BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Reen Wu	Professor
eRA COMMONS USER NAME (credential, e.g., agency login) REEN_WU	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
National Taiwan University, Taipei, Taiwan	B.S.	06/65	Agricultural Chemistry
National Taiwan University, SOM, Taipei, Taiwan	M.S.	06/68	Biochemistry
University of Arkansas, SOM, Little Rock, Ark.	Ph.D.	02/72	Biochemistry
University of California at San Diego, La Jolla, CA	(Post-Doct)	72-76	Mol. & Cell Biol.

A. PERSONAL STATEMENT

My laboratory is one of the laboratories that have developed a serum-free hormone-supplemented medium for culturing primary airway epithelial cells from various animal species and human. Utilizing the defined culture system, in 1983 and 1985, we were the first group to demonstrate new ciliogenesis and mucous cell differentiation in primary hamster tracheal epithelial cultures. In 1985. we have developed the "Whitcutt" chambers to be used for airway epithelial cells cultured under air-liquid interface (ALI) condition. In 1986, we were able to achieve the first pseudostratified mucociliary epithelial layer in this chamber. These successes lead to the current ALI protocol to mimic the *in vivo* biology of airway epithelial cells for *in vitro* studies in various laboratories. Since then, we have utilized both the *in vitro* and *in vivo* approaches to delineate the functional role of airway epithelial cells in response to various cytokines/mediators, environmental insults, and infections. We have used differential and subtractive hybridization approaches to identify differential gene expression associated with epithelial cell differentiation and cell injury. In 1995-1996, we have introduced the first microarray study for profiling gene expression in response to vitamin A and smoke exposure. These studies lead to the discovery of various novel genes associated with airway epithelium. These are small proline-rich protein genes, SPURT (PLUNC), retinol dehydrogenase, In 2003, we have discovered the significant role of IL-17 in the stimulation of airway mucin gene expression. This finding has led to the finding that IL-17 is the most potent inducer for various epithelial host defense molecules in addition to the pro-inflammatory effects. We have demonstrated IL-17(A) is coordinately regulating both beta-defensin 2 and CCL20 for both apical and basolateral secretion, respectively. The significance of this phenomenon is related to the recruitment of CCR6+ Th17 and immature dendritic cells by these only two ligands. In addition, the use of ALI cultures allows us to expose cells under the physiological condition to smoke exposure. Using the microarray and the bioinformatics, we have delineated an injury/repair pathway. Further studies with clinical tissues from cancer patients, we are able to characterize differential expression and the significance of the interactone of these differential genes. Recent work has observed the persistence of cell differentiation, especially mucin gene expression, associated with smoke and vitamin A treatments. Because of these activities, there is a need to carry out further study at the global, genome-wide level, especially in relating to the persistent changes in gene expression. Because of these current interests, our lab is actively engaged in RNA-seq and MIRA-seq analyses and studies at our Genome building (GBSF) and at Cancer Center at our UCD Medical Center.

I have been funded from NIH since 1984, my research projects are always multidisciplinary and mechanistic-drive ones. We have been recognized for our work with a NIH merit award in 1995 and a Recognition Award for Scientific Accomplishment by American Thoracic Society in 2011. In addition, I have served as a regular member of several NIH study sections, including the genome-wide microarray, epigenetic mechanism-related study sections, Lung Biology and Pathology (LBPA) study sections in the past, and more recently, Lung Cellular, Molecular and Immunology (LCMI) study section and NHLBI Institutional Training Mechanism (NITM) Review Panel.

B. POSITIONS AND HONORS

Positions and Employment

1976-1978 Assistant. Research Biologist, Department of Biology, UC San Diego
1978-1982 IPA, Research Chemist & Group Leader, Pulmonary Cell Biology Group, Laboratory of Pulmonary Function and Toxicology, National Institute of Environmental Health Science, Research Triangle Park, North Carolina
1983-1985 Senior Scientist, W. Alton Jones Cell Science Foundation, Lake Placid, New York
1985- Associate Professor, Professor, Division of Pulmonary & Critical Care Medicine, Department of Internal Medicine, and Veterinary Anatomy, Physiology & Cell Biology, University of California at Davis
2005-2011 Chair, Comparative Pathology Graduate Group, University of California at Davis

