

University of California San Francisco School of Medicine
FULL ACADEMIC CURRICULUM VITAE

Updated: 11/06

NAME: Clifford A. Lowell

PERSONAL Date of birth: February 8, 1958 (Tacoma, WA)
Married: Kerry Koller, Ph.D. Children: Benjamin (age 18) and Katie (age 14)
Home address: 1215 27th Ave. San Francisco, CA 94122

Position: Professor and Chair
Department of Laboratory Medicine
University of California, San Francisco School of Medicine

Address: Room HSE590, Box 0100
Department of Laboratory Medicine
University of California, San Francisco
San Francisco, CA 94143-0100
Voice: (415) 476-2963
FAX: (415) 502-5462
email: Clifford.Lowell@ucsf.edu
www: <http://www.ucsf.edu/lowell/lab.html>

EDUCATION:

1975-1979	Stanford University	B.S. - Honors (Biology),
1979-1986	Johns Hopkins University School of Medicine	M.D.
1979-1986	Johns Hopkins University School of Medicine	Ph.D. Biochemistry, Cellular and Molecular Biology

LICENSES, CERTIFICATION:

1990	Medical license, State of California G 67944
1990	Diplomat of American Board of Internal Medicine

PRINCIPAL POSITIONS HELD:

1986 - 1989	Osler Medical House Officer (Internship and Residency), Department of Medicine, The Johns Hopkins Hospital. Department Chairman: Dr. John D. Stobo.
1989 - 1995	Post-Doctoral Research Fellow, Department of Microbiology and Immunology University of California, San Francisco. Laboratory of Dr. Harold Varmus. Project: Targeted Disruption of Src-Family Kinases.
1995 - 2001	Assistant Professor in Residence, Department of Laboratory Medicine Univ. of California, San Francisco, Director of Clinical Immunology Laboratory
2001 - 2005	Associate Professor in Residence, Department of Laboratory Medicine Univ. of California, San Francisco, Director of Clinical Immunology Laboratory
2005 - 2006	Professor, Department of Laboratory Medicine Univ. of California, San Francisco, Director of Clinical Immunology Laboratory
2006 - present	Professor and Chair, Department of Laboratory Medicine Univ. of California, San Francisco

OTHER POSITIONS HELD CONCURRENTLY:

- 1976 - 1979 Undergraduate Research Assistant, Stanford University, Department of Pathology, Laboratory of Dr. David Clayton. Honors Thesis: Mechanisms of Mitochondrial DNA Replication.
- 1981 - 1984 Graduate Research, The Johns Hopkins University School of Medicine, Dept. of Molecular Biology and Genetics, Dept. Chairman, Dr. Thomas Kelly. Thesis: Structure and Expression of the Murine Serum Amyloid A Gene Family. Fellow Medical Scientist Training Program
- 1988 - 1989 Residency Research Program, Dept. of Medicine, The Johns Hopkins University School of Medicine, Laboratory of Dr. Douglas Fearon
Project: Analysis of the Epstein-Barr Virus/Complement Receptor.
- 1990 - 1992 Clinical Oncology Fellow, University of California, San Francisco

HONORS AND AWARDS:

- 1977 N.C.A.A. All-American, Swimming, Stanford University.
- 1979 Phi Beta Kappa, Stanford University.
- 1979 B.S. with University Distinction and Departmental Honors, Stanford University.
- 1979 - 1986 Awardee Medical Scientist Training Program Scholarship, The Johns Hopkins University School of Medicine.
- 1986 Alpha Omega Alpha, The Johns Hopkins University School of Medicine.
- 1989 Awardee Bristol-Meyers Cancer Research Fellowship
- 1992 Awardee Howard Hughes Physician Scientist Training Fellowship
- 1995 Member, Program Biological Sciences, UCSF
- 1995 Member, Program in Biomedical Sciences, UCSF
- 1997 American Society of Hematology Junior Faculty Scholar Award
- 2000 Stewart Family Trust Scholar Award
- 2001 Leukemia/Lymphoma Society Scholar Award
- 2003 UCSF Program in Immunology: Student-selected Faculty Speaker
- 2005 Federation of American Societies for Experimental Biology (FASEB)
Elected organizer for 2007 Meeting “Signal Transduction in Immune System”

CLINICAL ACTIVITIES

Medical Director of the Clinical Immunology Laboratory, Dept. of Laboratory Medicine. The laboratory performs diagnostic testing using immunologic methods including serologic testing, infectious disease screening in blood donors and flow cytometry. The responsibilities of the Medical Director include diagnostic interpretation of test results (mainly for hematopoietic malignancy), teaching of pathology residents and evaluating diagnostic tests offered by the Laboratory. The laboratory performed over 1300 flow cytometric analysis of patient samples for leukemia/lymphoma diagnosis in 2005. Additional major improvements made in the clinical laboratory within the last year include the development a new multi-parameter flow testing for leukemia/lymphoma, automation of routine flow cytometry, improvements in a number of standard ELISA-type assays, and institution of molecular assays for HPV infection.

