

BIOGRAPHICAL SKETCH

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NAME Edwards, III, Carl Keith		POSITION TITLE Associate Professor of Dermatology	
eRA COMMONS USER NAME Edwardsck			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education</i>)			
INSTITUTION AND LOCATION	DEGREE (<i>if applicable</i>)	YEAR(s)	FIELD OF STUDY
Colorado State University	B.S.	1980	Microbiology
University of Colorado at Boulder	M.A.	1984	Immunology
University of Illinois at Urbana-Champaign	Ph.D.	1989	Immunophysiology
University of Indiana Medical School	Post-Doctoral	1990	Immunology

A. Positions and Honors.**Positions and Employment**

1990-1995	Senior Research Scientist, Department of Immunology, Marion Merrell Dow Research Inst.
1990-1993	Assistant Professor, Department of Medicine, University of Kansas School of Medicine
1993-1995	Associate Professor, Department of Medicine, University of Cincinnati School of Medicine
1995-2003	Senior Research Fellow, Department of Inflammation, Amgen, Inc.
2003-2004	Senior Scientific Research Director, Department of Dermatology, Schering AG
2005-	Associate Professor, Department of Dermatology, School of Medicine, University of Colorado Health Sciences Center at Fitzsimons, Aurora, CO U.S.A.

Other Experience and Professional Memberships

1987-1989	NIH Fellowship, University of Illinois at Urbana-Champaign, Urbana, IL, USA
1991-	Elected Research (Full) Member, American College of Rheumatology
1995-1997	Chief Scientist/Clinical Leader, Tumor Necrosis Factor Binding Protein (TNFbp), Amgen, Inc.
1997-2002	Chief Scientist/Clinical Leader, PEG sTNF-RI, Amgen, Inc.
1999-2002	Chief Scientist/Clinical Leader, IL-1ra/PEG sTNF-RI, Amgen, Inc.
2003-	Elected Member, Society for Investigative Dermatology

Honors

1988	Finalist, A.L. Neuman Outstanding Graduate Student Award, Division of Veterinary Pathobiology, College of Veterinary Medicine, University of Illinois at Urbana-Champaign, USA
1998	Symposium Panelist/Speaker, Biologics in RA Therapy, American College of Rheumatology Annual Meeting, San Diego, CA, USA
2000	Symposium Speaker, "Biology of TNF-Alpha in Health and Disease" American College of Rheumatology Annual Spring Clinical Meeting, Seattle, WA, USA
2002	Symposium Speaker, Scientific Basis of Rheumatology, Royal College of Physicians, London, United Kingdom
2003	FDA Advisory Panel Selected Consultant, "Anti-TNF Therapies and Potential Side Effects".

B. Selected peer-reviewed publications (in chronological order; selected from a total of 107 refereed journal articles and/or scholarly chapters in books).

- Gangadharam PRJ and **Edwards III CK**. Release of superoxide anion (O_2^-) from resident and activated mouse peritoneal macrophages infected with *Mycobacterium intracellulare*. *American Review of Respiratory Diseases*. 1984; 130:834-838.
- Edwards III CK**, Hedegaard HB, Zlotnik A, Gangadharam PRJ, Johnston Jr RB, Pabst MB. Chronic infection due to *Mycobacterium intracellulare* in mice: association with macrophage release of prostaglandin E_2 and reversal by injection of indomethacin, muramyl dipeptide, or interferon- γ . *Journal of Immunology*. 1986; 136:1820-1827.

