# August 2006

## **CURRICULUM VITAE**

## MARK DAMIAN WEWERS, M.D.

### Title:

John A. Prior Professor of Medicine The Ohio State University College of Medicine

# **Mailing Address:**

110L Davis Heart and Lung Research Institute 473 West 12<sup>th</sup> Avenue Columbus, Ohio 43210

# **Telephone:**

(614) 293-4925 FAX: (614) 293-4799

### **Personal:**

March 2, 1950

### **Education:**

1964-1968	Subiaco Academy, Subiaco, Arkansas (Valedictorian)
1968-1970	St. Louis University, St. Louis, Missouri
1970-1972	B.A., Zoology, University of Arkansas, Fayetteville, Arkansas
1972-1976	M.D., University of Arkansas School of Medicine, Little Rock, Arkansas

## **Postgraduate Training:**

1976-1977	Intern, Internal Medicine
	University of Arkansas Medical Sciences, Little Rock, Arkansas
1977-1979	Resident, Internal Medicine
	University of Arkansas Medical Sciences, Little Rock, Arkansas
1979-1981	Fellowship, Pulmonary Disease
	University of Arkansas Medical Sciences, Little Rock, Arkansas

# **Academic Positions:**

1981-1983	Visiting Professor, Pulmonary Branch, National Heart, Lung and Blood Institute, Bethesda, Maryland.
1983-1986	Senior Investigator, Pulmonary Branch, National Heart, Lung and Blood Institute, Bethesda, Maryland.
1986-1990	Assistant Professor of Medicine, Pulmonary and Critical Care Division, Ohio State University College of Medicine, Columbus, Ohio.
1990-1995	Associate Professor of Medicine, Pulmonary and Critical Care Division, Ohio State University College of Medicine, Columbus, Ohio.
1995	Professor of Medicine, Pulmonary and Critical Care Division, Ohio State University College of Medicine, Columbus, Ohio.

2001-present	Joint Appointment, Department of Molecular Virology, Immunology and Medical Genetics, The Ohio State University.
1996-2002	Director, Division of Pulmonary and Critical Care, Ohio State University College of Medicine.
1997-2005	Deputy Director, Davis Heart and Lung Research Institute, The Ohio State University.
2000-2002	Interim Director, Davis Heart and Lung Research Institute, The Ohio State University
2002-present	Graduate Faculty, Interdisciplinary Program in Biophysics, The Ohio State University.
2005-present	Executive Associate Director, Davis Heart and Lung Research Institute, The Ohio State University.

#### **Board Certification and Licensure:**

1980	Diplomate, American Board of Internal Medicine
1982	Diplomate, American Board of Internal Medicine
	Subspecialty - Pulmonary Disease
1989	Diplomate, American Board of Internal Medicine
	Subspecialty - Critical Care Medicine (recertified 2004-2014)
1986-present	Licensed to Practice Medicine, State of Ohio

### **Professional Memberships:**

American Thoracic Society
European Respiratory Society
American College of Chest Physicians
Ohio Thoracic Society
Alpha-1 Association
American Academy for the Advancement of Science
The Ohio State University Comprehensive Cancer Center
American Association of Immunologists
International Cytokine Society
Davis Heart Lung Research Institute, Investigator.

# **Honors and Scientific Recognition:**

1973 McGuire Scholarship Recipient; University of Arkansas, Little Rock, Arkansas AOA, University of Arkansas 1976.

Unverferth Award for Leadership in Research, Department of Internal Medicine, 1998.

Lung Biology/Pathology A Study Section, NHLBÎ, permanent member 1996-2000

Associate Editor, Journal of Immunology 1999-2003.

Promotions and Tenure Committee, Department of Internal Medicine 1995-1997. Promotions and Tenure Committee, Department of Internal Medicine 1999-2002

Appointments, Promotion and Tenure Committee, College of Medicine 1998-2003.

Member, Ohio State University Vice President for Research Advisory Group, 2000-2002.

Member, College of Medicine Council of Chairs, 2000-2002.

John A. Prior Professorship 2000-present.

Member, Investigation Committee, College of Medicine 2003-present

Distinguished Mentor Award, Davis Heart and Lung Research Institute, 2003.

Appointments, Promotions and Tenure Committee, Department of Internal Medicine 2004-Collaborative Leader Award, 2006, DHLRI

#### **Research Interests:**

Regulation of macrophage caspases Macrophage biology NOD-like receptor biology

#### **Grant Review:**

NIH, National Heart, Lung and Blood, Pathology A and Pulmonary Ad Hoc Reviewer 1989-1995.

Canadian Cystic Fibrosis Foundation 1994.

Veteran's Administration Merit Review Board, 1994-1995.

American Lung Association, National Grant Review Board 1994-1996

NIH, Specialized Center of Research Interstitial Lung Disease Ad Hoc Reviewer, 1992

NIH, Program Project Reviewer, 1993.

American Lung Association of Ohio, Research and Awards Review Committee Chairman, 1998.

NIH, Lung Biology Pathology A Study Section Member, 1996-2000.

NIH, Specialized Center for Research for Pathobiology of Interstitial Lung Disease, Study Section Member, January 2001.

American Lung Association of Ohio, Research and Awards Review Committee Chairman, 2001 and 2002.

NIH, Special Emphasis Panel, ZRG1 Resp, 2001.

Burroughs Wellcome, Grant Review, ad hoc, 2001.

NIH, NHLBI, Program Project Review, 2002.

NIH, NIAID, Ad Hoc Reviewer, 2002.

Swiss National Science Foundation, Ad Hoc Reviewer 2004

NIH, Inflammation and Innate Immunity Study Section, ad hoc, February 2005

NIH, Lung Cellular and Molecular Immunobiology Study Section, ad hoc, February 2006

NIH, NIGMS, Glue Grant Review Committee, March 2006.

British Lung Foundation, Ad Hoc Reviewer May 2006.

Alpha-1 Foundation, Grants Advisory Committee, July 2006- June 2008.

