BIOGRAPHICAL SKETCH

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NAME:	Heather Dale Jones, MD
eRA COMMONS USER NAME:	JONESH2
POSITION TITLE:	Assistant Professor, 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	Completion Date	FIELD OF STUDY
University of California, Berkeley Berkeley CA	B.A.	06/1992	Molecular and Cell Biology
Medical Col of Pennsylvania/Hahnemann Univ Philadelphia PA	M.D.	06/1998	Medicine
Boston Medical Center Boston MA	Residency	06/2001	Internal Medicine
Johns Hopkins Hospital Baltimore MD	Clinical Fellowship	12/2002	Pulmonary and Critical Care Medicine
Pulmonary-Critical Care Medicine Branch, NHLBI/NIH, Bethesda MD	Research Fellowship	05/2006	Pulmonary and Critical Care Medicine

A. PERSONAL STATEMENT

I study Acute Respiratory Distress Syndrome, or ARDS. I take care of many patients with ARDS in my clinical work in the intensive care unit, and unfortunately this disease has few to no effective therapies and carries a mortality rate of 30%. Because ARDS often develops in the setting of sepsis and mechanical ventilation, we developed a mouse model of acute lung injury that mimics these conditions. I am now using this model to examine the complex relationship between non-infectious inflammation from mechanical ventilation, the inflammatory response to bacterial infection, and the effects of these inflammatory responses on lung function. I am currently focused on the role of inflammatory cytokines in the development of severe hypoxemia in patients with ARDS, and recently (December 2014) received an NIH K08 grant to support this work. I have worked closely with Drs. Debiao Li and Wafa Tawackoli in the Biomedical Imaging Research Institute to develop *in vivo* lung imaging techniques for measuring ventilation and perfusion abnormalities during acute lung injury in mice as a part of this work. I am also collaborating with Dr. Fouras on both small animal and human research projects involving 4Dx imaging, because 4Dx imaging significantly advances our ability to study and understand mechanisms of lung disease by providing functional information never before possible. Below are two of my most important publications in the field of acute lung injury.

1. **Jones HD**, Crother TR, Gonazalez R, Jupelli M, Chen S, Dagvadorj J, Arditi M, Shimada K. The NLRP3 Inflammasome is required for the development of hypoxemia in LPS/mechanical ventilation acute lung injury. Am J Respir Cell Mol Biol. 2013. PubMed PMID: 24007300.
2. **Jones HD,** Yoo J, Crother TR, Kyme P, Ben-Shlomo A, Khalafi R, Tseng C, Parks WC, Arditi M, Liu G, Shimada K. Nicotinamide exacerbates hypoxemia in ventilator-induced lung injury independent of neutrophil infiltration. . PLoS One. 2015 PubMed PMID: 25875775.

B. POSITIONS AND HONORS

Positions and Employment

1992-1994 Laboratory Manager and Scientist, Dept of Physiology and Biochemistry
University of California, San Francisco
2006-2007 Assistant Clinical Investigator, Pulmonary-Critical Care Medicine Branch,
NHLBI/NIH, Bethesda MD

2007-2015 Medical Director, Intensive Care Unit, Division of Pulmonary/Critical Care Medicine
2010-now Member, Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles CA
2009-now Health Sciences Assistant Clinical Professor, David Geffen School of Medicine, UCLA

Local Clinical Committees

2007-2011 Critical Care Committee, Cedars-Sinai Medical Center
2008-2009 Chair, Critical Care Committee, Cedars-Sinai Medical Center
2012-2013 Chair, Critical Care Committee, Cedars-Sinai Medical Center
2008-2013 Chair, CS-Link ICU Task Force
2010-2014 Chair, Cedars-Sinai Medicine Sepsis Task Force

Professional Memberships

2008-now American College of Chest Physicians
2008-now American Thoracic Society
2013-now World Molecular Imaging Society

Honors (partial list)

2007-2008 NIH NCRR-Cedars-Sinai General Clinical Research Center CReFF award
2008-2010 Cedars-Sinai Leadership Development Program (graduate)
2009-2011 Cedars-Sinai Clinical Scholars Program (graduate)
2012-2013 UCLA Clinical and Translational Science Institute grant
2002 NIH Award for identifying bronchoscope contamination
2002-2006 NIH Loan Repayment Scholarship Award Support
1998 Alpha Omega Alpha Honor Medical Society
1998 Maurice C. Clifford, M.D. Leadership Award
1998 The Women's Health Education Award for excellence in Women's Health
1998 Janet M. Glasgow Memorial Achievement Citation of the AMWA
1996-1998 Women's Health Student Research Fellowship, Institute for Women's Health
1997 "Preventive Medicine in Women's Health" Abstract accepted for oral presentation at the National Medical Student Research Forum, Galveston, Texas.
1990-1991 President's Undergraduate Research Fellowship
1992 I.L. Chaikoff Award for Outstanding Undergraduate Research in Molecular and Cell Biology
1992 Honors in Molecular and Cell Biology
1992 Distinction in General Scholarship

