BIOGRAPHICAL SKETCH

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NAME: Lauren M. Aleksunes

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

POSITION TITLE: Professor

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 Connecticut, Storrs, CT	B.S.	05/2000	Pharmacy Studies
University of Connecticut, Storrs, CT	Pharm.D.	05/2002	Pharmacy
University of Connecticut, Storrs, CT	Ph.D.	12/2006	Pharmacology & Toxicology
Univ. of Kansas Medical Center, Kansas City, KS	Postdoctoral Fellow	08/2009	Pharmacology & Toxicology

A. Personal Statement

I am a board-certified toxicologist with expertise in both basic and clinical toxicology. I was the first recipient of dual Pharm.D. and Ph.D. degrees at the Univ. Connecticut. My postdoctoral training in mechanistic toxicology was completed at the Univ. Kansas Medical Center. Since arriving at Rutgers University in 2009, the research of my laboratory has aimed to identify mechanistic roles for xenobiotic transporters in target organ toxicities with particular focus on the blood-brain and blood-placental barriers. Our research addresses the impact of interindividual variation in transporter expression and function, due to life stage, genetics/epigenetics, diet, environment, and pre-existing disease, on susceptibility to chemical toxicity. Our laboratory has been highly productive in the fields of transporter biology and toxicology with 130 publications (h-index: 44). In 2010, I published a review article on xenobiotic transporters in *Pharmacological Reviews* that has been cited over 750 times. In 2019, I received the Outstanding Young Investigator Award from the Society of Toxicology Women in Toxicology and the Richard Okita Early Career Award in Drug Metabolism and Disposition from the American Society for Pharmacology and Experimental Therapeutics.

I have a long-standing track record investigating biomarkers and susceptibility factors for drug-induced nephrotoxicity in animals and cancer patients. We have recently characterized a humanized mouse line for its ability to recapitulate the renal toxicities of immune checkpoint inhibitors observed in patients. We recently received a NJ Health Foundation grant to validate this model.

- Wen X, Buckley B, McCandlish E, Manautou J, Goedken M, **Aleksunes L** (2014) Transgenic expression of the human MRP2 transporter reduces cisplatin accumulation and nephrotoxicity in Mrp2-null mice. *Am J Pathol.* 184:1299-308. PMCID:PMC4005989.
- George B, Wen X, Mercke N, Gomez M, O-Bryant C, Bowles D, Hu Y, Hogan S, Joy M, **Aleksunes L** (2017) Profiling of kidney injury biomarkers in patients receiving cisplatin: time-dependent changes in the absence of clinical nephrotoxicity. *Clin Pharm Ther.* 101:510-8. PMCID:PMC5359028.
- George B, Wen X, Mercke N, Gomez M, O'Bryant C, Bowles D, Hu Y, Hogan S, Joy M, **Aleksunes L** (2020) Time-dependent changes in kidney injury biomarkers in patients receiving multiple cycles of cisplatin. *Toxicol Rep.* 7:571-576. PMCID:PMC32382514.
- Ibrahim M, Chang C, Hu Y, Hogan S, Mercke N, Gomez M, O'Bryant C, Bowles D, George B, Wen X, Buckley B, **Aleksunes L**, Joy M (2019) Pharmacokinetic determinants of cisplatin-induced subclinical kidney injury in oncology patients. *Euro J Clin Pharmacol.* 75(1):51-57. PMCID:PMC6656531.

- Chang C, Hu Y, Hogan S, Mercke N, Gomez M, O-Bryant C, Bowles D, George B, Wen X, **Aleksunes** L, Joy M (2017) Pharmacogenomic variants influence the urinary excretion of novel kidney injury biomarkers in patients receiving cisplatin. *Int J Mol Sci.* 18(7). PMCID:PMC5535826.