#### **Journal Review:**

Journal of Immunology (Associate Editor 1999-2003) American Journal of Respiratory and Critical Care Medicine American Journal of Respiratory Cell and Molecular Biology American Journal of Physiology **CHEST** Cytokine Journal of Immunological Methods Blood Genes and Immunity Journal of Clinical Investigation Critical Care Medicine New England Journal of Medicine Proceedings of the National Academy of Sciences Infection and Immunity

## **Grant Support (Current):**

"Regulation of Macrophage Interleukin-1ß Production" **Principal Investigator**: Mark D. Wewers, M.D. National Institutes of Health, R01 HL40871, 2/01/02 through 12/31/06, Annual Direct Cost, \$200,000. Total Cost, \$900,000.

"Macrophage Inflammasome Regulation"

**Principal Investigator:** Mark D. Wewers, M.D.

NIH NHLBI 1 R01 HL076278 12/15/04 through 12/15/08 Annual Direct Cost: \$250,000. Total directs \$1,000,000

"Molecular Mechanisms of Lung Inflammation", Principal Investigator: Mark D. Wewers, M.D. National Institutes of Health, 1 T32 HL07946-01 07/01/00 - 06/30/05Direct costs: \$157,215.

"Macrophage Inflammasome Activation in Tularemia" Principal Investigator (Project 2): Mark D. Wewers, M.D. University of Chicago subcontract, Great Lakes RCE National Institutes of Health, 5U54AI057153-03 01/01/06 - 2/28/08Annual Direct Costs: \$83,000.

"Induction of Inflammation by Mitochondrial Proteins" Principal Investigator: Elliott Crouser, M.D. Co-Investigator: Mark D. Wewers, M.D. NIH NIAIĎ R03 AI062740-01A1 07/01/2005 - 06/30/2007

Total Direct Costs: \$149,500

"Alveolar macrophage proteomics in HIV-induced emphysema" **Principal Investigator:** Philip Tomas Diaz, M.D.

Co-Investigator: Mark D. Wewers, M.D.

NIH/NHLBI R01 HL083478 09/29/2005 – 06/30/2010 Annual Direct costs: \$411,125.

"Cytolytic Attack Against Lung Parenchyma in Emphysema"

**Principal Investigator**: Daren Knoell, Pharm.D. National Institutes of Health K08 HL044620-01

Mentor: Mark D. Wewers, M.D. Direct Costs: \$125,565 annual Total Direct Costs: \$658,317

"Fibroproliferative ARDS: mechanisms of cell death and repair."

**Principal Investigator**: Ruairi Fahy, M.B.

NIH NHLBI K23HL69899-01

04/01/02 -03/01/07

Mentor: Mark D. Wewers, M.D. Direct Costs: \$ 129,060 annual Total Direct Costs: \$644,490

"Exercise as an anti-inflammatory therapy for asthma" **Principal Investigator:** John Mastronarde, M.D.

10/01/04- 7/31/06

Mentor: Mark D. Wewers, M.D.

Direct Costs: \$109,987

"HIV-1 induction of intracellular host defense mechanisms"

Principal Investigator: Raquel Raices

National Institutes of Health, NIAID F31 AI061828-01

Mentor: Mark D. Wewers 12/01/04 – 11/30/07 Amount: \$30,448, annual.

"Monocyte Pyrin Expression in Human Sepsis"

Principal Investigator: Mark W. Hall, M.D.

Co-mentors: Mark D. Wewers, M.D. and Wolfgang Sadee, Ph.D.

NIH NHLBI K08

Direct costs annually: \$122,500.

#### **Pending Applications:**

"Innate Immunity, Stress, and Chronic Lung Disease"

Principal Investigator: Clay B. Marsh, M.D. Project 2 Director: Mark D. Wewers, M.D.

NIH, NHLBI, SCCOR 12/01/2006 – 11/30/2011

Total Direct Costs: \$19,852,477.

"Effect of Cigarette Smoking on Tumor Suppressor Genes and Cytokines""

**Principal Investigator**: Elizabeth J. Corwin, Ph.D.

Co-I: Mark D. Wewers, M.D. 3% effort

NIH NINR

**Direct Costs Program** (requested): \$1,083,875.

"Zinc Importer SLC39A8 and Lung Epithelial Cell Survival"

**Principal Investigator**: Beth Besecker, M.D. Primary Mentor: Mark D. Wewers, M.D.

Co Mentors: Daren Knoell, Pharm.D. and Wolfgang Sadee, Ph.D.

Direct Costs: \$117,532.

"Induction of Inflammation by Mitochondrial Proteins"

**Principal Investigator**: Elliott Crouser, M.D. Co-Investigator: Mark D. Wewers, M.D.

NIH/NIAID R03 AI062740 Direct costs: \$74,750 annually.

"Molecular Mechanisms of Lung Inflammation", **Principal Investigator:** Mark D. Wewers, M.D. National Institutes of Health, 1 T32 HL07946-06 07/01/06 – 06/30/11

## **Completed Projects:**

"Lymphocytic Alveolitis, IL-1β Regulation and Lung Injury" **Principal Investigator**: Mark D. Wewers, M.D. NIH NHLBI R01 HL53229 August 1994-July 1999, Principal Investigator

Direct costs: \$875,464. Total costs: \$1,278,177.

"Monocyte Fcgamma Receptors and Vascular Sclerosis", **Principal Investigator** of Project 2, Mark D. Wewers, M.D., NIH PO1 AI 40105-01 Basic Mechanisms of Chronic Allograft Rejection 8/31/96-7/31/02

Direct costs: \$384,887. Total costs: \$561,934

"HIV Surveillance Affects Macrophage Function", **Principal Investigator:** Mark D. Wewers, M.D. National Institutes of Health, 1 R01 HL62054 9/30/98 – 8/31/03

Direct costs: \$200,000. Total costs: \$274,358. Year 1.

Direct costs: \$1,000,000. Total costs: \$1,371,790. Total project.

"Macrophage HIV Infection in the Lung Microenvironment",

**Principal Investigator:** Mark D. Wewers, M.D. National Institutes of Health, 1 RO1 HL63649-01

7/01/99 - 6/30/04

Direct costs: \$200,000. Total costs: \$274,358. Year 1. Direct costs: \$1,000,000. Total costs: \$1,371,790.

