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: Laura S. Van Winkle

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

POSITION TITLE: Professor/Professor-in-Residence

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 California, Santa Barbara CA	B.S. (honors)	06/1987	Pharmacology
University of California, Davis CA	Ph.D.	06/1995	Pharmacology & Toxicology
University of California, Davis CA	Postdoctoral	08/1997	Comparative Respiratory Biology & Medicine

A. Personal Statement My training is in inhalation toxicology and cell biology of the lung in health and disease. My research interests have focused on injury and repair in the lung and how this relates to respiratory disease following environmental exposures to air pollution or toxic chemicals. I have been both a PI and a collaborator on national, foundation and state-funded grants from NIH, TRDRP, CARB, FAMRI and/or USEPA continuously since my faculty appointment in 1997. These grants have focused on lung cell biology and toxicology of naphthalene, fine and ultrafine particulate matter, near roadway vehicle exhaust, second hand tobacco smoke, ozone, allergens such as house dust mite and ovalbumin, inhaled engineered nanomaterials single and multi-walled carbon nanotubes and silver oxide nanoparticles. In general my laboratory focuses on biochemical and histologic in vivo and ex vivo approaches to tease a part lung cellular responses, with a special focus on distal conducting airways. My lab is also known for excellence in imaging and histology and I run a campus-wide Cellular and Molecular Imaging Core to assist other investigators with their tissue analysis needs. Recently we successfully received an S10 equipment grant to purchase a Cytoviva Hyperspectral imaging system which will allow localization of nanosized objects including carbonaceous PM (such as that from vehicle exhaust) in tissues. Currently, I am a PI (multi-PI, with Kent Pinkerton and Sara Thomasy) of the UC Davis component of the NIEHS Centers for Nanotechnology Health Implications Research (NHIR) Consortium. This consortium has a major focus on engineered nanomaterials including dose response and biological effect as well as biodistribution studies of nanosilver and carbon nanotubes. I am the co-leader of the UC Davis P30 Environmental Health Sciences Center Pilot Project Program and a member of the Centers leadership team. I have a long standing interest in graduate education and am a faculty member of 4 graduate groups at UC Davis: 1) Pharmacology and Toxicology, 2) Molecular, Cellular and Integrative Physiology, 3) Integrative Pathobiology and 4) Forensic Science. I am also a training faculty on 5 institutional T32s and an undergraduate IMSD grant and am chairing the committee on educational policy for the Pharmacology and Toxicology graduate group where I also serve on the Executive Committee.

B. Positions and Honors

Positions and Employment

1987-1990 Research Assistant, Amgen, Thousand Oaks, CA Preclinical Pharmacology: pharmaco-kinetics and biodistribution

1997-2003 * Assistant Research Cell Biologist, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis (*2000 6 mos Family Leave)

2001-2005 Lecturer, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis

2003-2005	Associate Research Cell Biologist, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis
2005-2012	Associate Adjunct Professor, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis
2005-2012	Associate Research Cell Biologist, Center for Health and the Environment, UC Davis
2013-2015	Chair, Academic Federation at UC Davis
2012-2016	Adjunct Professor, School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis
2012- present	Research Cell Biologist, Center for Health and the Environment, UC Davis
2016- present	Professor of Respiratory Toxicology/Professor-in-Residence School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, UC Davis

Other Experience and Professional Memberships

Diplomate, American Board of Toxicology (DABT), Recertified 2007, 2012, 2017

American Thoracic Society – ATS Environmental Health Policy Committee 2010-2015

- Environmental , Occupational and Public Health Program Committee 2018-present

Society of Toxicology - Elected councilor for Inhalation and Respiratory Specialty Section 09-11

- Elected secretary for Inhalation and Respiratory Specialty Section 15-17

American Physiological Society (APS), AAAS, American Society for Cell Biology (ASCB)