B. Positions, Scientific Appointments, and Honors

Positions

2019-Pres Lead, Workforce Development Core, NJ Alliance for Clinical and Translational Science (CTSA), New Brunswick, NJ
2019-Pres Professor, Rutgers University, Piscataway, NJ
2015-Pres Director, Joint Graduate Program in Toxicology, Rutgers University, Piscataway, NJ
2014-2019 Associate Professor with Tenure, Rutgers University, Piscataway, NJ
2009-2014 Assistant Professor, Rutgers University, Piscataway, NJ
2007-2009 Postdoctoral Fellow, University of Kansas Medical Center, Dept. Pharmacology and Toxicology, Kansas City, KS
2003-2004 Poison Information Provider, Connecticut Poison Control Center, Farmington, CT
2002-Pres Licensed Pharmacist, Connecticut
2002-2006 Staff Pharmacist, CVS Pharmacy, Kensington and Mansfield, CT
2002-2006 Predoctoral Fellow, University of Connecticut, Dept. Pharmaceutical Sciences, Storrs, CT

Scientific Appointments

2019-2025 Vice Chair and Chair, Gordon Research Conference, Multidrug Efflux Systems
2017-Pres External Advisory Boards, Toxicology T32 graduate programs at the University of Arizona, University of Colorado and Michigan State University
2015-2017 Rutgers Leadership Academy
2013-Pres Ad hoc NIH Grant Reviewer: ZES1 LKB-K(S) NIEHS Superfund, ZRG1 CB-L (55) R, ZES1 LKB-J (R), XNDA, ZES1 LAT-K (R) 1, EMNR-C (02), ZES1 JAB-D (C) 1, ZRG1 IMM-N (50) R
2013-2015 NIH NICHD Pediatrics Transporter Ontogeny Working Group: Extrapolation Subgroup
2012-Pres International Federation of Placenta Associations Member
2012-Pres Diplomat of the American Board of Toxicology (DABT Certification)
2010-Pres Cancer Institute of New Jersey, Clinical Investigations, Associate Member
2010-Pres NIEHS Center for Environmental Exposures and Disease, Member
2009-Pres Environmental and Occupation Health Sciences Institute, Member of the Toxicology Division
2009-Pres American Association for the Advancement of Science
2014-2016, Drug Transporter Focus Group Member
2009-Pres North Jersey Drug Metabolism Discussion Group
2009-Pres, Steering Group Member
2015-2016, Chair
2009-Pres American Society for Pharmacology and Experimental Therapeutics
2011-2013, Drug Metabolism Division, Councilor
2015-2016, Toxicology Division, Secretary/Treasurer
2017-2020, Finance Committee
2008-Pres American Association of Colleges of Pharmacy
2003-Pres Society of Toxicology (SOT)
2011-2014, Membership Committee
2013-2015, Councilor, Mechanisms Specialty Section
2013-2016, Councilor, MidAtlantic Regional Chapter
2016-2020, Program Committee
2018-2019, Education Committee, Graduate Education Subcommittee
2019-2023, Presidential Chain, MidAtlantic Regional Chapter

Honors

2022 Special Section about Aleksunes Lab Transporter Research, *Drug Metabolism and Disposition*
2021 William and Helen Levine Teacher of the Year Award, Ernest Mario School of Pharmacy
2021 Advisor Award, Lambda Kappa Sigma Professional Pharmacy Organization
2020 Chancellor Educator of the Year Award, Rutgers Biomedical Health Sciences
2019 Outstanding Young Investigator Award, Society of Toxicology Women in Toxicology

2019 Richard Okita Early Career Award in Drug Metabolism and Disposition, American Society for Pharmacology and Experimental Therapeutics
2019 Excellence in Research Award, NJ Health Foundation
2018 Excellence in Teaching Award, NJ Health Foundation
2018 Award of Merit, Lambda Kappa Sigma Professional Pharmacy Organization
2016 Achievement Award, Society of Toxicology
2015 Global Scientific Achievement Award in Drug Metabolism, Xenotech
2015 Mentor of the Year, American Foundation for Pharmaceutical Education
2014 Board of Trustees Research Fellowship for Scholarly Excellence
2014 Presidential Fellowship for Teaching Excellence
2012 Graduate of the Last Decade (G.O.L.D.) Award, Alumni Association, University of Connecticut
2011 NIEHS Outstanding New Environmental Health Scientist (ONES) Award