**Sponsor** for James N. Allen, M.D. NIH, Clinical Investigator Award, July 1992-June 1997, Indirect costs: \$ 360,000.

**Sponsor** for Clay B. Marsh, M.D. Francis Families Foundation Fellowship July 1995-June 1998, Indirect costs: \$105,000.

**Sponsor** of David Ralston, M.D. American Heart Association Fellowship July 1996- June 1998. \$35,000 annually.

**Sponsor** for Ruairi Fahy, M.D. Glaxo Wellcome Pulmonary Fellowship July 1998- June 1999. \$35,000.

**Director**, Study Center at Columbus, Ohio, NIH NHLBI National Alpha-1-antitrypsin Deficiency Registry

### **PUBLICATIONS**

#### A. Refereed Articles:

- 1. **Wewers MD,** Hiller CH, Wilson FW, Bone RC. Hemophilus influenzae infection of an existing lung cyst. **South Med Journal** 1982; 75:736-737.
- 2. **Wewers MD**, Rennard SI, Hance AJ, Bitterman PB, Crystal RG. Normal human alveolar macrophages obtained by bronchoalveolar lavage have a limited capacity to release interleukin-1. **J Clin Invest** 1984; 74:2208-2218.
- 3. Pelham F, **Wewers M,** Crystal RG, Buist SA, Janoff A. Urinary excretion of desmosine (elastin crosslinks) in subjects with PiZZ alpha-1-antitrypsin deficiency, a phenotype associated with hereditary predisposition to pulmonary emphysema. **Am Rev Resp Dis** 1985; 132:821-823.
- 4. Straus SD, Fells GA, **Wewers MD**, et al. Evaluation of recombinant DNA-directed E. coli produced alpha 1-antitrypsin as an anti-neutrophil elastase for potential use as replacement therapy for alpha 1-antitrypsin deficiency. **Biochem Biophys Res Comm** 1985; 130:1177-1184.
- 5. Bitterman PB, **Wewers MD**, Rennard SI, Adelberg S, Crystal RG. Modulation of alveolar macrophage-driven fibroblast proliferation by alternative macrophage mediators. **J Clin Invest** 1986; 77:700-708.
- 6. Bitterman PB, Rennard SI, Keogh BA, **Wewers MD**, Adelberg S, Crystal RG. Familial idiopathic pulmonary fibrosis: evidence of lung inflammation in unaffected family members. **N Engl J Med** 1986; 314:1343-1347.
- 7. **Wewers MD,** Gadek JE, Keogh BA, Fells GA, Crystal RG. Evaluation of danazol therapy for patients with PiZZ alpha-1-antitrypsin deficiency. **Am Rev Resp Dis** 1986; 134:476-480.
- 8. **Wewers MD**, Saltini C, Sellers S, et al. Evaluation of alveolar macrophages in normals and individuals with active pulmonary sarcoidosis for the spontaneous expression of the interleukin-1 beta gene. **Cell Immunol** 1987; 107:479-488.
- 9. Casolaro MA, Fells G, **Wewers MD**, et al. Augmentation of lung antineutrophil elastase capacity with recombinant human alpha-1-antitrypsin. **J Appl Physiol** 1987; 63:2015-2023.
- 10. **Wewers MD**, Brantly ML, Casolaro MA, Crystal RG. Evaluation of tamoxifen as a therapy to augment alpha-1-antitrypsin concentrations in Z homozygous alpha-1-antitrypsin deficient individuals. **Am Rev Resp Dis** 1987; 135:401-402.
- 11. **Wewers MD**, Casolaro MA, Sellers SE, et al. Replacement therapy for alpha 1-antitrypsin deficiency associated with emphysema. **N Engl J Med** 1987; 316:1055-1062.
- 12. **Wewers MD**, Casolaro MA, Crystal RG. Comparison of alpha-1-antitrypsin levels and antineutrophil elastase capacity of blood and lung in a patient with the alpha-1-antitrypsin phenotype null-null before and during alpha-1-antitrypsin augmentation therapy. **Am Rev Resp Dis** 1987; 135:539-543.

- 13. Bernaudin J-F, Yamauchi K, **Wewers MD**, Tocci MJ, Ferrans VJ, Crystal RG. Demonstration by in situ hybridization of dissimilar IL-1 beta gene expression in human alveolar macrophages and blood monocytes in response to lipopolysaccharide. **J Immunol** 1988; 140:3822-3829.
- 14. Davis WB, Husney RM, **Wewers MD**, Herzyk DJ, Sagone AL. Effect of oxygen partial pressure on the myeloperoxidase pathway of neutrophils. **J Appl Physiol** 1988; 65:1995-2003.
- 15. **Wewers MD**, Herzyk DJ, Gadek JE. Alveolar fluid neutrophil elastase activity in the adult respiratory distress syndrome is complexed to alpha-2-macroglobulin. **J Clin Invest** 1988; 82:1260-1267.
- 16. Allen JN, **Wewers MD**. HIV-associated bronchiolitis obliterans organizing pneumonia. **Chest** 1989; 96:197-198.
- 17. Sagone AL, Husney RM, **Wewers MD**, Herzyk DJ, Davis WB. Effect of dimethylthiourea on the neutrophil myeloperoxidase pathway. **J Appl Physiol** 1989; 67:1056-1062.
- 18. She Z-W, **Wewers MD**, Herzyk DJ, Sagone AL, Davis WB. Tumor necrosis factor primes neutrophils for hypochlorous acid production. **Am J Physiol** 1989; 257:L338-L345.
- 19. **Wewers MD**, Herzyk DJ. Alveolar macrophages differ from blood monocytes in human interleukin 1 beta release: quantitation by enzyme linked immunoassay. **J Immunol** 1989; 143:1635-1641.
- 20. **Wewers MD**, Herzyk DJ, Gadek JE. Comparison of smoker and nonsmoker lavage fluid for the rate of association with neutrophil elastase. **Am J Respir Cell Mol Biol** 1989; 1:423-429.
- 21. Allen JN, **Wewers MD**. Acute myocardial infarction with cardiogenic shock during pregnancy: treatment with intra-aortic balloon counterpulsation. **Crit Care Med** 1990; 18:888-889.
- 22. Anderson CL, Shen L, Eicher DM, **Wewers MD**, Gill JK. Phagocytosis mediated by three distinct Fcgamma receptor classes on human leukocytes. **J Exp Med** 1990; 171:1333-1345.
- 23. **Wewers MD**, Rinehart JJ, She Z-W, et al. Tumor necrosis factor infusions in humans prime neutrophils for hypochlorous acid production. **Am J Physiol Lung Cell Mol Physiol** 1990; 259:L276-L282.
- 24. Allen JN, Herzyk DJ, **Wewers MD**. Colchicine has opposite effects on interleukin-1β and tumor necrosis factor α production. **Am J Physiol Lung Cell Mol Physiol** 1991;5:L315-L321.
- 25. Allen JN, Herzyk DJ, Allen ED, **Wewers MD**. Human whole blood interleukin-1β production: kinetics, cell source and comparison with TNF-α. **J.Lab.Clin.Med.** 119:538-546, 1992.
- 26. Herzyk DJ, Berger A, Allen JN, **Wewers MD**. Sandwich ELISA formats designed to detect 17 kDa IL-1β significantly underestimate 35 kDa IL-1β. **J.Immunol.Methods.** 148:243-254, 1992.