Other Experience and Professional Memberships

1988-95 Member, California Lung Association Fellowship Training Committee
1993-96 Member, Lung Biology and Pathology Study Section, National Institute of Health
1993- Member, Editorial Board of American Journal of Physiology: Lung Cellular and Molecular Physiology
1993-2004 Member, Editorial Board of Pulmonary Pharmacology & Therapeutics
1994-96 Member, American Thoracic Society Annual Meeting Program Committee
1997- Member, Technical Review Committee for Nebraska Cancer and Smoking Disease Research Program
1998- Member, Editorial Board of American Journal of Respiratory Cell and Molecular Biology
1998-2000 Member, Scientific Advisory Committee, Institute of Zoology, Academia Sinica, Taipei, Taiwan
2000- Member of National Health Research Institute's Scientific Review Committee, Zuhnan, Taiwan
2004- Program Director for T32 HL07013, Training in Comparative Lung Biology and Medicine
2006-2008 Member, Editorial Board, Journal of Immunology
2006-2010 Member, Lung Cellular, Molecular and Immunology (LCMI) study section, NIH
2007-2010 Member, VA Joint Biomedical Laboratory Research and Development and Clinical Science Research and Development Scientific Merit Review Board, Dept. of Veterans Affairs
2006-2011 Member, Advisory Committee of the Division of Environmental Health and Occupational Medicine, National Health Research Institute, Zuhnan, Taiwan
2007-2011 Member, NHLBI Institutional Training Mechanism (NITM) Review Panel, NIH-NHLBI

Honors

1972-74 American Cancer Society Postdoctoral Fellowship
1974-76 NIH National Research Service Award
1993 Joan Oettinger Memorial Award, School of Medicine, University of California at Davis
1995 Merit Award, NIH R37-HL35635
1996 Faculty Research Award, UC Davis, School of Medicine
2006 Pfizer Award for Research Excellence, VM School, UC Davis
2007 Dean's Award for Excellence in Mentoring, School of Medicine, UC Davis
2011 American Thoracic Society Recognition Award for Scientific Accomplishment

C. SELECTED PEER-REVIEWED PUBLICATIONS

1. Miller LA, Zhao YH, and **Wu R**. Inhibition of TGF-alpha gene expression by vitamin A in airway epithelium. J. Clin Invest. 97(6):1429-35. 1996. PMID: 8617875
2. Yoneda, K., Peck, K., Chang M. M-J, Chmiel, K., Sher, Y.P., Chen, J., Chen, Y., and **Wu, R**. Profiling smoke-and hydrogen peroxide-induced gene expression patterns in human bronchial epithelial cells by high density DNA microarray membrane. Am. J. Respir. Crit. Care Med., 164: S85-S89. 2001. PMID: 12874447
3. Chen, Y., Zhao, Y.H., and **Wu, R.** *In silico* Cloning of mouse *Muc5b* gene and its upregulation of gene expression in mouse asthma model. Am. J. Respir. Crit. Care Medicine, 164: 1059-1066. 2001.
4. Kao, C.Y, Chen, Y., Zhao, Y.H., and **Wu, R.** ORFeome based search of airway epithelial cell-specific novel human β-defensin genes. Am. J. Respir. Cell Mol. Biol. 29: 71-80, 2003. PMID: 12600824