C. CONTRIBUTIONS TO SCIENCE

1. Yeast morphology and microscopy. I began bench research as an undergraduate at the University of California, Berkeley. Live microscopy techniques were in their infancy at that time and had only been used in mammalian cells. I applied these techniques to the much smaller, single-celled organism *S. cerevisiae* for the first time, and demonstrated that these cells could be imaged and that novel features of their growth and division could be characterized in this way. I used immunofluorescence microscopy to understand and categorize the effects of site-directed mutations in actin in *S. cerevisiae* on morphogenesis and mitochondrial organization.

a. **Jones HD**, Schliwa M, Drubin DG. Video microscopy of organelle inheritance and motility in budding yeast. Cell Motil Cytoskeleton. 1993;25:129-42. PubMed PMID: 8324829.
b. Drubin DG, **Jones HD**, Wertman KF. Actin structure and function: roles in mitochondrial organization and morphogenesis in budding yeast and identification of the phalloidin-binding site. Mol Biol Cell. 1993;4:1277-94. PubMed Central PMCID: PMCPMC275764.

2. Cell cycle regulation. I joined Dr. Morgan's laboratory as a research technician when cell cycle proteins were just beginning to be understood. I purified cyclin-dependent kinase 2, a key mammalian cell cycle protein, for crystallization, and I performed kinetics experiments to characterize the interaction of two inhibitors with this kinase.

c. De Bondt HL, Rosenblatt J, Jancarik J, **Jones HD**, Morgan DO, Kim SH. Crystal structure of cyclin-dependent kinase 2. Nature. 1993;363:595-602. PubMed PMID: 8510751.

d. Schulze-Gahmen U, Brandsen J, **Jones HD**, Morgan DO, Meijer L, Vesely J, Kim SH. Multiple modes of ligand recognition: crystal structures of cyclin-dependent protein kinase 2 in complex with ATP and two inhibitors, olomoucine and isopentenyladenine. Proteins. 1995;22(4):378-91. PubMed PMID: 7479711

3. GTP-exchange proteins in vesicular trafficking. As a research fellow in the Pulmonary-Critical Care Medicine Branch of the NHLBI, I studied the role of brefeldin A-inhibited guanine nucleotide-exchange proteins BIG1 and BIG2 in the regulation of vesicular trafficking and discovered several putative protein kinase A (PKA) binding sites for BIG1 and BIG2. I performed site-directed mutagenesis to prove that PKA binding to BIG1 and BIG2 regulates vesicular trafficking.

e. **Jones HD**, Moss J, Vaughan M. BIG1 and BIG2, brefeldin A-inhibited guanine nucleotide-exchange factors for ADP-ribosylation factors. Methods Enzymol. 2005;404:174-84. PubMed PMID: 16413268.

f. Citterio C, **Jones HD**, Pacheco-Rodriguez G, Islam A, Moss J, Vaughan M. Effect of protein kinase A on accumulation of brefeldin A-inhibited guanine nucleotide-exchange protein 1 (BIG1) in HepG2 cell nuclei. Proc Natl Acad Sci U S A. 2006;103:2683-8. PubMed Central PMCID: PMCPMC1413798.

g. Islam A, **Jones H**, Hiroi T, Lam J, Zhang J, Moss J, Vaughan M, Levine SJ. cAMP-dependent protein kinase A (PKA) signaling induces TNFR1 exosome-like vesicle release via anchoring of PKA regulatory subunit RIIbeta to BIG2. J Biol Chem. 2008;283:25364-71. PubMed Central PMCID: PMCPMC2533074.

4. Bronchoscope contamination. As a clinical fellow at Johns Hopkins Hospital, I discovered that a number of my patients had respiratory cultures from bronchoscopy that suggested bronchoscope contamination. I reported my suspicions to hospital epidemiology, and the subsequent investigation confirmed my suspicions of bronchoscope contamination, and led to a nation-wide recall of the bronchoscope model. Many involved credited me as contributing significantly to the health of patients with pulmonary issues throughout the country through my discovery and diligence in making a report.

h. Srinivasan A, Wolfenden LL, Song X, Mackie K, Hartsell TL, **Jones HD**, Diette GB, Orens JB, Yung RC, Ross TL, Merz W, Scheel PJ, Haponik EF, Perl TM. An outbreak of Pseudomonas aeruginosa infections associated with flexible bronchoscopes. N Engl J Med. 2003;348:221-7. PubMed PMID: 12529462.