- 27. Herzyk DJ, Allen JN, Marsh CB, **Wewers MD.** Macrophage and monocyte IL-1β regulation differs at multiple sites: mRNA expression, translation, and posttranslational processing. **J.Immunol** 149:3052-3058, 1992.
- 28. Herzyk D.J., and **Wewers MD**. ELISA detection of IL-1β in human sera needs independent confirmation: false positives in hospitalized patients. **Am.Rev.Resp.Dis.** 147:139-142, 1993.
- 29. Kindt, GC, Moore SA, She Z-W, **Wewers MD.** Endotoxin priming of monocytes augments Fcγ receptor cross-linking induced TNFα and IL-1β release. **Am.J.Physiol** 265:L178-L185, 1993.
- 30. Diaz, P, **Wewers MD**, Clanton TC. Tumor necrosis factor and endotoxin do not directly affect in vitro diaphragm function. **Am.Rev.Resp.Dis**. 148:281-287, 1993.
- 31. Allen JN, Moore SA, **Wewers MD.** Taxol enhances but does not induce interleukin-1β and tumor necrosis factor-α production. **J.Lab.Clin.Med.** 122:374-381, 1993.
- 32. **Wewers MD**, Pope HA, Miller DK. Processing proIL-1β decreases detection by a proIL-1β specific ELISA but increases detection by a conventional ELISA. **J.Immunol.Meth**. 165:69-278, 1993.
- 33. She Z.-W., **Wewers MD,** Herzyk DJ, Davis WB. Tumor necrosis factor increases the elastolytic potential of adherent neutrophils: a role for hypochlorous acid. **Am.J.Resp.Cell Mol.Biol.** 9:386-392, 1993.
- 34. Overdahl M, **Wewers MD**. Acute occlusion of a mainstem bronchus by a rapidly expanding foreign body. **Chest** 105:1600-1602, 1994.
- 35. Marsh CB, **Wewers MD**. Cytokine induced interleukin-1 receptor antagonist release in mononuclear phagocytes. **Am.J.Resp.Cell Mol.Biol.** 10:521-525, 1994.
- 36. Marsh CB, Moore SA, Pope HA and **Wewers MD**. Interleukin-1 receptor antagonist decreases endotoxin induced interleukin-1β and tumor necrosis factorα release from mononuclear phagocytes. **Am.J.Physiol.** 11:L39-L45, 1994.
- 37. Marsh CB, Pope HA, **Wewers MD**. Fc gamma receptor crosslinking downregulates IL-1ra and induces IL-1β in mononuclear phagocytes stimulated with endotoxin or Staphylococcus aureus. **J.Immunol.** 152:4604-4611, 1994.
- 38. Allen JN, Moore SA, Pope-Harman AL, Marsh CB, **Wewers MD**. Immunosuppressive properties of surfactant and plasma on alveolar macrophages. **J.Lab.Clin.Med.** 125:356-369, 1995.
- 39. O'Brien JM, **Wewers MD**, Moore SA, Allen JN. Taxol and colchicine increase LPS-induced pro-IL-1β production, but do not increase IL-1β secretion: a role for microtubules in the regulation of IL-1β production. **J. Immunol.** 154:4113-4122, 1995.
- 40. Altenberger EA, Pope HA, **Wewers MD**. Detection of soluble type II receptor in the presence of its natural ligand IL-1β: quantification by sandwich ELISA. **J. Immunol. Meth.** 185:115-122, 1995.