5. Yoneda, K., Chang, M. M.J., Chmiel, K., Chen, Y., and **Wu, R.** Application of high density DNA microarray to study smoke- and hydrogen peroxide-induced injury and repair in human bronchial epithelial cells. J. Am. Soc. Nephrology, 14: S284-S289. 2003. PMID: 12874447
6. Chen, Y., Zhao, Y.H., Kalaslavadi, T.J., Hamati, E., Nehrke, K., Le, A.D., Ann, D.K., and **Wu, R.** Genome-wide search of novel gel-forming mucin genes and identification of MUC19/Muc19 as a new glandular tissue-specific mucin gene. Am. J. Respir. Cell Mol. Biol., 30: 155-165. 2004. PMID: 12882755
7. Kao CY, Huang F., Chen Y., Thai P, Wachi, S, Kim C, Tam L and **Wu R.** Up-regulation of CC chemokine ligand 20 expression in human airway epithelium by IL-17 through a JAK-independent but MEK/NF-kappaB-dependent signaling pathway. J. Immunol. 175: 6676-6685. 2005. PMID: 16272323
8. Wachi S., Yoneda K, and **Wu R.** Interactome-transcriptome analysis reveals the high centrality of genes differentially expressed in lung cancer tissues. Bioinformatics, 21(23):4205-8. 2005. PMID:16188928
9. Chen,Y., Hamati, E., Lee, W.M., Wachi, S., Schnurr, D., Shigeo, Y., Dolganov, G., Boushey, H., and **Wu, R.** Transcriptional profiling of gene expression in rhinovirus infected human primary airway epithelial cells: Elevation of innate defense molecules through both dsRNA and interferon dependent pathways. Am. J. Respir. Cell Mol. Biol. 34: 192-203. 2006. PMID: 16210696
10. Chen,Y., Hamati, E., Lee, W.M., Wachi, S., Schnurr, D., Shigeo, Y., Dolganov, G., Boushey, H., and **Wu, R.** Rhinovirus induces airway epithelial gene expression through double-stranded RNA and IFN-dependent pathways. Am. J. Respir. Cell Mol. Biol. 34: 192-203. 2006. PMID: 16210696
11. Wu, D.Y-C, **Wu, R.,** Reddy, S.P., Lee, Y.C., and Chang, M. M-J. Distinctive EGFR/ERK-Independent and Dependent Signaling Pathways in the Induction of Airway MUC5B and MUC5AC Expression by PMA. Am. J. Pathol. 170(1) 20-32. 2007. PMID:17200179
12. Huang F, Kao CY, Wachi S, Thai P, Ryu J and **Wu, R**. Requirement for both JAK-mediated PI3K signaling and ACT1/TRAF6/TAK1-dependent NF-κB activation by IL-17A in enhancing cytokine expression in human airway epithelial cells. J. Immunol. 179: 6504-6513. 2007. PMID:17982039
13. Zhu L, Pi J, Wachi S, Andersen ME, **Wu R**, and Chen Y. Identification of Nrf2-dependent airway epithelial adaptive response to proinflammatory oxidant-hypochlorous acid challenge by transcription profiling. Am J Physiol Lung Cell Mol Physiol. 294(3):L469-77. 2008. PMID: 18156441
14. Thai P, Loukoianov A, Wachi S and **Wu R**. Regulation of airway mucin gene expression, Annual Rev. Physiology, 70: 405-429. 2008. PMID:17961085
15. Lee YC, Chuang CY, Lee PK, Lee JS, Harper RW, Buckpitt AB, **Wu R**, and Oslund KL. TRX-ASK1-JNK signaling regulation of cell density-dependent cytotoxicity in cigarette smoke-exposed human bronchial epithelial cells. Am J Physiol Lung Cell Mol Physiol. 294(5):L921-31. 2008. PMID: 18281606
16. Kao CY, Kim C, Huang F, **Wu R**. Requirements for two proximal NF-kappa B binding sites and Ikappa B-zeta in IL-17A-induced human beta -defensin 2 expression by conducting airway Epithelium. J Biol Chem. 283(22):15309-18. 2008. PMID:18362142
17. Huang F, Wachi S, Thai P, Loukoianov A, Tan KH, Forteza RM, **Wu R**. Potentiation of IL-19 expression in airway epithelia by IL-17A and IL-4/IL-13: important implications in asthma. J Allergy Clin Immunol. 121(6):1415-21. 2008. PMID: 18539194
18. Hung LY, Velichko S, Huang F, Thai P and **Wu R.** Regulation of airway innate and adaptive immune responses: the IL-17 paradigm, Critical Reviews in Immunology, 28(4): 269-279. 2008. PMID:19166380
19. Fujisawa, T., Velichko S, Thai P, Hung LY, Huang F and **Wu, R**. Regulation of airway MUC5AC expression by IL-1β and IL-17A: the NF-κB paradigm. J Immunol. 2009 Nov 15;183(10):6236-43. Epub 2009 Oct 19'. PMID: 19841186
20. Oslund KL, Adamson G, **Wu R**. Evaluation of MUC5AC expression and upregulation in airway epithelial cells of horses. Am J Vet Res. 71(6):690-6. 2010. PMID: 20513186.
21. Lee YC, Oslund KL, Thai P, Fujisawa T, Duong T, Denison MS, and **Wu R**. TCDD induced MUC5AC expression: Aryl hydrocarbon receptor-independent/EGFR-dependent MAPK signaling pathway. Am. J. Respir. Cell Mol Biol. 2011 Aug;45(2):270-6. Epub 2010 Oct 22. PMID: 20971882
22. Fujisawa T, Chang MM, Velichko S, Thai P, Hung LY, Huang F, Phuong N, Chen Y, and **Wu R**. NF-{kappa}B Mediates IL-1β- and IL-17A-induced MUC5B Expression in the Airway Epithelial Cells. Am. J. Respir. Cell Mol. Biol. 2011 Aug;45(2):246-52. Epub 2010 Oct 8. PMID: 20935193
23. Plopper C, Joad J, Miller L, Schelegle E, Fanucchi M, Van Winkle L, Tyler N, Avdalovic M, Evans M, Lasley W, Buckpitt A, Pinkerton K, Tarkington B, Davis S, Nishio S, Gershwin L, **Wu R**, and Hyde D. Lung effects