C. Contributions to Science

1. ***Drug-Induced Liver Injury.*** My dissertation research investigated the modulation of hepatobiliary transporters during drug-induced liver injury in mice and humans. I demonstrated that uptake carriers and efflux pumps were differentially regulated during acetaminophen and carbon tetrachloride hepatotoxicity. Liver injury leads to the induction of efflux transporters on canalicular and sinusoidal plasma membranes of hepatocytes – a concerted effort to reduce the chemical burden of stressed hepatocytes. My research also demonstrated that the Nrf2 transcription factor is a critical regulator of efflux transporter expression and shown to positively regulate that expression of Mrp3 and Mrp4. The final studies aimed at characterizing the signaling of Nrf2 and the expression of efflux transporters in livers from patients with fulminant hepatic failure due to acetaminophen intoxication, two studies that validated the mechanistic work performed in mouse models.
   - **Aleksunes L**, Scheffer G, Jakowski A, Pruimbroom-Brees I, Manautou J (2006) Coordinated expression of multidrug resistance associated proteins (Mrps) in mouse liver during toxicant–induced injury. *Toxicol Sci.* 89:370-379. Cited: 50+ times
   - Barnes S, **Aleksunes L** (co-first authors), Augustine L, Scheffer G, Goedken M, Pruimboom-Brees I, Jakowski A, Cherrington N, Manautou J (2007) Induction of hepatobiliary efflux transporters in acetaminophen-induced acute liver failure cases. *Drug Metab Disp.* 35:1963-1969.
   - **Aleksunes L**, Barnes S, Goedken M, Manautou J (2008) Acquired resistance to acetaminophen hepatotoxicity is associated with induction of multidrug resistance protein 4 (Mrp4) in proliferating hepatocytes. *Toxicol Sci.* 104:261-73. PMCID:PMC2734298.
   - **Aleksunes L**, Slitt A, Maher J, Augustine L, Goedken M, Chan J, Cherrington N, Klaassen C, Manautou, J (2008) Induction of Mrp3 and Mrp4 transporters during acetaminophen hepatotoxicity is dependent on Nrf2. *Toxicol Appl Pharm.* 226:74-83. Cited: 105+ times

2. ***Drug-Induced Nephrotoxicity.*** Paramount to understanding the mechanisms employed by nephrotoxicants is characterizing their disposition within proximal tubules. A number of these toxicants are actively secreted and reabsorbed by uptake and efflux transporters in the kidneys. As a postdoctoral fellow and an independent investigator, I have identified renal toxicants as substrates of transporters and characterized the regulation of kidney transporters during injury. Translational studies with cancer patients prescribed the nephrotoxic drug cisplatin have documented novel time-dependent secretion patterns of protein biomarkers of acute kidney injury and revealed important pharmacogenomic factors that are associated with altered susceptibility to nephrotoxicity.
   - Wen X, Gibson C, Buckley B, Goedken M, Richardson JR, **Aleksunes L** (2014) MDR1 transporter protects against paraquat-induced toxicity in human and mouse proximal tubule cells. *Toxicol Sci.* 141:475-83. PMCID:PMC4271045.
   - Wen X, Buckley B, McCandlish E, Manautou J, Goedken M, **Aleksunes L** (2014) Transgenic expression of the human MRP2 transporter reduces cisplatin accumulation and nephrotoxicity in Mrp2-null mice. *Am J Pathol.* 184:1299-308. PMCID:PMC4005989.
   - George B, Wen X, Mercke N, Gomez M, O-Bryant C, Bowles D, Hu Y, Hogan S, Joy M, **Aleksunes L** (2017) Profiling of kidney injury biomarkers in patients receiving cisplatin: time-dependent changes in the absence of clinical nephrotoxicity. *Clin Pharm Ther.* 101:510-8. PMCID:PMC5359028.

- Wen X, Kozlosky D, Zhang R, Doherty C, Buckley B, Barrett E, **Aleksunes L** (2021) BCRP/ABCG2 transporter regulates accumulation of cadmium in kidney cells: role of the Q141K variant in modulating nephrotoxicity. *Drug Metab Disp.* 49:629-637. PMCID: PMC8382159.