PROFESSIONAL ACTIVITIES

Membership Professional Societies (Current)

- 1996-curr American Society of Hematology
- 1997-curr American Association of Laboratory Immunologists
- 1998-curr Society for Leukocyte Biology
- 2000-curr American Association of Immunologists
- 2000-curr American Society for Cell Biology

INVITED PRESENTATIONSINTERNATIONAL (since faculty appointment)

- 8/95 EMBL Symposia on Mouse Molecular Genetics, Heidelberg, FRG. "Altered Hematopoiesis in Src-family Kinase Deficient Mice"
- 10/96 American/European Society for Leukocyte Biology, Verona, Italy. Session Chair "Impaired Macrophage Adhesion in Hck/Fgr Deficient Mice"
- 10/96 University of Cologne, Cologne, FRG. "Lyn as a Negative Regulator of B-cell Antigen Receptor Signaling"
- 5/98 International Congress on Leukocyte Adhesion, Lake Garda, Italy. "Src-family Kinases Hck, Fgr and Lyn are Required for α 1 Integrin Signaling in Murine Macrophages"
- 5/98 Pfizer Pharmaceutical Corp., Sandwich, England, UK. "Kinases and Neutrophil Function"
- 9/03 European Immunology Association, Annual Symposia. Signal Transduction Mechanisms. "Src-family and Syk Tyrosine Kinases in Neutrophil Activation". Sopron, Hungary.
- 9/03 Semmelweis University, Budapest, Hungary. Dept. of Physiology Faculty Speaker. "Neutrophil Signaling Mechanisms"
- 9/05 European Federation of Immunologic Societies, "Signal Transduction in the Immune System" Lake Balaton, Hungary
- 9/05 Semmelweis University, Budapest, Hungary. Dept. of Physiology Faculty Speaker. "Integrin Signaling Mechanisms"

NATIONAL (since faculty appointment)

- 7/95 7th Annual International Meeting on Oncogenes: Fredrick, MD "Regulation of Immune Cell Adhesion by Cytoplasmic Tyrosine Kinases".
- 8/95 Amgen Corporation, Bolder, CO. "LPS Signaling and Src-family Kinases"
- 3/96 Keystone Symposia -- B-Cell Development and Function: Hilton Head, SC "Role of the Lyn Kinase in B-cell Activation"
- 6/97 The Albany Medical College, Dept. Physiology/Cell Biology, Albany, NY. "Signal Transduction by Cell Adhesion Receptors"
- 7/97 FASEB Conference on Hematologic Malignancies: Saxton River, Vermont Session Chair "Tyrosine Kinase Regulation of Hematopoietic Cell Adhesion"
- 8/97 American Association Laboratory Immunology, San Francisco, CA. Session Organizer. "Immune Functions Regulated by Cell Adhesion"
- 12/97 Millennium Pharmaceuticals, Boston, MA. "Signal Transduction by Integrin Receptors".
- 5/98 The Scripps Institute, Dept. of Immunology, San Diego, CA. "LPS and Adhesion Receptor Signal Transduction in Macrophages".
- 6/98 Merck Pharmaceuticals, Rahway, NJ. "Role of Src-family Kinases in Neutrophil Activation"
- 8/98 Society for Leukocyte Biology, National Meeting: San Diego, CA. "Neutrophil Adhesion and Signal Transduction".
- 10/98 New York University Blood Center, New York, NY. "Chemoattractant Signal Transduction by the Src-family Tyrosine Kinases".
- 2/99 Sugen Corp, Redwood City, CA. "Src-family Kinases and Myeloid Cell Signaling".
- 5/99 Onyx Pharmaceuticals, Richmond, CA. "Signal Transduction by Leukocyte Integrins"
- 10/99 Boehringer-Ingelheim Pharmaceuticals, New Groton, CT. "Regulation of Myeloid Leukocyte Activation by Src-family Kinases"
- 2/00 Parke-Davis/Onyx Pharmaceuticals, Berkeley, CA RMC conference: "Targeting Syk Kinase"
- 3/00 ICOS Pharmaceuticals, Seattle, WA. "Src-family Kinases and Leukocyte Trafficking"
- 10/00 University of California, Berkeley Cell and Molecular Biology Seminar Series. "Regulation of Leukocyte Activation by the Syk Tyrosine Kinase".
- 11/00 University of Pennsylvania School of Medicine, Immunology Colloquium Seminar Series. "Cytoplasmic Tyrosine Kinases and Leukocyte Adhesion".
- 2/01 Gordon Conference – Fibronectins, Integrins and Related Molecules. Ventura, CA "Regulation of Leukocyte Activation by Syk and Src-family Kinases"
- 3/01 La Jolla Institute of Allergy and Immunology. "Regulation of Leukocyte Integrin Signaling" Immunology Seminar Series.
- 4/01 American Association of Immunology, Annual Meeting, Orlando, FL. Symposia Organizer:

