BIOGRAPHICAL SKETCH

NAME:	Parks, William C.
eRA COMMONS USER NAME:	wparks
POSITION TITLE:	Professor

EDUCATION & TRAINING

INSTITUTION AND LOCATION	DEGREE	COMPLETION DATE	FIELD OF STUDY
College of St Thomas, St Paul, MN	BA	12/1976	Biology
Medical College of Wisconsin, Milwaukee, WI	PhD	06/1982	Anatomy and Cell Biology
Michigan State University, East Lansing, MI	Postdoc	04/1985	Cancer Biology
Washington University, St Louis, MO	Postdoc	06/1986	Extracellular Matrix Biology

A. PERSONAL STATEMENT

As co-investigator on this project, I and my lab will assist Dr. Jorth with mouse models of *P. aeruginosa* infection and establishment and use of airway organotypic (ALI) cultures, models my lab has used for years. In fact, my lab for ALI culture core services at both Wash. Univ. and UW. Research in my lab focuses on the role of matrix metalloproteinases (MMPs) in epithelial repair, host defense, and inflammation with emphasis on macrophage activation in lung diseases. Our lab has made several contributions to our basic knowledge of the control of MMP expression and activity. I have edited 6 books or serials devoted to MMPs or proteinase biology. Below are four of my most cited publications.

1. Pilcher BK, Dumin JA, Sudbeck BD, Krane SM, Welgus HG, Parks WC. 1997. The activity of collagenase-1 is required for keratinocyte migration on a type I collagen matrix. ***J Cell Biol*** 137:1445-57.
2. Wilson CL, Ouellette AJ, Satchell DP, Ayabe T, López-Boado YS, Stratman JL, Hultgren SJ, Matrisian LM, Parks WC. 1999. Regulation of intestinal α-defensin activation by the metalloproteinase matrilysin in innate host defense. ***Science*** 286:113-7.
3. Li Q, PW Park, CL Wilson, WC Parks. 2002. Matrilysin shedding of syndecan-1 regulates chemokine mobilization and transepithelial efflux of neutrophils in acute lung injury. ***Cell*** 111:635-46 *(cover article)*.
4. Parks WC, CW Wilson, YS Lopéz-Boado. 2004. Matrix metalloproteinases as modulators of inflammation and innate immunity. ***Nat Rev Immunol*** 4:617-29.

B. POSITIONS AND HONORS

Positions and Employment

2013 - now Professor of Medicine (Pulmonary and Critical Care Medicine) and Biomedical Sciences
Scientific Director, Women's Guild Lung Institute
2013 - 2017 Executive Vice Chair for Research, Department of Medicine
2016 - now Director, Graduate Program in Biomedical and Translational Sciences
2018 - now Associate Dean for Graduate Research Education
Cedars-Sinai Medical Center, Los Angeles CA

2013 - now Professor of Medicine (tenured)
David Geffen School of Medicine at UCLA, Los Angeles CA

2004 - 2013 Professor (tenured) of Medicine (Pulmonary and Critical Care Medicine)
Director, Center for Lung Biology
Endowed Chair in Pulmonary Disease Research (2011-13)
University of Washington, Seattle WA

1999 - 2004 Professor of Pediatrics (Allergy & Pulmonary Med), Medicine, and Cell Biology & Physiology
1994 - 1999 Associate Professor (tenured) of Medicine (Dermatology) and Cell Biology & Physiology
1987 - 1994 Assistant Professor of Medicine (Dermatology) and Cell Biology & Physiology
1986 - 1987 Instructor of Medicine (Pulmonary and Critical Care Medicine)
Washington University, St Louis MO

Other Experience (partial list)