3. **Edwards III CK**, Ghiasuddin SM, Schepper JM, Yunger LM, Kelley KW. A newly defined property of somatotropin: priming of macrophages for production of superoxide anion. *Science*. 1988; 239:769-771.
4. **Edwards III CK**, Lorrence RM, Dunham DM, Yunger LM, Greager JA, Walter RJ, Kelley KW. Hypophysectomy inhibits the synthesis of tumor necrosis factor- α production by rat macrophages: Partial restoration by exogenous growth hormone or interferon. *Endocrinology*. 1991; 128:989-996.
5. **Edwards III CK**, Yunger LM, Lorrence RM, Dantzer R, Kelley KW. The pituitary gland is required for protection against the lethal effects of *Salmonella typhimurium*. *Proceedings of the National Academy of Sciences (USA)*. 1991; 88:2274-2277.
6. **Edwards III CK**, Ghiasuddin SM, Blum A, Yunger LM, Lorrence RM, Kelley KW. *In vivo* administration of recombinant growth hormone or interferon- γ activates macrophages: Enhanced resistance to experimental *Salmonella typhimurium* infection is correlated with the generation of reactive oxygen intermediates. *Infection and Immunity*. 1992; 60:2514-2521.
7. Zhou T, Bluethmann H, **Edwards III CK**, Mountz JD. Defective maintenance of T-cell tolerance to a superantigen in MRL-*lpr/lpr* mice. *Journal of Experimental Medicine*. 1992; 176:1063-1072.
8. Mountz JD, **Edwards III CK**. Murine models of autoimmunity: T cell and B cell defects. *Current Opinions in Rheumatology*. 1992; 4:612-620.
9. Mountz JD, Edwards III CK. Murine models of autoimmunity. *Current Opinions in Rheumatology*. 1992; 4:621-629.
10. Parmely MJ, Zhou WW, **Edwards III CK**, Borcharding DR, Silverstein R, Morrison DC. Adenosine and a related carbocyclic nucleoside analogue selectively inhibit tumor necrosis factor- α production and protect mice against endotoxin challenge. *Journal of Immunology*. 1993; 151:389-396.
11. Mountz JD, Zhou T, Long RE, Bluethmann H, Koopman WJ, **Edwards III CK**. T-cell influence superantigen-induced arthritis in MRL-*lpr/lpr* mice. *Arthritis and Rheumatism*. 1994; 37:113-124.
12. Bradshaw M, Rutherford M, Schook LB, Borcharding DR, McWhinney CD, Hoepfer BJ, **Edwards III CK**. Specific transcriptional inhibition of bone marrow-derived macrophage (BMDM ϕ) TNF- α gene expression and protein production using novel enantiomeric carbocyclic nucleoside analogues. *Journal of Pharmacology and Experimental Therapeutics*. 1995; 273:1506-1518.
13. Mountz, J.D., T.J. Baker, D.R. Borcharding, H. Bluethmann, T. Zhou, and **Edwards III CK**. Increased susceptibility of *fas* mutant MRL-*lpr/lpr* mice to *Staphylococcal enterotoxin B*-induced Septic Shock. *Journal of Immunology*. 1995; 155: 4829-4837.
14. McWhinney CD, Bradshaw M, De M, Borcharding DR, Dudley M, Bowlin TL, Peet N, Schook LB, **Edwards III CK**. Activation of adenosine A₃ receptors on macrophages inhibits tumor necrosis factor- α . *European Journal of Pharmacology*. 1996; 310:209-216.
15. Zhou T, **Edwards III CK**, Yang P, Wang Z, Bluethmann H, Mountz JD. Greatly accelerated lymphadenopathy and autoimmune disease in *lpr* mice lacking tumor necrosis factor receptor I. *Journal of Immunology*. 1996; 156: 2661-2665.
16. **Edwards III CK**, Zhou T, Zhang J, Baker TJ, De M, Long RE, Borcharding DR, Bowlin TL, Bluethmann H, Mountz JD. Inhibition of superantigen-induced proinflammatory cytokine production and inflammatory arthritis in MRL-*lpr/lpr* mice by a transcriptional inhibitor of tumor necrosis factor- α . *Journal of Immunology*. 1996; 157:1758-1772.
17. Grom AA, Murray KJ, Luyrink L, Emery H, Passo MH, Glass DN, Bowlin T, **Edwards III CK**. Patterns of expression of tumor necrosis factor- α , tumor necrosis factor- α , and their receptors in synovia of patients with juvenile rheumatoid arthritis and juvenile spondylarthropathy. *Arthritis and Rheumatism*. 1996; 39:1703-1710.
18. Solorzano CC, Kaibara A, Hess PJ, Edwards PD, Ksontini R, Frazier J, Trujillo D, Kieft G, Kohno H, Cosenza, M. Clare-Salzler, MacKay SLD, Moldawer LL, **Edwards III CK**. Pharmacokinetics, immunogenicity and efficacy of dimeric TNF receptor binding proteins in healthy and bacteremic baboons. *Journal of Applied Physiology*. 1998; 84: 1119-1130.
19. Kuiper S, Joosten LAB, Bendele AM, **Edwards III CK**, Arntz OJ, Helsen MMA, van de Loo FAJ, van den Berg WB. Different roles of tumor necrosis factor- α and interleukin-1 in murine streptococcal cell wall arthritis. *Cytokine*. 1998; 10: 690-702.
20. McComb J, Gould T, Chlipala E, Senello R, Frazier J, Kieft G, Seely J, Edwards III CK, Bendele AM. Antiarthritic activity of soluble TNF receptor type I form in adjuvant arthritis: correlation of plasma levels with efficacy. *Journal of Rheumatology*. 1999; 26:1347-1351.
21. **Edwards, III CK**. PEGylated recombinant human soluble tumor necrosis factor receptor type I (rHu-sTNF-RI): A novel high-affinity TNF receptor designed for chronic inflammatory diseases. *Annals of Rheumatic Diseases*. 1999; 58: (Suppl I) I73-I81.
22. Moreland LW, McCabe D, Caldwell JR, Sach M, Weisman M, Henry G, Seely J, Martin SW, Yee C, Bendele AM, Frazier J, Kohno T, Cosenza ME, Lyons S, Dayer J-M, Cohen A, **Edwards III CK**. Phase I/II trial of recombinant methionyl human tumor necrosis factor binding protein PEGylated dimer (TNFbp Dimer) in patients with active refractory rheumatoid arthritis. *Journal of Rheumatology*. 2000; 27: 601-609.

