expression by miR-126. *Front Immunol.* 2020;11:566. Published 2020 Apr 29. doi:10.3389/fimmu.2020.00566

Hoover DB, Poston MD, Brown S, Lawson SE, Bond CE, Downs AM, **Williams DL, Ozment**

TR. Cholinergic leukocytes in sepsis and at the neuroimmune junction in the spleen. *Int Immunopharmacol.* 2020 Apr;81:106359. doi: 10.1016/j.intimp.2020.106359. Epub 2020 Mar 3. PubMed PMID: 32143148; PubMed Central PMCID: PMC7315439.

Lu, X., He, Y., Tang, C. et al. Triad3A attenuates pathological cardiac hypertrophy involving the augmentation of ubiquitination-mediated degradation of TLR4 and TLR9. *Basic Res Cardiol* 115, 19 (2020). <https://doi.org/10.1007/s00395-020-0779-1>

Zhao Q, Yang J, Chen H, et al. Peli1 induction impairs cardiac microvascular endothelium through Hsp90 dissociation from IRE1 α . *Biochim Biophys Acta Mol Basis Dis.* 2019;1865(10):2606-2617. doi:10.1016/j.bbadis.2019.06.017

Zhong Y, Mohan K, Liu J, Al-Attar A, Lin P, Flight RM, Sun Q, Warmoes MO, Deshpande RR, Liu H, Jung KS, Mitov MI, Lin N, Butterfield DA, Lu S, Liu J, Moseley HNB, Fan TWM, **Kleinman ME**, Wang QJ. Loss of CLN3, the gene mutated in juvenile neuronal ceroid lipofuscinosis, leads to metabolic impairment and autophagy induction in retina pigment epithelium [published online ahead of print, 2020 Jun 24]. *Biochim Biophys Acta Mol Basis Dis.* 2020;165883. doi:10.1016/j.bbadis.2020.165883

B. Books or Chapters

C. Proceedings

PAPERS, ABSTRACTS, AND/OR PRESENTATIONS

A. Regional and National

Fan M, Yang K, Wang Y, Tu F, Ha T, Liu L, Kalbfleisch J, Williams DL, Li C. Endothelial Hspa12b and Yap Cooperatively Promote Angiogenesis Following Myocardial Infarction. Abstract submitted to AHA Scientific Sessions, Nov. 16-18, 2019, Philadelphia, PA.

Gill PS, Hall JV, Ozment TR, Williams DL. Age-Related Changes in the Gut Microbiome are Reversed by Innate Immune Training. Abstract submitted to Shock Society Annual Meeting, 2020.

Gill PS, Ozment TR, Williams DL. Innate immune training modulates myeloid derived cell (MDSC) populations in polymicrobial sepsis. Abstract submitted to INTRIM meeting, Nijmegen, The Netherlands, Oct. 31- Nov. 2, 2019.

Gill PS, Hall JV, Ozment TR, Williams DL. Training the innate immune system reverses age related changes to the fecal microbiome. Abstract submitted to INTRIM meeting, Nijmegen, The Netherlands, Oct. 31- Nov. 2, 2019.

Grey E, Lee J, Hodge M, Drain placement during Bariatric surgery: Helpful or Harmful? Abstract submitted to Southeastern Surgical Conference, 2/8/2020 – 2/11/2020. New Orleans, LA.

Tarwater S, Hopkins S. Ultraputative management of sympathetic chain cecal schwannoma during carotid endarterectomy. Submitted for presentation at the Southeastern Surgical Congress, 2/8/2020 – 2/11/2020. New Orleans, LA.

Wang Y, Yang K, Gill S, Fan M, Tu F, Ha T, Liu L, Kalbfleisch J, Williams DL, Li C. Endothelial Cell Specific Hspa12b Promotes Macrophage Polarization Toward To A Regenerative Phenotype Following Myocardial Infarction. Abstract submitted to AHA Scientific Sessions, Nov. 16-18, 2019, Philadelphia, PA.

Yang K, Xu J, Tu F, Wang X, Fan M, Ha T, Kalbfleisch J, Williams D, Li C. Lactate suppresses macrophage pro-inflammatory response to LPS stimulation by inhibition of YAP and NF-kB activation via GPR81 mediated signaling. Abstract submitted to Shock Society Meeting, 2020.