2007-2011	Associate Editor, Toxicology Letters
2008	Chair and organizer of Society of Toxicology symposium “Developmental Basis of Disease: Persistent Effects of ETS exposures”
2008	NIH SEP Study Section Systemic Injury by Environmental Exposure
2010	NIH S10 Study Section Confocal Microscopy and Advanced Imaging (Equipment grants)
2011	NIH LCMI ZRG Study Section (member conflicts), Ad hoc member
2011, 2012	NIH ZRG1 Study Section AREA Applications: Cardiovascular and Respiratory Sciences
2009-2011	NIH SBIR Study Section Respiratory Sciences
2012, 2013	NIH Study Section Lung Injury Repair and Remodeling, Ad hoc member
2014	NIH SEP Study Section Systemic Injury by Environmental Exposures
2014	NIH S10 Study Section Confocal Microscopy and Advanced Imaging (Equipment grants)
2014-2015	NIH Study Section ZRG1 Tobacco Control Regulatory Research
2015	NASA Research Grant Review Panel, Ad hoc Member
2015	NIH Director’s Early Independence Award, Ad hoc write in reviewer
2015	NIH ZRG1 DKUS-C AREA Applications
2015	SOT, Hookah Issues Statement Writing Team
2015	Appointed member, Chancellors Special Committee on Diversity and Inclusion
2015	Appointed member, Chancellors Committee on Visioning the Campus of the 21st Century
2016	Facilitator, Poster session “Smoking and particulates impact on lung health” 2016 Annual meeting of the American Thoracic Society in San Francisco
2016-2022	Standing Member, NIH Study Section Systemic Injury by Environmental Exposures (SIEE)
2017-	Associate Editor, Toxicological Sciences
2018	NIH Study section, Cardiovascular and Pulmonary Research on E-cigarettes

Honors

1997-1999	American Lung Association Research Fellow, UC Davis
2008	Young Investigator Award, Inhalation and Respiratory Specialty Section, Society of Toxicology
2010	UC Davis AF Professional Development Leave Award (to MSU and UConn)
2018	Mentoring Award, Women in Toxicology Special Interest Group, Society of Toxicology

C. Contribution to Science (selected from over 90 peer reviewed publications and 8 book chapters)

1. My early publications focused on the effect of chemicals on distal airway Club (Clara) cells. In particular my lab is known for developing the naphthalene injury and repair model to study wound healing in the deep lung.

This well-characterized, reproducible model in mice is widely used to understand the processes involved in cell injury, progenitor cell relationships and also paracrine factors involved in conducting airway epithelial repair.

a. **Van Winkle, LS**, AR Buckpitt, SJ Nishio, JM Isaac and CG Plopper. **1995** The cellular response in naphthalene-induced Clara cell injury and bronchiolar epithelial repair in the mouse. *Am. J. Physiol. (Lung Cell. Mol. Physiol.* 13): L800-L818.
b. **Van Winkle, LS**, JM Isaac and CG Plopper. **1997** Distribution of EGF receptor and ligands during naphthalene-induced Clara cell injury and repair. *Am J Pathol.* 151:443-459.
c. Greeley, M, **LS Van Winkle**, PC Edwards, CG Plopper. **2010** Airway Trefoil Factor Expression during Naphthalene Injury and Repair. *Tox Sciences* 113(2):453-467

2. I have developed and utilized methods to study airway site specific responses including mRNA expression, live and enzymatically active cells and toxicity in situ. These approaches have subsequently been employed to understand intrinsic, sex-specific and site-specific changes in nasal and conducting airway epithelium following exposures to inhaled and ingested environmental toxicants, including the traffic related PAH naphthalene. A special focus is the impact of cytochrome P450 monooxygenases and detoxification enzymes in different lung regions on bioactivation of chemicals.

a. **Van Winkle LS,** Gunderson AD, Shimizu JA, Baker GL, Brown CD. **2002** Gender differences in naphthalene metabolism and naphthalene-induced acute lung injury. *American journal of physiology*. *Lung Cellular and Molecular Physiology*, 282(5): L1122-34.
b. Sutherland, KM, PC Edwards, TJ Combs, **LS Van Winkle**. **2012** Sex differences in the development of airway epithelial tolerance to naphthalene. *Am J Physiol Lung Cell Mol Physiol* 302 (1) L68-81. Note: Images chosen for journal cover
c. **Van Winkle, LS**, JS Kelty, CG Plopper. **2017** Preparation of specific compartments of the lungs for pathologic and biochemical analysis of toxicologic responses. *Curr Protoc Toxicol*. 2017 Feb 1;71:24.5.1-24.5.26.
d. Kovalchuk, N, J Kelty, L Li, M Hartog, QY Zhang, P Edwards, **L Van Winkle**, X Ding. **2017** Impact of hepatic P450-mediated biotransformation on the disposition and respiratory tract toxicity of inhaled naphthalene. Toxicol Appl Pharmacol. Aug 15;329:1-8
e. Li, L, SA Carratt, M Hartog, N Kovalchuk, K Jia, Y Wang, Q-Y Zhang, P Edwards, **LS Van Winkle**, X Ding. **2017** Human CYP2A13 and CYP2F1 Mediate Naphthalene Toxicity in the Lung and Nasal Mucosa of CYP2A13/2F1-Humanized Mice. *Environmental Health Perspectives.* 125(6);067004 doi: 10.1289/EHP844