23. Bendele AM, Chlipala E, Scherrer J, Frazier J, Sennello G, Rich WJ, **Edwards III CK**. Combination benefit of treatment with the cytokine inhibitors Interleukin-1 receptor antagonist (IL-1ra) and PEGylated Soluble Tumor Necrosis Factor Receptor Type I (sTNF-RI) in animal models of rheumatoid arthritis. *Arthritis and Rheumatism*. 2000; 43:2648-2659.
24. Vigers GPA, Dripps DJ, **Edwards III CK**, Brandhuber BJ. X-ray crystal structure of a small antagonist peptide bound to the Type - I interleukin-1 receptor. *Journal of Biological Chemistry*. 2000; 275:36927-36933.
25. Frishman JI, **Edwards III CK**, Sonnenberg MG, Kohno T, Cohen AM, Dinarello CA. Tumor necrosis factor (TNF)- α -induced interleukin-8 in human blood cultures discriminates neutralization by the p55 and p75 TNF soluble receptors. *The Journal of Infectious Diseases*. 2000; 182: 1722-1730.
26. Hyka N, Dayer J-M, Modoux C, Kohno T, **Edwards III CK**, Roux-Lombard P, Burger D. Apolipoprotein A-I (ApoAI) inhibits the production of IL-1 β and TNF- α by blocking contact-mediated activation of monocytes by T lymphocytes. *Blood*. 2001; 97: 2381-2389.
27. Vazquez-Torres A, Fantuzzi G, Holden D, **Edwards III CK**, Dinarello CA, Fang FC. Defective localization of the NADPH Phagocyte Oxidase to *Salmonella*-containing phagosomes in TNFp55 receptor-deficient macrophages. *Proceedings of the National Academy of Sciences (USA)*. 2001; 98: 2561-2565.
28. Dayer JM, Feige U, **Edwards III CK**, Burger D. Anti-Interleukin-1 therapy in rheumatic diseases. *Current Opinions in Rheumatology*. 2001; 13:170-176.
29. Rosenberg JJ, Martin SW, Gaines GC, Fukuzuka K, Rose J, Frazier J, Seely J, Amicone A, Boyle W, Kieft G, Cosenza ME, Kohno T, Moldawer LL, **Edwards III CK**. Development of a novel, non-immunogenic soluble human TNF receptor type I construct that blocks pathological effects of systemic TNF- α in the juvenile *papio*. *Journal of Applied Physiology*. 2001; 91: 2213-2223.
30. Schultz MJ, Rijneveld AW, Florquin S, **Edwards III CK**, Dinarello CA, van der Poll T. Role of Interleukin 1 in the pulmonary immune response during *Pseudomonas aeruginosa* pneumonia. *American Journal of Physiology-Lung Cellular and Molecular Physiology*. 2002; 282:L285-L290.
31. Rijneveld AW, Florquin S, Speelman P, **Edwards III CK**, Dinarello CA, van der Poll T. Treatment with recombinant interleukin-1 receptor antagonist only transiently impairs antibacterial defense in murine pneumococcal pneumonia. *Eur. Cytokine Network*. 2003; 14:242-245.
32. **Edwards III CK**, Martin SW, Seely J, Kinstler O, Buckel S, Bendele AM, Feige U, Kohno T. Design of PEGylated soluble tumor necrosis factor receptor type I (PEG sTNF-RI) for chronic inflammatory diseases. *Advanced Drug Delivery Reviews: Site Specific PEGylation of Polypeptides*. 2003; 55:1315-1336.