2015 - 2018	Associate Editor, *American Journal of Pathology*
2013 - 2015	Editor-in-Chief (founding editor), *Metalloproteinases in Medicine*
2013 - now	Associate Editor, *Matrix Biology*
2012 - now	Consulting Editorial Board, *Journal of Clinical Investigation*
2009 - 2015	Editorial Board, *American Journal of Pathology*
2009 - 2013	Editor-in-Chief (founding editor), *Journal of Inflammation Research*
2008 - 2012	Chair, member: Lung Injury, Repair and Remodeling (LIRR) Study Section, CSR/NIH
2008 - 2018	Member: Shriner's Hospitals Research Review Board
2006 - 2013	Chair, member: Pulmonary Study Section, California Tobacco-Related Disease Res Program
2003 - 2007	Chair, member: Committee on Cell Structure and Metastasis, American Cancer Society
2000 - 2012	Past Pres. (11-12); Pres. (09-10), Pres-elect (07-08), Treasurer (00-06): Am Soc for Matrix Biol
1999 - 2003	Member, Pathobiochemistry C (PBC) Study Section, CSR/NIH
1998 - 2016	Deputy Editor (2001-04, 2015-16)/Associate Editor (other yrs), *Am J Resp Cell & Mol Biol*

Honors (partial list)

2015	Scientific Achievement Award, American Thoracic Society
2011-13	Endowed Chair in Pulmonary Disease Research, University of Washington
2003	Chair, Gordon Research Conference on Tissue Repair and Regeneration
2001	Johns Hopkins Scholar in Lung Biology
1998, 2008	Triangle Area Pulmonary Scholar, Duke, UNC, NCS
1997	Chair, Gordon Research Conference on Elastin and Elastic Tissue
1997	Lester I. Conrad Foundation Award in Dermatology Research
1993-98	Genentech Scholar/American Lung Association Career Investigator Award

C. CONTRIBUTIONS TO SCIENCE

1. MMPs as Effectors of Inflammation and Macrophage Activation. Our lab was among the first to propose and demonstrate (citations 2-4 above) that MMPs function more to control precise processes of immunity and inflammation than to degrade ECM. Studying MMPs in inflammation, with an emphasis on macrophage activation, has been a focus of our lab for several years.

a. Gill SE, Gharib SA, Bench EM, Sussman SW, Wang RT, Rims C, Birkland TP, Wang Y, Manicone AM, McGuire JK, Parks WC. 2013. Tissue inhibitor of metalloproteinases 3 (TIMP3) moderates the pro-inflammatory status of macrophages. ***Am J Respir Cell Mol Biol*** 49:768-77.

b. Rohani MG, McMahan RS, Hurtz AL, Razumova MV, Cieslewicz M, Pun SH, Wang Y, Birkland TP, Parks WC. 2015. Stromelysin-2 (MMP-10) regulates the collagenolytic activity of alternatively activated resident macrophages. ***J Invest Dermatol*** 135:2377-84.

c. McMahan RS, Birkland TP, Smigiel KS, Vandivort TC, Manicone AM, McGuire JK, Gharib SA, Parks WC. 2016. Stromelysin-2 (MMP10) moderates inflammation by controlling macrophage activation. ***J Immunol*** 197:899-909.

d. Rohani MG, Dimitrova E, Beppu A, Wang Y, Jefferies CA, Parks WC. 2018. Macrophage MMP10 regulates tolerance to TLR7 signaling. *Front Immunol*, in press.

2. MMPs in Skin Repair My entry into MMP biology began with studies on human ulcerations and normal skin wounds. Our principal findings, including citation 1 above, demonstrated an essential role for MMP1 in closure of human wounds and how this proteinase promotes re-epithelialization by affecting the nature of specific cell:matrix interactions. We are now studying how MMPs functions to control macrophage activation and the resolution of scar tissue.

e. Sudbeck BD, Pilcher BK, Welgus HG, Parks WC. 1997. Induction and repression of collagenase-1 by keratinocytes is controlled by distinct components of different extracellular matrix compartments. ***J Biol Chem*** 272:22103-10.

f. Dumin JA, Dickeson SK, Stricker TP, Bhattacharyya-Pakrasi M, Roby JD, Santoro SA, Parks WC. 2001. Procollagenase-1 (MMP-1) binds the integrin $\alpha_2\beta_1$ upon release from keratinocytes migrating on type I collagen. ***J Biol Chem*** 276:29368-74.