3. ***Placental Biology.*** The placenta provides nutrients critical for fetal growth and protects against xenobiotic exposures. Transporters in the placenta and fetal membranes including the BCRP protein regulate the maternal-fetal transfer of some toxicants. Recently, we have made critical discoveries into the genetic, transcriptional, and post-translational mechanisms that regulate the expression and function of BCRP in the human placenta. We have also identified the mycoestrogen zearalenone as a novel substrate for the placental BCRP transporter.
   - Francois L, Gorczyca L, Du J, Bircsak K, Yen E, Wen X, Tu M, Yu A, Illsley N, Zamudio S, **Aleksunes L** (2017) Down-regulation of the placental BCRP/*ABCG2* transporter in response to hypoxia signaling. *Placenta*. 51:57-63. PMCID:PMC5354084.
   - Bircsak K, Moscovitz J, Wen X, Archer F, Yuen, P, Mohammed M, Fisher S, Memon N, Weinberger B, Saba L, Vetrano A, **Aleksunes L** (2018) Interindividual regulation of the BCRP/*ABCG2* transporter in term human placentas. *Drug Metab Disp.* 46(5):619-627. PMCID:PMC5896368.
   - Szilagyi J, Gorczyca L, Brinker A, Buckley B, Laskin J, **Aleksunes L** (2019) Placental BCRP/ABCG2 transporter prevents fetal exposure to the estrogenic mycotoxin zearalenone. *Toxicol. Sci.* 168:394-404. PMCID:PMC6432861.
   - Szilagyi J, Composto G, Joseph L, Wang B, Rosen T, Laskin J, **Aleksunes L** (2019) Anandamide down-regulates placental transporter expression through CB2 receptor-mediated inhibition of cAMP synthesis. *Pharmacol. Res.* 141:331-342. PMCID:PMC6391190.

4. ***Blood-Brain Barrier and Microglial Transporters.*** Within the CNS, there are multiple transporters responsible for the uptake and efflux of drugs and chemicals. In fact, expression patterns vary from cell type to cell type and in response to pathologies and pharmacological interventions. Our laboratory focuses on 1) regulation and function of the MDR1 transporter at the blood-brain barrier and 2) transporter regulation and function in quiescent and activate microglia. In particular, we hypothesize that transporters represent a unique target involved in gene-environment interactions in neurodegeneration.
   - You D, Wen X, Morris A, Richardson J, **Aleksunes L** (2019) Up-regulation of MDR1 transporter expression in human brain endothelial cells through enhanced histone acetylation and activation of aryl hydrocarbon receptor signaling. *Mol Neurobiol.* 56:6986-7002. PMCID:PMC6728213.
   - You D, Mosaad F, Shin H, Richardson J, **Aleksunes L** (2019) Brain region-specific regulation of histone acetylation and efflux transporters in mice. *J Biochem Mol Toxicol.* e22318. PMCID:PMC6754812.
   - Gibson C, Richardson J, **Aleksunes L** (2012) Inflammatory regulation of ABC efflux transporter expression and function in microglia. *J Pharmacol Exp Ther.* 343:650-660. PMCID:PMC3500534.

5. ***Xenobiotic Disposition During Pregnancy.*** Our laboratory has identified molecular changes in xenobiotic metabolism and transport that occur during pregnancy. Using mice, we have characterized dynamic changes in hepatic and renal nuclear receptors, Phase-I, Phase-II, and transport genes and proteins. More recent studies have aimed to understand how activation of transcriptional pathways or disease states can alter pregnancy-induced changes in chemical disposition.
   - **Aleksunes L,** Yeager R, Wen X, Cui Y, Klaassen C (2012) Repression of hepatobiliary transporters and differential regulation of classic and alternative bile acid pathways in mice during pregnancy. *Toxicol Sci.* 130:257-268. PMCID:PMC3498745.
   - **Aleksunes L,** Xu J, Lin E, Wen X, Goedken M, Slitt A (2013) Pregnancy represses induction of hepatobiliary efflux transporters in livers of diabetic mice. *Pharm Res.* 30: 2209-2220. Invited manuscript. PMCID:PMC3644534.
   - Moscovitz J, Kong B, Buckley K, Buckley B, Guo G, **Aleksunes L** (2016) Restoration of enterohepatic bile acid pathways in pregnant mice following activation of Fxr by GW4064. *Toxicol Appl Pharmacol.* 310:60-67. PMCID:PMC5064858.

Complete List of Published Work (Over 135) in My Bibliography:
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