- 41. Marsh CB, Gadek JE, Kindt GC, Moore SA, **Wewers MD.** Monocyte Fc gamma receptor crosslinking induces interleukin-8 production. **J. Immunol.** 155:3161-3167, 1995.
- 42. Pue CA, Mortensen RF, **Wewers MD**. Acute phase levels of C-reactive protein enhance IL-1β and IL-1ra production by human blood monocytes but inhibit IL-1β and IL-1ra production by alveolar macrophages. **J. Immunol.** 156:1594-1600,1996.
- 43. Allen JN, Liao Z, **Wewers MD**, Altenberger EA, Moore SA, Allen ED. Detection of interleukin-5 and interleukin-1 receptor antagonist in bronchoalveolar lavage in acute eosinophilic pneumonia. **Journal of Allergy and Clinical Immunology**. 97:1366-1374, 1996.
- 44. Marsh CB, Anderson CL, Lowe MP, **Wewers MD**. Monocyte IL-8 release is induced by two independent FcyR-mediated pathways. **J. Immunol**. 157:2632-2637, 1996.
- 45. Brown EA, Dare HA, **Wewers MD**. The combination of endotoxin and dexamethasone induces Type II interleukin-1 receptor (IL-1RII) in monocytes: a comparison to interleukin-1β (IL-1β) and interleukin-1 receptor antagonist (IL-1ra). **Cytokine** 8:826-836, 1996.
- 46. Allen JN, Moore SA, Jurist UA, Liao Z, **Wewers MD**. Changes in mononuclear phagocyte microtubule stability and composition after endotoxin stimulation: I. Changes in microtubule stability. **Am.J. Resp.Cell Mol.Biol**. 16:119-126, 1997.
- 47. Allen JN, Moore SA, Jurist UA, Liao Z, **Wewers MD**. Changes in mononuclear phagocyte microtubule stability and composition after endotoxin stimulation: II. Changes in microtubule stability. **Am.J. Resp.Cell Mol.Biol**. 16:127-132, 1997.
- 48. Marsh, C.B., **Wewers, M.D**., Tan, L.C., and Rovin, B.H. Fc gamma receptor cross-linking induces peripheral blood mononuclear cell MCP-1 expression: role of Fc gamma RIII. **J.Immunol**. 158:1078-1084, 1997
- 49. Ralston, DR, Marsh CB, Lowe MP, and **Wewers MD**. Antineutrophil cytoplasmic antibodies induce monocyte IL-8 release: role of surface proteinase-3, alpha-1 antitrypsin, and Fcgamma receptors. **J. Clin. Invest.** 100:1416-1424, 1997.
- 50. **Wewers, MD**, Dare HA, Winnard AV, Parker JM, and Miller DK. IL-1β converting enzyme (ICE) is present and functional in human alveolar macrophages: macrophage IL-1β release limitation is ICE independent. **J. Immunol.** 159:5964-5972, 1997.
- 51. Marsh CB, Lowe MP, Rovin BH, Parker JM, Liao Z, Knoell DL, **Wewers MD**. Lymphocytes produce IL-1 beta in response to Fc gamma receptor cross-linking: effects on parenchymal cell IL-8 release. **J. Immunol**. 160:3942-3948, 1998.
- 52. Knoell, DL, Ralston DR, Coulter KR, and **Wewers MD**. Alpha 1-antitrypsin and protease complexation is induced by LPS, IL-1β and TNFα in monocytes. **Am. J. Resp. Crit. Care Med.** 157:246-255, 1998.

- 53. **Wewers MD**, Diaz PT, Wewers ME, Lowe MP, Nagaraja HN, Clanton TL. Cigarette smoking in HIV infection induces a suppressive inflammatory environment in the lung. **Am. J. Resp. Crit. Care Med.** 158:1543-1549, 1998.
- 54. Coulter KR, **Wewers MD**, Lowe MP, Knoell DL. Extracellular regulation of IL-1β through lung epithelial cells and defective interleukin-1β type II receptor expression. **Am. J. Resp. Cell and Mol. Biol**. 20:964-975, 1999.
- 55. **Wewers MD**, Winnard AV, Heidi A. Dare. Endotoxin stimulated monocytes release multiple forms of IL-1beta including a proIL-1beta form whose detection is affected by export. **J. Immunol**. 162:4858-4863, 1999.
- 56. Marsh CB, Pomerantz RP, Parker JM, Winnard AV, Mazzaferri EL, Jr., Moldevan N, Kelley T, Beck E, **Wewers MD**. Regulation of monocyte survival in vitro by deposited IgG: role of macrophage colony stimulating factor. **J. Immunol**. 1999 162:6217-6225.
- 57. Diaz PT, King MA, Pacht ER, **Wewers MD**, Gadek JE, Neal D, Nagaraja HN, Drake J, Clanton TL. The pathophysiology of pulmonary diffusion impairment in human immunodeficiency virus infection. **Am. J. Resp. Crit. Care Med.** 160:272-277, 1999.
- 59. Fahy, RJ, Doseff A, **Wewers MD**. Spontaneous human monocyte apoptosis utilizes a caspase-3 dependent pathway which is blocked by endotoxin and is independent of caspase-1. **J. Immunol.** 163:1755-1767, 1999.
- Coulter KR, Wewers MD, Lowe MP, Knoell DL. Extracellular regulation of interleukin (IL)-1 through lung epithelial cells and defective IL-1 type II receptor expression. Am.J.Resp.Cell Mol.Biol. 1999;20:964-975.
- 62. Coulter KR, Allen ED, Hart J, **Wewers MD**, Castile RG, Knoell DL. Induction of interleukin-8 release by lung epithelium with cystic fibrosis epithelial lining fluid is marginally affected by inhibitors of interleukin-1beta. **Pharmacotherapy.** 2000;20:64-74.
- 63. Diaz PT, King MA, Pacht ER, **Wewers MD**, Gadek JE, Nagaraja HN, Drake J, Clanton TL. Increased susceptibility to pulmonary emphysema among HIV-seropositive smokers. **Ann.Intern.Med** 2000;132:369-372.
- 64. Diaz PT, King ER, **Wewers MD**, Gadek JE, Neal D, Drake J, Clanton TL. HIV infection increases susceptibility to smoking-induced emphysema. **Chest** 2000; 117: 285S
- 65. Swaan PW, Knoell DL, Helsper F, **Wewers MD**. Sequential processing of human proIL-1β by caspase-1 and subsequent folding determined by a combined in vivo and in silico approach **Pharmaceutical Research** 2001;18:1083-1090.
- 66. Cooper MA, Fehniger TA, Ponnappan A, Mehta V, **Wewers MD**, Caligiuri MA. Interleukin-1β costimulates interferon-γ production by human natural killer cells. **Euro. J. Immunol.** 2001;31:792-801.