g. Krampert M, Bloch W, Sasaki T, Bugnon P, Rülicke T, Wolf E, Aumailley M, Parks WC, Werner S. 2004. Activities of the matrix metalloproteinase stromelysin-2 (MMP-10) in matrix degradation and keratinocyte organization in wounded skin. ***Mol Biol Cell*** 15:52454. PMCID: PMC532007

h. Rohani MG, Pilcher BK, Chen P, Parks WC. 2014. Cdc42 inhibits ERK-mediated matrix metalloproteinase-1 (MMP-1) expression in collagen-activated keratinocytes. ***J Invest Dermatol*** 134:1230-7. PMCID: PMC3989453

3. MMP in Lung Repair and Disease. Our findings in skin wounds led us to explore how these proteinases function in repair of lung and gut. Our work on MMPs in lung biology and repair have been one of our most productive and recognized areas or research. Among our discoveries, we determined that MMP7 functions to control the transepithelial movement of neutrophils (citation 3 above) and promotes re-epithelialization by affecting the nature of specific cell:matrix interactions.

i. McGuire JK, Li Q, Parks WC. 2003. Matrilysin-mediated cleavage of E-cadherin ectodomain is associated with mucosal re-epithelialization. ***Am J Pathol*** 162:1831-43. PMCID: PMC1868120

j. Chen P, Abacheri LE, Nadler ST, Wang Y, Li Q, Parks WC. 2009. Matrilysin shedding of syndecan-1 facilitates re-epithelialization by affecting $\alpha_2\beta_1$ integrin activation. ***PLoSOne*** 4:e6565. PMCID: PMC2719060

k. Gharib SA, Altemeier WA, Van Winkle LS, Plopper CG, Schlesinger SY, Buell CA, Brauer R, Lee V, Parks WC, Chen P. 2012. MMP7 coordinates airway epithelial injury response and modulates ciliogenesis. ***Am J Respir Cell Mol Biol*** 48:390-6.

l. Gharib SA, Loth DW, Artigas MS, Birkland TP, Wilk JB, Wain LV, Obeidat M, Tang W, Rawal R, Boezen HM, Imboden M, Huffman JE, Lahousse L, Manichaikul A, Hui J, Smith AV, Surakka I, Vitart V, Evans DM, Strachan, DP, Hofman A, Gläser S, Wilson JF, North KE, Zhao JH, Heckbert SR, Jarvis DL, Probst-Hensch N, Schulz H, Barr RG, Jarvelin M-R, O'Connor GT, Kähönen M, Cassano PA, Dupuis J, Hayward C, Psaty BM, Hall IP*, Parks WC*, Tobin MD*, London SJ*. 2015. Pathway genomics of lung function and airflow obstruction. ***Hum Molec Genet*** 24:6836-48. (*co-senior authors).

4. MMP28, Epilysin. Our lab discovered MMP28, the last human MMP. We named it epilysin, as we cloned from epithelial libraries and determined it is broadly expressed among epithelia. However, we since determined it is prominently expressed by macrophages and functions to control macrophage activation.

m. Lohi J, Wilson CL, Roby JD, Parks WC. 2001. Epilysin: A novel matrix metalloproteinase (MMP-28) expressed in testis and keratinocytes and in response to injury. ***J Biol Chem*** 276:10134-44.

n. Manicone AM, Birkland TP, Lin M, Betsuyaku T, van Rooijen N, Lohi J, Keski-Oja J, Wang Y, Skerrett SJ, Parks WC. 2009. Epilysin (MMP-28) restrains early macrophage recruitment in *Pseudomonas aeruginosa* pneumonia. ***J Immunol*** 182:3866-76. PMCID: PMC2721855

o. Gharib SA, Johnston LK, Huizar I, Birkland TP, Hanson J, Wang Y, Parks WC, Manicone AM. 2014. MMP28 promotes macrophage polarization toward M2 cells and pulmonary fibrosis. ***J Leukoc Biol*** 95:9-18. *(Leading Edge Research article)*

p. Manicone AM, Gharib SA, Eddy W, Gong K, Long M, Frevert CW, Altemeier WA, Parks WC, Houghton AM. 2017. MMP28 is a key contributor to COPD pathogenesis. ***Am J Pathol*** 187:1288-1300.