33. **Edwards III CK**. Drug discovery and development for inflammatory diseases: Meeting highlights. *Expert Opin. Ther. Targets*. 2004; 8:151-163.
34. Schottelius AJG, Moldawer LL, Dinarello CA, Asadullah K, Steery W, **Edwards III CK**. Biology of Tumor Necrosis Factor- α (TNF- α): Implications for psoriasis. *Experimental Dermatology*. 2004; 13:193-222.
35. **Edwards, III, C.K.** 2004. Drug discovery and development for inflammatory diseases: Meeting highlights. *Expert Opin. Ther. Targets*. 8:151-163.
36. Efron, P.A., H. Tsujimoto, Ungaro, F.R. Bahjat, R. Ungaro, J. Debernardis, C. Tannahill, H.V. Baker, **C.K. Edwards, III**, and L.L. Moldawer. 2005. Differential maturation of murine bone marrow derived dendritic cells with lipopolysaccharide and tumor necrosis factor- α . *Infection and Immunity. In the Press*.
37. Furst, D., R. Fleischman, E. Kopp, M. Schiff, **C.K. Edwards, III**, A. Solinger, M. Macri, and T. Joh. 2005. Dose-Finding study of PEGylated recombinant methionyl human soluble tumor necrosis factor type I (Pegsunercept) in Rheumatoid Arthritis patients. *J. Rheumatology. In the Press*.
38. **Edwards, III, C.K.** 2005. Pegsunercept: A high-affinity, recombinant E. coli-derived, human soluble tumor necrosis factor type I [p55] monomeric receptor designed for chronic inflammatory diseases. *J. Controlled Release. In the Press*.
39. Hamada, K., E. Vannier, T. Yamada, D.E. Smith, L.W. Abad, M. Tokuriki, **C.K. Edwards, III**, J.G. Cannon, and R. Roubenoff. 2005. Inflammatory cachexia regulates sarcoactive cytokine gene expression in rat skeletal muscle tissue. *Journal of Applied Physiology. In the Press*.
40. Wang, X., A. Tousson, H.-C. Hsu, **C.K. Edwards, III**, A. Schottelius, Y.-Y. Y. Li, D.R. Kelly, P. Yang, J. Chen, H. Xu, D.A. Norris, C.A. Elmetts and J.D. Mountz. 2005. Evaluation of effector T cell migration by in vivo imaging using the oxazolone-induced mouse Atopic dermatitis model. *Journal of Investigative Dermatology. In the Press*.
41. Li, Y-Y. Y, J-F. Chang, Y. Yang, C. Garrison Fathman, M. Bao, **C.K. Edwards, III**, and J.R. Parnes. 2005. Murine splenic B lymphocyte activation using different activation stimuli induces *in vitro* splicing of Tumor Necrosis Factor- α nuclear pre mRNA. *Molecular Immunology. In the Press*.
42. **Edwards, III, C.K.**, A.M. Bendele, L.I. Reznikov, G. Fantuzzi, E.S. Chlipala, L.L. Moldawer, J.D. Mountz, and C.A. Dinarello. 2005. Soluble human TNF p55 and p75 receptors reverse spontaneous arthritis in transgenic mice expressing transmembrane TNF- α by the p55 and p57 soluble Human TNF receptors. *Arthritis & Rheumatism. In the Press*.