of inhaled corticosteroids in a rhesus monkey model of childhood asthma. Clinic.Exp. Allergy. 42(7):1104-18. 2012 Jul. PMID: 22702509.

24. Zeki, A, Thai P, Kenyon NJ, **Wu R**. Differential effects of simvastatin on IL-13-induced cytokine gene expression in primary mouse tracheal epithelial cells. Respir Res. 2012 May 14;13(1):38. [Epub ahead of print]. PMID: 22583375.
25. Lee JG and **Wu R**. Combination erlotinib-cisplatin and Atg3-mediated autophagy in erlotinib resistant lung cancer, PLOS ONE e48532. doi:10.1371/journal.pone.0048532.

D. RESEARCH SUPPORT

Ongoing Support:

RO1 HL096373 Wu (PI) 04/01/10-03/31/14
NIH/NHLBI $250,000/year (direct cost)
Regulation of airway mucin gene expression by epigenetic mechanism
The application seeks to elucidate the role of DNA methylation and changes in chromatin content in the regulation of airway mucin gene expression, especially *MUC5AC*, in human airways, and the nature of the persistent elevation of *MUC5AC* expression associated with smoking
Role: PI

R01 HL077902 Wu (PI) 08/01/05-06/30/09; 07/01/10-06/30/14
NIH/NHLBI $250,000/year (direct cost)
Title: Roles of IL-17-Induced gene expression in airway epithelial host defense
The goal of this application is to test the hypothesis that the proinflammatory cytokine, IL-17, plays an essential role in the regulation of airway host defense against bacterial infection. IL-17 is a major inducer for various epithelial innate molecules that are responsible for anti-microbial activity. In addition, these innate molecules are also responsible for Th17 cell recruitment. Through this autocrine/paracrine mechanism, airway host defense against bacterial infection is achieved.
Role: PI

RO1 HL105573 Kenyon, N (PI) 12/01/11-11/30/16
NIH/NHLBI $250,000/year (direct cost)
Title: L-Arginine as a therapy in severe asthma
The goal is to improve the care of adult severe asthmatics and to further our understanding of the mechanisms of L-arginine metabolism and nitric oxide biology in the lung. If we demonstrate that L-arginine supplementation can decrease asthma attacks in a subset of severe asthmatics, it will have great implications for future research as well as for the daily lives of patients with asthma
Role: Co-Investigator

T32 HL07013 Wu (PI) 7/1/04-6/30/09 (y26-30); 7/1/09-6/30/14 (y31-35)
NIH/NHLBI $380,000/year (direct cost)
Training in Comparative Lung Biology and Medicine
This program provides the multidisciplinary training in pulmonary research for pre-doctoral and post-doctoral fellows.
Role: Program Director and Training faculty

RO1 HL097087 (MPI) Wu and Miller (Co-PI) 09/01/09-07/31/13
NIH/NHLBI $250,000/year (direct cost)
Role of epithelium in airway immunity
The application proposes to elucidate the role of conducting airway epithelium in the development of a pathologic immune response to inhaled allergens in maturing lung and its contribution to the initiation of childhood asthma. Three specific aims are: 1) the developmental regulation of CCL20 in infant airway epithelium, 2) characterization of CCR6+ lymphocyte population in infant monkey lung following allergen exposure, and 3) the impact of IL-17A.IL-12 imbalance in allergen exposed infant monkey.
Role: Co-PI