3. My lab has a long standing interest in pollution effects on the lung, particularly when pollution exposures include early postnatal development. We have studied ozone, particulate matter, tobacco smoke, near roadway vehicle exhaust and bisphenol A with a specific focus on morphologic assessment of cellular changes in the respiratory tract, including changes in secretory and P450 containing cells and antioxidant enzymes in response to pollution exposures.

a. Chan, JKW, Fanucchi, MV, DS Anderson, A Abid, CD Wallis, TJ Combs, BM Kumfer, IM Kennedy, AS Wexler, **LS Van Winkle**. **2011** Inhaled ultrafine premixed flame particulates induce age-specific cellular responses in neonatal and adult rats. *Tox Sciences* Dec 124 (2):472-86
b. Chan, JKW JG Charrier, SD Kodani, CF Vogel, SY Kado, DS Anderson, C Anastasio, and **LS Van Winkle.** **2013** Combustion-derived ultrafine soot generates reactive oxygen species and activates Nrf2 antioxidants differently in neonatal and adult rat lungs. *Particle and Fibre Tox* 1;10(1):34. (Note: Highly accessed)
c. Murphy, SR, KT Oslund, DM Hyde, LA Miller, **LS Van Winkle**, and ES Schelegle. **2014** Ozone Induced Airway Epithelial Cell Death, the Neurokinin-1 Receptor Pathway and the Postnatal Developing Lung. *AJP Lung*2014 Sep 15;307(6):L471-81. doi: 10.1152/ajplung.00324.2013.
d. Murphy SR, Schelegle ES, Miller LA, Hyde DM, **Van Winkle LS**. **2013** Ozone exposure alters serotonin and serotonin receptor expression in the developing lung. *Toxicological Sciences*, 134(1): 168-79

4. I have added a new research direction in the last 5 years, from studies of predominantly particulate air pollution to studies of nanoparticle health effects on the respiratory system of adult rats. This research has been aided by my role as the PI of the UC Davis component of a national consortium to study nanomaterials health effects that is funded by NIEHS. The consortium meets several times a year to exchange ideas and methodology and this has greatly enhanced my abilities to study nanoparticulate aerosols. Much of this

research uses inhalation exposures that we generate with engineered nanomaterials to model real world occupational exposures and their effects on the lung. My expertise on histopathology/ imaging as well as my understanding of various respiratory tract microenvironments in relation to ultrafine PM deposition has been key to these studies which have demonstrated long persistence of inhaled silver nanoparticles in lung tissues and have developed novel tracer particles to enhance our understanding of ultrafine particle dosimetry.

a. Abid AD, Anderson DS, Das GK, **Van Winkle LS**, Kennedy IM. **2013** Novel lanthanide-labeled metal oxide nanoparticles improve the measurement of in vivo clearance and translocation. *Part Fibre Toxicol.* Jan 10;10:1. doi: 10.1186/1743-8977-10-1
b. Anderson, DS, RM Silva, D Lee, PC Edwards, A Sharmah, T Guo, K E Pinkerton and **LS Van Winkle**, **2015** Persistence of Silver Nanoparticles in the Rat Lung: Influence of Dose, Size and Chemical Composition. *Nanotoxicology* Aug;9:591-602
c. Anderson, DS, ES Patchin, RM Silva, DL Uyeminami, A Sharmah, T Guo, GK Das, JM Brown, J Shannahan, T Gordon, LC Chen, KE Pinkerton and **LS Van Winkle**. **2015** Influence of Particle Size on Persistence and Clearance of Aerosolized Silver Nanoparticles in the Rat Lung. *Toxicological Sciences* Apr;144(2):366-81
d. Das, GK, DA Anderson, CD Wallis, SA Carratt, IM Kennedy, **LS Van Winkle** **2016** Novel Multi-functional Europium-Doped Gadolinium Oxide Nanoparticle Aerosols Facilitate the Study of Deposition in the Developing Rat Lung *Nanoscale* 8(22), 11518 - 11530
e. Patchin, ES, DS Anderson, RM Silva, DL Uyeminami, GM Scott, T Guo, **LS Van Winkle** an KE Pinkerton. **2016** Size-dependent deposition, translocation and microglial activation of inhaled silver nanoparticles in the rodent nose and brain. *Environmental Health Perspectives* Dec;124(12):1870-1875.

List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/sites/myncbi/laura.vanwinkle.1/bibliography/44203609/public/?sort=date&direction=ascending.