5. Host-Pathogen Interactions. In addition to our 1999 *Science* paper (#2 above), we have explored various mechanisms of defensin activation and how bacteria interact with host cells and matrix.

q. López-Boado YS, Wilson CL, Hooper LV, Gordon JI, Hultgren SJ, Parks WC. 2000. Bacterial exposure induces and activates matrilysin in mucosal epithelial cells. ***J Cell Biol*** 148:1305-15. PMCID: PMC2174301

r. Gounder AP, Myers ND, Treuting PM, Bromme BA, Wilson SS, Wiens ME, Lu W, Ouellette AJ, Spindler KR, Parks WC, Smith JG. 2016. Defensins potentiate a neutralizing antibody response to enteric viral infection. ***PLoS Pathogens*** 12:e1005474-20. PMCID: PMC4774934

s. Secor PR, Sweere J, Michaels LA, Malkovskiy AV, Lazzareschi D, Katznelson E, Arrigoni A, Braun KR, Evanko SP, Kaminsky W, Singh PK, Parks WC*, Bollyky PL*. 2015. Filamentous bacteriophage promote biofilm assembly and tolerance to desiccation and antibiotics. ***Cell Host Microbe*** 18:549-59 (*co-senior authors).

t. Secor PR, Michaels LA, Smigiel KS, Rohani MG, Jennings LK, Hisert KA, Arrigoni A, Braun KR, Birkland TP, Lai Y, Hallstrand TS, Bollyky PL, Singh PK, Parks WC. 2016. Filamentous bacteriophage produced by *Pseudomonas aeruginosa* alters the inflammatory response and promotes non-invasive infection *in vivo*. ***Infect Immun*** 85:e00648-16. *(Cover article)*

Complete List of Published Work (172 peer-reviewed original papers; 49 reviews, chapters; 6 books/serials)**:** http://www.ncbi.nlm.nih.gov/sites/myncbi/william.parks.2/bibliography/41193975/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

R01 HL120947 (Chen) 1-14 to 12-17
Syndecan-1 Regulation of Influenza Infection
The goals of this project are to determine the mechanisms by which syndecan-1 moderate apoptotic pathways in airway epithelium in response to viral infection.
Role: Co-investigator

NIH R01 AI072726 (Arditi) 2-16 to 1-21
Role of IL-1 in Bacterial Ligand-induced Vasculitis and Myocarditis
The goals of this project are to determine how IL-1α and IL-1β promote development of vasculitis, aneurysm and myocarditis.
Role: Co-investigator

NIH T32 GM118288 (Parks) 7-17 to 6-22
Graduate Program in Biomedical and Translational Sciences
Pre-doctoral institutional training grant; 4 slots/year.
Role: PI

NIH R01 HL137076 (Chen; Schroer) 1-18 to 11-21
Dynactin 4 regulation of lung injury
This project focuses on the mechanism by which the mutant DCTN4 impairs airway repair, remodeling, and response to infection.
Role: Co-investigator

NIH R01 HL141078 (Parks) 4-18 to 3-22
Control of Macrophage Activation in Lung Disease
This project focuses on the mechanisms controlling the ability of macrophages to degrade extracellular matrix in fibrotic lung disease.
Role: PI

NIH P01 HL108793 (Noble) 8-18 to 6-23
Epithelial-Mesenchymal Interactions in Pulmonary Fibrosis and Chronic Allograft Dysfunction (CLAD)
The goals of this Program are to uncover mechanisms that contribute to disease progression and identity novel therapeutic targets to combat lung fibrosis whether it occurs in the airway or in the interstitium of the lung.
Role: Co-investigator (Projects 1 and 3)

Completed Research Support (partial list)

NIH R56 HL128995 (Parks) 9-1-15 to 8-31-16
Role of MMP10 in Macrophage Activation
The goals of this 1-yr project were study aspects of MMP10 control of macrophage activation. Data formed the foundation of R01 HL141078.
Role: PI

NIH P01 HL098067 (**Ziegler**) 8-1-10 to 5-31-15
Regulation of Pulmonary Inflammation by Leukocytes and Extracellular Matrix
Project 3: Role of Stromelysin-2 (MMP10) in Lung Immunity (Parks)
This project focuses on how MMP10 governs proinflammatory macrophage activation in response to *P. aeruginosa* infection.
Role: Project PI