- 67. Fahy RJ, **Wewers MD**. Bronchoalveolar lavage and serum IgG levels in healthy asymptomatic HIV infected patients. **Chest** 2001;119:196-201.
- 68. Mehta VB, Hart J, **Wewers MD**. ATP stimulated release of IL-1β and IL-18 requires priming by LPS and is independent of caspase-1 cleavage. **J. Biol. Chem.** 2001; 276:3820-3826.
- 69. Tridandapani, S., Siefker, K., Teillaud J.-L., Carter JE, **Wewers MD**, Anderson CL. Regulated expression and inhibitory function of FcgammaRIIb in human monocytic cells. **J. Biol. Chem**. 2002; 277:5082-5089.
- 70. Coulter, K.R., Doseff, A., Sweeney, P., Wang, Y., Marsh, C.B., **Wewers, M.D.**, Knoell, D.L. Opposing effect by cytokines on Fas-mediated apoptosis in A549 lung epithelial cells. **Am J Respir Cell Mol Biol** 2002;26:58-66.
- 71. Crouser, E.D., Julian, M.W., Joshi, M.S., Bauer, J.A., **Wewers, M.D.**, Hart, J.M., Pfeiffer, D.R. Cyclosporin A ameliorates mitochondrial ultrastructural injury in the ileum during acute endotexmia. **Crit Care Med** 2002; 30:2722-2728.
- 72. Fahy RJ, Lichtenberger F, McKeegan CB, Nuovo GJ, Marsh CB and **Wewers MD**. The acute respiratory distress syndrome: a role for TGF-β1. **Am.J.Resp. Cell Mol Biol** 2003; 28(4):499-503.
- 73. Spragg RG, Lewis JF, Wurst W, HŸfner D, Baughman RP, **Wewers MD** and Marsh JJ. Treatment of the acute respiratory distress syndrome with rSP-C surfactant. **Am J Resp Crit Care Med.** 2003; 167:1562-1566.
- 74. Diaz PT, **Wewers MD**, Pacht ER, Drake J, Nagaraja HN, Clanton TL. Respiratory symptoms among HIV-seropositive individuals. **Chest** 2003; 123(6):1977-1982.
- 75. Doseff AI, Bourgeois TA, **Wewers MD**. IL-4-induced apoptosis entails caspase activation and suppression of ERK phosphorylation. **Am.J.Resp. Cell Mol Biol** 2003;29:367-374.
- Crouser ED, Julian MW, Huff JE, Joshi MS, Bauer JA, Gadd ME, Wewers MD, Pfeiffer DR. Abnormal permeability of inner and outer mitochondrial membranes contribute independently to mitochondrial dysfunction in the liver during acute endotoxemia. Crit Care Med 2004;32(2):478-488.
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- 78. Elssner A, Carter JE, Yunger TM, **Wewers MD**. HIV infection does not impair human alveolar macrophage phagocytic function unless combined with cigarette smoking. **Chest** 2004;125:1071-1076.
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#### **B.** Reviews

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#### **D.** Abstracts

### 2002-present

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Kim H-J, Hart J. Knatz N, Hall MW, Wewers MD. Janus kinase 3 downregulates LPS induced ICE activation by autocrine IL-10; **AJRCCM** 2004; A34.

Fahy RJ, Karavanov A, Schneider GP, Wewers MD. Proteomic patterns of BAL fluid in early acute respiratory distress syndrome. **AJRCCM** 2004; A44.

Knoell DJ, Bao SY, Kim H-J, Wewers MD. Modulation of barrier function during death receptor mediated apoptosis in differentiated human lung epithelial cells. **AJRCCM** 2004; B55.

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Kim HJ, Gavrilin MA, Hart JM, Wewers MD. Tyrosine 82 in CARD domain of caspase-1 negatively regulates caspase-1 activation. **The FASEB Journal** 19 (4): A335, 2005.

Seshadri S, Gavrilin MA, Hart J, Duncan MD and Wewers MD. Pyrin expression is suppressed with monocyte to macrophage differentiation. **The FASEB Journal** 19 (5): A1445, 2005.

Fahy RJ, Yang L, Duncan MD, Gavrilin MA and Wewers MD. Monocyte mRNA expression in early septic shock. **Proceedings of the American Thoracic Society** 2:A42, 2005.

Bouakl IJ, Gavrilin MA, and Wewers MD. Intracellular activation of the human monocyte inflammasome by Francisella. **Proceedings of the American Thoracic Society** 2:A306, 2005.

Bao SY, Lai JP, Knoell DL, and Wewers MD. Zinc deficiency suppresses the PI3K/Akt pathway and enhances apopotosis in differentiated human lung epithelial cells. **Proceedings of the American Thoracic Society** 2:A324, 2005.

Gavrilin MA and Wewers MD. Internalization and phagosome escape required for Francisella to induce human monocyte IL-1β processing and release. Keystone Symposium: Innate Immunity 60, 2006. Fahy RJ, Gavriin MA, Bhatt NU, Joshi P, Seshadri, Nagaraja HN and Wewers MD. Monocyte inflammasome mRNA expression and survival from septic shock. **Proceedings of the American Thoracic Society** 3:A35, 2006.

Raices R, Sarkar A, Bao S, Hart J, Knoell D and Wewers MD. Relative ability of lung epithelial cells and monocytes to sense Toll ligands. **Proceedings of the American Thoracic Society** 3:A321, 2006.

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Kim H-J, Hart J and Wewers MD. Kinases, Lyn and Syk are involved in monocyte caspase-1 activation induced by wheat germ agglutinin. **Proceedings of the American Thoracic Society** 3:A323, 2006.

Sarkar A, Bao S, Raices R, Wewers MD and Knoell DL. NOD-like receptor proteins coordinate the inflammasome response in human lung epithelial cells. **Proceedings of the American Thoracic Society** 3:A325, 2006.

Kim H-J, Hart J, Wewers MD. Mutation of conserved tyrosine residue in p20 domain of caspase-1 causes dysfunction. **Proceedings of the American Thoracic Society** 3:A324, 2006.

Exline MC, Fahy R, Gavriin MA, Duncan MD, and Wewers MD. Anti-apoptotic peptide humanin suppressed in monocytes of septic patients. **Proceedings of the American Thoracic Society** 3:A328, 2006.

Magalang UJ, Rajappan R, Varadharaj S, Hunter MG. Kutala VK Kuppusamy P, Wewers MD, Marsh CB, Parinandi NL. Adiponectin inhibitis superoxide generation by human neutrophils. **Proceedings of the American Thoracic Society** 3:A353, 2006.