D. Research Support

Ongoing Research Support

1U01 ES027288 Multi-PI Pinkerton (Contact)/Van Winkle/Thomasy 9/30/16-8/31/21
NIEHS
Respiratory and Ocular Toxicity of Inhaled Nanomaterials
Our goal is to compare molecular, cellular and pathologic effects of aerosolized nanomaterials, to be defined by the consortium, on the eye and the lung. This application has a focus on wound healing and how nanomaterials impact this process in target organs and in cells from the target organs in vitro. Role: PI

R01 ES020867-01A1 Multi-PI: X Ding (contact)/Van Winkle 08/20/13-04/30/19
NIEHS
Metabolic mechanisms of naphthalene toxicity in lung
The goal is to define the role of different cytochrome P450 enzymes in the metabolic activation of naphthalene in the lung and liver using transgenic mouse models with lung and liver P450s knocked out or human P450s inserted. Naphthalene is a component of fossil fuel combustion and smoke. Role: PI

3R01ES020867-S1 Multi-PI: X Ding (contact)/Van Winkle 5/5/15-4/30/19
NIEHS/NHLBI
ViCTER Supplement to R01 Metabolic mechanisms of naphthalene toxicity in lung
The overall theme of this ViCTER supplement is to study mechanisms of lung toxicity, including tolerance, induced by naphthalene, in order to improve assessment of human lung cancer risks from NA. Three Aims are proposed, 1) to define whether NA is a genotoxic carcinogen through a direct mechanism; 2) to test the role of inflammatory cell estrogen production in NA-induced lung toxicity and tolerance; and 3) to identify cellular stress response for NA-induced lung toxicity and tolerance. Role: PI

NIEHS P30 Core Center (Hertz-Piccioto) 4/1/15-3/31/20
UC Davis Center for Environmental Health Sciences
Environmental Exposures, Mechanisms, and the Development of Disease

The goal of a NIEHS core center is to provide research resources that facilitate the work of NIEHS funded investigators. Role: Van Winkle Leader of Pilot Projects Program, participant in respiratory health theme area, recipient of pilot project to study ozone effects during lung development

R01 CA092596-10 (X Ding) 4/1/2016 – 3/31/21
NCI
Human Cyp2A and respiratory tract xenobiotic toxicity
This is the renewal of Dr. Ding's (SUNY Poly) R01 that studies the role of P450s in lung carcinogenesis following exposure to ETS using novel transgenic mice that contain a human P450 gene CYP2A13(SUNY Poly) and on lung pathology (tumor formation and DNA adducts, UC Davis).
Role: Co-investigator, lead UCD subcontract.

CMA1 (Van Winkle) 2/1/2017- 1/31/2020
Chloropicrin Manufacturer's Association
Evaluation of the effect of chloropicrin on the lungs of mice
The goal is to create a better understanding of chloropicrin mechanism of cytotoxicity observed in the respiratory tract of mice following inhalation of chloropicrin vapor, particularly in relation to the formation of tumors. Role: PI

R01ES014901S1A1 Lein 11/01/2017-10/31/2020
NIEHS ViCTER Supplement
Molecular and Cellular Basis of PCB Developmental Neurotoxicity
The goal of this application is to explore new directions in PCB developmental neurotoxicity using cutting edge methods and the lung as a target organ for vapor exposures. Dr. Van Winkle is the leader of Aim 3 which will examine the effect of PCB vapor on lung development. Role: Co investigator

Completed Research Support last 3 yrs

U01 ES02027 Multi-PI: Pinkerton (contact)/Van Winkle 10/1/10-3/31/16
NIEHS Engineered Nanomaterials: Linking Physical and Chemical Properties to Biology.
The goal is to systematically explore the influence of physicochemical properties of engineered nanomaterials (ENMs), including single walled carbon nanotubes (SWCNT) and other materials as specified by the consortium (silver NM and MWCNT) in rats. A special emphasis at UC Davis is on inhalation. This grant generated 21 in vivo publications. Role: PI

R21 ES021600 (Van Winkle, L) 09/18/12-08/31/15
NIEHS
Prenatal Bisphenol A and Lung Maturation
The goal is define how fetal BPA exposure changes secretory product maturation in Clara cells and mucous cells of the lung in both a mouse and a rhesus monkey model. Role: PI

California Air Resources Board (Wexler, Pinkerton, Tablin, Wilson, Van Winkle co-PIs) 1/2011-6/30/15
Health Effects of Central Valley Particulate Matter
The major goals are to collaboratively evaluate the differences in both systemic and lung specific inflammation and antioxidant responses between PM2.5 collected in Davis and Sacramento (winter) in an intra-tracheal mouse model system. Unique particle extraction methods that retain PAH are used. Role: PI

American Beverage Association (Van Winkle) 04/01/15- 06/30/17
Investigations on the lung effects of 4-MEI
This grant is designed to determine if acute lung toxicity from 4-MEI occurs and affects distal airway Club cells.
Role: PI