5. The NLRP3 Inflammasome in host defense and in mechanisms of hypoxemia in acute lung injury. The lab of my K08 mentor, Dr. Moshe Arditi, has focused on mechanisms of host defense in the lung and I have contributed to several papers on this topic since joining the lab, listed below. My work, reflected in citations 1 and 2 in Section A, contributes to understanding the role of host defense mechanisms in the development of hypoxemia during acute lung injury. Prior to my work, it was thought that hypoxemia in acute lung injury was due to edema and acute inflammatory cell infiltration of the lungs. My research has shown a disconnect between these factors and the development of hypoxemia. I demonstrated that hypoxemia requires the production of the cytokine interleukin-1β, and that hypoxemia can develop in the absence of neutrophil infiltration into the lungs. My K08 is focused on understanding the mechanisms underlying these observations.

i. Jupelli M, Shimada K, Chiba N, Slepenkin A, Alsabeh R, **Jones HD**, Peterson E, Chen S, Arditi M, Crother TR. Chlamydia pneumoniae infection in mice induces chronic lung inflammation, iBALT formation, and fibrosis. PLoS One. 2013;8:e77447. PubMed Central PMCID: PMCPMC3808399.

j. Chiba N, Shimada K, Chen S**, Jones HD**, Alsabeh R, Slepenkin AV, Peterson E, Crother TR, Arditi M. Mast Cells Play an Important Role in Chlamydia pneumoniae Lung Infection by Facilitating Immune Cell Recruitment into the Airway. J Immunol (2015, Epub ahead of print)

k. Tumurkhuu G, Dagvadorj J, **Jones HD**, Chen S, Shimada K, Crother TR, Arditi M. Alternatively Spliced Myeloid Differentiation Protein-2 Inhibits TLR4-Mediated Lung Inflammation. J Immunol 194:1686-94 (2015).

l. Dagvadorj J, Shimada K, Chen S, **Jones HD**, Tumurkhuu G, Zhang W, Wawrowsky KA, Crother TR and Arditi M. Lipopolysaccharide induces alveolar macrophage necrosis via CD14 and the P2x7 receptor leading to Interleukin 1-α release. Immunity 2015; 42(4):640-53. NIHMSID: NIHMS678996

Complete List of Published Work (Note: link does not work in Safari):
http://www.ncbi.nlm.nih.gov/sites/myncbi/14uBQwULIxoQu/bibliography/44144318/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

NIH/NHLBI 1K08HL125806-01 2014-2019
IL-1beta in the Development of Hypoxemia in Acute Lung Injury
Goal: Determine the mechanisms of IL-1β-dependent hypoxemia in a two-hit murine model of acute lung injury.
Role: PI

Completed Research Support

NIH/NCATS UCLA CTSI UL1TR000124 2013-2014
Role of IL-1β and the NLRP3 Inflammasome in the Development of Hypoxemia in Acute Lung Injury
Goal: Explore the role of IL-1β and the NLRP3 inflammasome in hypoxemia in ventilator-induced lung injury (VILI) with sepsis.
Role: PI

NIH/NCATS UCLA CTSI UL1TR000124 2014-2015
Using in vivo imaging to determine the mechanism of IL-1β-dependent hypoxemia in ARDS
Goal: Develop in vivo imaging method to map IL-1b-dependent pulmonary perfusion and ventilation mismatching in a murine two-hit model of acute lung injury.
Role: PI

Plum Foundation 2013-2014
Dissecting the Mechanism of Severe Hypoxemia in Acute Respiratory Distress Syndrome
Goal: Determine which factors are responsible for hypoxemia in VILI with sepsis
Role: PI

NIH/NCRR/NCATS UCLA CTSI UL2TR000122 2012-2013
Acute Lung Injury and Effects of NAMPT and NAM in Modulating Lung Inflammation
Goal: Explore the role of nicotinamide and NAMPT in a mouse model of VILI.
Role: PI

Plum Foundation 2012-2013
Dissecting the Role of the Inflammasome in Acute Respiratory Distress Syndrome
Goal: Determine if inhibitors of the NLRP3 inflammasome or IL-1β attenuate VILI.
Role: PI

CSMC Research Institute/Eigler-Mann-Whiting Grant Award 2011-2012
Acute Lung Injury and Ventilation induced Lung Injury and Modulation of Lung Inflammation.
Goal: Assessed the effects of immunomodulators in VILI. Supported the data used for my current NIH KL2 award.
Role: PI

NIH/NCRR RR00425 General Clinical Research Center 2007-2008
The use of traditional acupuncture for sedation and analgesia in mechanically ventilated patients.
Goal: Evaluated the efficacy of daily acupuncture as an adjunctive therapy to sedatives and analgesics in patients requiring mechanical ventilation.
Role: PI

Breathe LA Foundation 2009-2010
Yoga as an adjunctive therapy in COPD
Goal: To determine whether instruction in gentle yoga improves symptoms in patients with COPD who are participating in a pulmonary rehabilitation program.
Role: PI