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#### **PRESENTATIONS**

## A. National Meetings:

North American Society for Pediatric Gastroenterology, Chicago, IL, November 1984."Alpha 1-antitrypsin deficiency - 15 years later".

National Institutes of Health Internal Medicine Board Review Course, Bethesda, MD, January 1985. "Pulmonary vascular disorders and sleep apnea."

American Thoracic Society, Symposium: Symposium on Alpha 1-antitrypsin Deficiency: From the Gene to the Bedside, Anaheim, CA, May 1985. "Re-establishment of the Anti-Elastase Screen of the Lower Respiratory Tract".

American Thoracic Society, Symposium: Sarcoidosis, New Orleans, LA, May 1987. "Interleukin 1 beta and Sarcoidosis".

American College of Chest Physicians, Symposium on Alpha 1-antitrypsin Deficiency, Atlanta, Georgia, October 1987. "Pathogenesis of Emphysema: Assessment of Basic Concepts Through Clinical Investigation".

American College of Allergy and Immunology, Los Angeles, CA, November 1988. "Proteases and Their Effect on the Fragile Lung."

American Thoracic Society, Symposium: Cytokines and Cytokine Networks in the Lung, Cincinnati, OH, May 1989. "Interleukin 1 beta and the Lung".

American College of Chest Physicians Annual Scientific Meeting, Boston, MA, October 31, 1989, "Recent Advances in the Treatment of Alpha-1-antitrypsin Deficiency and Future Advances on the Horizon".

American Thoracic Society International Conference, Miami, FL, May 17, 1992. "Alveolar Macrophage IL-1 Regulation".

American College of Chest Physicians Annual Scientific Meeting, Symposium on New Concepts of Pathogenesis and Treatment of Emphysema, Orlando, FL, October 28, 1993, "Role of Alpha-1-antitrypsin in Cystic Fibrosis and Adult Respiratory Distress Syndrome".

Fifth Charleston Lung Symposium, Charleston, SC, March 21, 1994, "Pulmonary Vasculitis Update".

American Thoracic Society International Symposium, Boston, MA: May 22, 1994, "New Concepts in IL-1β Regulation: A receptor antagonist, an ICE inhibitor and a decoy receptor".

American Physiological Society Conference: Physiology of the Release and Activity of Cytokines, Yale University, New Haven, CT, Invited Speaker, May 22, 1994, "ProIL-1β Detection by ELISA".

International Symposium: Alpha-1-antitrypsin: A World View in 1994, Barcelona, Spain, October 7, 1994, "Clinical Implications of alpha-1-antitrypsin Gene Therapy".

American Thoracic Society International Conference, Seattle, WA, May 20, 1995. Symposium on Inflammatory Mechanisms in the Lung and Airways: Cells, Cytokines and Mediators, "Cytokines in Lung Inflammation".

American Thoracic Society International Conference, New Orleans. LA, May 11, 1996. Postgraduate Course: Inflammatory Mechanisms in the Lung and Airways: Cells, Cytokines and Mediators, "Cytokines in Airway Inflammation, Lung Injury, Lung Defense".

American Thoracic Society International Conference, New Orleans, LA, May 13, 1996, Featured Speaker, Advances in Macrophage Biology, "Macrophages and IL-1β: Braking the ICE".

Second International Symposium on the Etiology and Pathobiology of Transplant Vascular Sclerosis, Southhampton, Bermuda, March 8, 1997. Plenary Session. "Role of Antibody in Transplant Vascular Sclerosis."

Midwest American Federation for Medical Research, September 19, 1998. "Caspases: inflammatory and suicidal", State of the Art Lecture.

American Thoracic Society International Conference, San Diego, CA, April 28, 1999. "Caspases: executioners of apoptosis", Symposium Speaker.

American Thoracic Society International Conference, San Diego, CA, April 24, 1999. Speaker on "Cytokines in Lung Inflammation" Postgraduate Course 11: Inflammatory Mechanisms in the Lung and Airways: Cells, Cytokines and Mediators.

National Heart Lung and Blood Institute Workshop: Pulmonary Complications of HIV in the Era of HAART. October 25, 1999. Speaker on "Macrophages, role of smoking and emphysema".

National Heart Lung and Blood Institute RFA Meeting: Speaker on "Role of epithelium in regulating alveolar macrophage HIV infection". September 20, 2000.

National Institute of Environmental Health Sciences; Research Triangle Park, N.C.; Speaker on "ICE: on the crossroads of apoptosis and inflammation". October 3, 2000.

American Thoracic Society International Conference, San Francisco, CA, Postgraduate Course. "Cytokines in Lung Injury, Repair and Inflammation", May 19, 2001.

American Thoracic Society International Conference, San Francisco, CA, Symposium on Macrophage Biology, "Macrophages: Link Between Inflammation and Cell Death", May 20, 2001.

American Thoracic Society International Conference, San Francisco, CA, Minisymposium on HIV Infection and the Lung, "HIV Interactions with Lung Inflammatory and Parenchymal Cells.", May 21, 2001.

OMEN-TV presentation, "New Developments in the Treatment of Sepsis", April 3, 2002, Columbus, OH

American Thoracic Society International Conference, Orlando Fl. May 26, 2004, "CD4 lung lymphocytes predict survival in Asymptomatic HIV Infection. May 2004.