C. Research Support (Ongoing or completed during the last three years)

ACTIVE

1. Academic Enrichment Funds - University of Colorado Health Sciences Center at Fitzsimons (2005-2008)

PENDING

1. "Identity of Surface Activating Factors of T Cells (SAFTs) in Psoriasis"
Brief Statement: Purification of TCISM Ligand in Cell-Cell Contact Mechanisms

NIH-PHS398 RO1 A1067778-01:
\$282,000.00 per year – 12/01/05 through 11/30/10
(Submitted: February 1, 2005 – Pending)
2. "Cell-Cell Contact Mechanism Leading to Cytokine Production in Lupus"
Brief Statement: Purification of TCISM Ligand in Cell-Cell Contact Mechanisms

Lupus Research Foundation RFA 2005-
\$100,000.00 per year – 10/01/05 through 10/31/08
(Submitted: June 30, 2005 – Pending)
3. "Identification of T Cell Cytokine Inducing Surface Molecule (TCISM) in Rheumatoid Arthritis"
Brief Statement: Purification of TCISM Ligand in Cell-Cell Contact Mechanisms

ACR Academic Re-entry Award RFA 2005-
\$50,000.00 per year – 07/01/06-06/30/08
(Submitted: August 1, 2005 – Pending)
4. "Proinflammatory Cytokine Gene Expression Analysis in Alopecia Areata"
Brief Statement: Gene Expression Analysis to dissect AA patient subpopulations

National Alopecia Areata Association RFA 2005
\$50,000.00 per year – 01/01/06 -12/31/2006
(Submitted: August 9, 2005 – Pending)
5. "Mechanism of Action of Anti-TNF Therapies in Psoriasis"
Brief Statement: Elucidation of anti-TNF α Mechanisms in Chronic Plaque Psoriasis

American Skin Association RFA 2005
\$15,000.00 per year – 01/01/06 – 01/01/07
(Submitted: October 3, 2005 – Pending)
6. "Identification of T Cell Cytokine Inducing Surface Molecule (TCISM) in Psoriasis"
Brief Statement: Purification of TCISM Ligand in Cell-Cell Contact Mechanisms

National Psoriasis Foundation
\$30,000.00 per year – 01/01/06 – 12/31/06
(Submitted: October 14, 2005 – Pending)
7. "UV-Induced Cutaneous Inflammation in Bxd Lupus-Prone Congenic Mice"
Brief Statement: Effects of UV radiation in BXD mice which are predisposed to Lupus

Dermatology Foundation
\$55,000.00 per year – 07/01/06 – 06/31/07
(Submitted: October 17, 2005 – Pending)

PREVIOUS

(I.) RESEARCH GRANT PROJECT(S):

A. Academic:

1. Immunopathology of *M. intracellulare* diseases (NIAID) 1981-1983 (P.I. PRJ Gangadharam, Co-Investigator C.K. Edwards, III, National Jewish Hospital, Denver, CO, U.S.A.)
2. Immunopathology of *M. intracellulare* in AIDS (NIAID) 1983-1985 (P.I. PRJ Gangadharam, Co-Investigator C.K. Edwards, III, National Jewish Hospital, Denver, CO, U.S.A.)
3. Corticosteroid Pharmacologic Actions and Dispositions (NIH) 1983-1985 (P.I. SJ Szeffler, Co-Investigator C.K. Edwards, III, National Jewish Hospital, Denver, CO, U.S.A.)
4. Macrophage Activation in Periodontal Disease (NIAID) 1983-1985 (P.I. R.B. Johnston, Jr., Co-investigator C.K. Edwards, III, National Jewish Hospital, Denver, CO, U.S.A.)
5. Hormonal Restoration of Functional Thymus Gland During Aging (NIH) 1986-1991 (P.I. K.W. Kelley, Co-Investigator C.K. Edwards, III, University of Illinois at Urbana-Champaign, IL, U.S.A.)
6. Cincinnati Juvenile Rheumatic Diseases Center (NIH Grant IP20AR42632) 09/30/93 - 08/31/96. Project 3 Biomed: "Tumor Necrosis Factor- α (TNF- α) in JRA, "Co-Investigator/Consultant".
Direct funding (1994): \$290,180.00
Indirect funding (1994): \$113,900.00
Total funding (1994): \$404,080.00

B. Industrial (*Sponsored Research Grants*)

1. Effects of Carbocyclic Nucleosides on Rheumatoid Arthritis and other Debilitating Chronic Autoimmune Diseases (MMDRI, Kansas City, MO; budget of \$300,000 per year) 1990-1992
2. Neuroendocrinimmunology, Aging and Autoimmune Diseases (MMDRI, Kansas City, MO; budget of \$75,000 per year) 1991-1993
3. The Use of Novel Carbocyclic Nucleosides in Systemic Inflammatory Response Syndrome (SIRS) and Other Acute Inflammatory Diseases (MMDRI, Cincinnati, OH; budget of \$500,000 per year) 1992-1995
4. Regulation of Macrophage-Derived Cytokine Gene Expression by Novel Carbocyclic Nucleosides (MMDRI, Cincinnati, OH; budget of \$250,000 per year) 1993-1995