B. International

III. INVITED PRESENTATIONS

A. Grand Rounds

B. National or International Meetings

Williams DL. Visiting Professor at The University of Nottingham School of Medicine and Health Sciences. Presentation: Trained Immunity as a New Approach to the Management of Sepsis. (10/19/19 – 11/9/19)

IV. OTHER

National and International Peer-review Committees

Li, C. : NIH SAT Review Session for Cardiovascular Differentiation & Development

Kleinman, M. : EBM of Translational Vision Science and Technology and Tomography

Journal Reviewers:

Williams DL.

Li C.

Browder IW.

Kleinman, M.

V. VISITING PROFESSORS

IV. OTHER

VI. EXTRAMURAL FUNDING

Number of PI's on Funded Grants: 6

VI EXTRAMURAL FUNDING

Peer Review (NIH, AHA, etc.)

Faculty	Agency	Project Period	Current Year Award	Total Award
Li & Wms	NIH-R01 ¹	9/1/18-5/31/19	\$225,000	\$1,332,000
Ozment	NIH-R01 ⁴	5/1/19 – 4/30/20	\$195,000	\$1,443,000
Williams/ Sherwood	NIH-R01 ²	2/1/19 – 1/31/20	\$453,237	\$534,819

Li	NIH-R01 ³	3/1/19 – 2/28/20	\$359,612	\$2,128,904
Kleinman	BrightFocus Foundation ⁵	7/1/18 – 12/30/20	\$160,000	\$160,000
Kleinman	NIH-EY028206 ⁶	4/18 – 3/23	\$376,250	1,881,250
Total Funding Received:				
Total for Multi-Year Commitments:				

¹ 2R01GM083016-09 – Competing Renewal of “Innate Immunity and Cardiovascular Function in Sepsis” 9/1/18 - 5/31/22.

²R01 – Training Innate Immunity: A new approach to the treatment of sepsis, Unfunded extension

³R01 – Role of Toll-Like Receptor Signaling in Cardiac Ischemia, Year 1 of 4

⁴R01 – Cellular and Molecular Mechanisms of Fungal Sepsis in the Critically Ill Patient, Year 3 of 5

⁵BrightFocus – Dysregulation of the Acetylome in Age-Related Macular Degeneration

⁶NIH-EY028206 – The Role of Histone Deacetylases in Age-related Macular Degeneration

Other Sponsored Activities – Current (Chair of Carroll Long, RDC, etc.)

Faculty	Agency	Project Period	Current Year Award	Total Award
Williams	Carroll Long Chair	7/1/18-6/30/19	100,000	100,000
Williams	Subcontract with U of Montana	9/29/18 – 9/28/19	\$470,900 (DC)	\$696,932 (TC)
Total Funding Received:				
Total for Multi-Year Commitments:				

VII PENDING EXTRAMURAL APPLICATIONS

(Means proposed but unfunded.)

Faculty	Agency	Project Period	Request	Funded?
Li	NIH ¹	7/1/19 – 6/30/23	\$532,226	Yes
Williams	NIH ² S10	2/1/19 –	\$499,875.00	no

		1/31/20		
Li	NIH ³	1/1/20 – 12/31/24	\$2,854,962.00	yes
Williams	DOD Grant ⁴	1/1/20 – 12/31/22	\$3,626,364.00	no
DL Williams & Ivan Zanoni	NIH ⁵	2021-2026	820,446	no
TR Ozment	NIH ⁶	10/1/20 – 9/30/21	\$59,900	yes
Total Funding Received				
Total for Multi-Year Commitments				

¹Competing Renewal of “Role of Toll-Like Receptor Signaling in Cardiac Ischemia”

²Upgrade of 400 MHz NMR Spectrometer with high performance digital console and cryoprobe- S10 Proposal.

³Novel Role of Lactate for Cardiovascular dysfunction in sepsis

⁴Development of a Vaccine for the Prevention and/or Treatment of the Emerging Fungal Pathogen Candida auris

⁵Development of a vaccine against the emerging fungal pathogen Candida auris

⁶NIGMS Equipment Supplement 2020Equipment supplement request for Mesoscale QuickPlex SQ 120MM Reader