#### **B.** Other Academic Institutions:

- 1. Indiana American College of Physicians Annual Meeting, Indianapolis, IN, November 11, 1989, "Alpha-1-antitrypsin Deficiency: Diagnosis and Treatment".
- 2. University of Iowa, Department of Internal Medicine, Pulmonary Research Conference, December 11, 1995. "Multifaceted Components of IL-1β Regulation".
- 3. Winthrop University Hospital, Mineola, NY, December 3, 1992, "Role of the Macrophage in Interleukin-1 Regulation".
- 4. Combined Cleveland Clinic/The Ohio State University Immunology Seminar, Mohican State Park Lodge, OH, January 26, 1993. "IL-1β Production by the Lung".
- 5. Northeast Ohio University, College of Medicine Physiology Department Series, Rootstown, OH, March 14, 1994, "Role of Cytokines in ARDS".
- 6. University of Iowa, Pulmonary Research Conference. "Multifaceted components of IL-1β regulation", December 11, 1995, Iowa City, Iowa.
- 7. University of Arkansas Medical Sciences, Little Rock, AR, March 25, 1999, Medical Grand Rounds. "Mechanisms of Emphysema, New Paradigms."
- 8. University of Southern California, Los Angeles, CA, April 9, 1999; Center for Lung Biology Seminar. "Caspases: Role in Cell Death and Inflammation".
- 9. University of Nebraska, Omaha Neb., November 17, 2000; Medical Grand Rounds. "Emphysema, New Concepts for an Old Disease".
- 10. Northeast Ohio University College of Medicine, December 19, 2002. Physiology Department Seminar Series, Rootstown, OH, "Sepsis: the Role of ICE and CARDs".
- 11. Case Western Reserve University, Physiology and Biophysics Seminar Series, December 20, 2004. "Caspase-1: at the 'tipping point' of Inflammation".

12. Indiana University, Indianapolis, IN. June 22, 2005. Sunnyside Lecture: Medical Grand Rounds. "The Burden of Emphysema: How Does It Happen and What Should be Done?".

#### C. Ohio State University

- 1. Ohio State University Department of Internal Medicine Board Review Course, Columbus, Ohio, September 1987. "Pulmonary Vasculitis".
- 2. Ohio State University Department of Internal Medicine Board Review Course, Columbus, Ohio, September 1988. "Pulmonary Vasculitis".
- 3. Medical Grand Rounds: July 1985 "Diagnosis and Management of Alpha 1-antitrypsin Deficiency"
- 4. College of Nursing, "Quest for Excellence" Conference, Columbus, Ohio, October 1988. "Utility of Fiberoptic Bronchoscopy in the ICU".
- 5. Medical Grand Rounds: "Role of Cytokines in Sepsis", Ohio State University, Department of Internal Medicine, February 22, 1990.
- 6. Ohio State University, Panel Discussion: 1996 Scientific Integrity Workshop; featured discussant.
- 7. Immunology Seminar Program, March 31, 1998, "Caspases, inflammatory and suicidal!"
- 8. Medical Grand Rounds: July 23, 1998, "Destructive Lung Disease: New Paradigms", Ohio State University, Department of Internal Medicine.
- 9. "Pleural Disease", February 12, 1999. Pulmonary and Critical Care Division Continuing Medical Education Course. Hyatt Regency Hotel, Columbus, OH.
- 10. Family Genetics and the Future of Heart and Lung Disease: February 16, 2000, Ohio State University Heart and Lung Institute Seminar.
- 11. "Viral Respiratory Tract Infections", February 12, 2000, Pulmonary and Critical Care Divisions Continuing Education Course, Hyatt Regency Hotel, Columbus, OH.
- 12. Imunology Seminar Program, December 12, 2000, "ICE: On the crossroads of apoptosis and inflammation".
- 13. Microbiology Molecular Immunology Lecture Series, January 31, 2001, "MAIL: A new regulator of IL-1?"
- 14. Grantsmanship Workshop, Ohio State University Health Science Colleges, Program Coordinator and Moderator. May 11, 2001.
- 15. Ohio State University Internal Medicine Grand Rounds, October 18, 2001, "Sepsis Treatment: New Concepts".
- 16. Center for Microbial Interface Biology Seminar, February 2003, "Host Defense: A House of CARDs".

- 17. Davis Heart and Lung Research Institute, Discovery Series, August, 2003, "Intracellular control of inflammation: CATERPILLERS, CARDs and Pyrins".
- 18. Ohio State University Integrated Medical School Cutting Edge Seminar, September 19, 2003, "Innate Host Defense: New insights from the genome".
- 19. Pulmonary and Critical Care Medicine Update 2003, "Management of Sepsis: 2003", February 15, 2003, Columbus, OH.
- 20. Pulmonary and Critical Care Medicine Update 2004, "Pleural Disease Update", February 12, 2004.
- 21. Ohio State University, Distinguished Lecture Series, IBGP 797, "Fever and Inflammation: Hints from Plants and the Genome Project".
- 22. Ohio State University Internal Medicine Grand Rounds, July 1, 2004, "The Burden of Tobacco".
- 23. Davis Heart and Lung Research Institute, Tools of the Trade: The Art of Scientific Writing Seminar Series, September 22, 2004, "Coping with Rejection".
- 24. Davis Heart and Lung Research Institute, K Award Grants Seminar: "Dealing with the Review", April 20, 2006.
- 25. Davis Heart and Lung Research Annual Retreat: "Sepsis: Lessons from Flora", May 5, 2006.
- 26. Davis Heart and Lung Research Institute: "CATERPILLERS: New sensors of danger", June 30, 2006.

#### **D. Non-academic Institutions**

- 1. Miami Valley Hospital, "Alpha 1-antitrypsin Deficiency", September 27, 1989.
- 2. Symposium on Alpha-1-antitrypsin deficiency, Scanticon Conference Center, Minneapolis, MN, August 17, 1990, "Role of Alpha-1-antitrypsin Replacement Therapy".
- 3. Lung Disease Symposium, Akron General Hospital. Akron, OH, October 3, 1990, "Therapy for alpha-1-antitrypsin deficiency".
- 4. Doctor's North Hospital, Columbus, OH, April, 1996. "Alpha-1-antitrypsin Deficiency".
- 5. COPD Update 2001: American Lung Association of Ohio, June 1, 2001. "Alpha 1 Emphysema."
- 6. Ohio Thoracic Society /American Thoracic Society 53<sup>rd</sup> Annual Case Conference, "Alpha 1-antitrypsin Vignettes", September 21, 2003.

#### E. Other

1. Merck Research Labs Research Conference, Rahway, NJ, June 10, 1992. "ProIL-1β Detection and the Alveolar Macrophage".