- “Hematopoiesis and the Immune System”.
- 4/01 University of California, Irvine. “Regulation of Leukocyte Integrin Signaling” Dept. of Immunology Seminar Series.
- 2/02 Keystone Symposia on Molecular and Cellular Biology of Leukocyte Regulatory Receptors. Session chair “Src-family kinases and Leukocyte Inhibitory Receptors”. Lake Tahoe, CA.
- 4/02 American Association of Immunology, Annual Meeting, New Orleans, LO. Symposia Organizer: “Hematopoiesis and the Immune System”.
- 5/02 Rigel Biopharmaceuticals, S. San Francisco, CA. “The Src-family Tyrosine Kinases”.
- 11/02 PPD Pharmaceuticals, Menlo Park. “Syk and Inflammation”
- 1/03 Wyeth-Research, Cambridge, MA. “Src and Syk Kinase Regulation of Leukocyte Signaling”.
- 2/03 Gordon Conference – Fibronectins, Integrins and Related Molecules. Ventura, CA
“Negative regulation of leukocyte integrin signaling by the Lyn tyrosine kinase”
- 3/03 Los Angeles/UCLA Children’s Research Hospital. Immunology Seminar Series. “Tyrosine Kinases and Leukocyte Chemokine Signaling”
- 4/03 American Association of Immunology, Annual Meeting, Denver, CO. Symposia Organizer: “Hematopoiesis and the Immune System”.
- 7/03 FASEB Summer Research Conference. Aspen, CO. Immune Signaling Mechanisms. “Syk and Leukocyte Integrin Signaling”.
- 9/03 Rigel Biopharmaceuticals, S. San Francisco, CA. “Syk, Integrins and Osteoclasts”.
- 9/03 UCSF, Program in Immunology Seminar Series. Annual Student-selected Faculty Speaker. “The Ups and Downs of Leukocyte Signaling”.
- 10/03 Yale University, Department of Laboratory Medicine. Immunology Seminar Series “Webs in Leukocyte Tyrosine Kinase Based Signaling”.
- 3/04 Amgen Inc. Thousand Oaks, CA. “Src and Syk Family Kinases in Blood Cells”.
- 4/04 American Association of Immunology, Annual Meeting, Washington, DC. Symposia Organizer: “Hematopoiesis and the Immune System”.
- 2/05 University of Pennsylvania School of Medicine, Immunology Colloquium Seminar Series. “Coupling of Leukocyte Integrins to Downstream Signaling”.
- 6/05 FASEB Summer Research Conference, Aspen, CO. Signal Transduction in the Immune System. “Wiskott-Aldrich Syndrome and Neutrophil Dysfunction”
- 7/05 FASEB Summer Research Conference, Tucson, AZ, Immunoreceptors. “Convergence of Integrin and Immunoreceptor Signaling Pathways”
- 10/05 National Institutes of Health, National Institute of Allergy/Infectious Disease, Twinbrooke Campus, Immunology Invited Seminar Series. “Leukocyte Integrin Signaling Pathways”.
- 1/06 Roche Pharmaceuticals, Immunology Seminar Series, “Src, Syk and Immunoreceptor Signaling”
- 3/06 University of Michigan, Dept. Pharmacology, Invited Seminar Series “Positive and Negative Regulation of Intracellular Signaling by Src-family Kinases”.
- 4/06 FASEB Annual Meeting, San Francisco, CA, Leukocyte Migration Session, “Role of WASp in Neutrophil Integrin Function”
- 11/06 Scripps Research Institute, La Jolla, CA. Dept. of Immunology, Immunology Seminar Series. “Leukocyte Integrins Utilization ITAM Sequences for Signal Transduction”.
- 11/06 University of Virginia, Robert M. Berne Cardiovascular Research Center. Immunology Program Seminar Series. “Src-family and Syk Kinases in Innate Immune Cells”.
- 12/06 Medical College of Georgia, Immunology Center Seminar Series. “Integrin Signaling in Neutrophils and Macrophages Utilizes an ITAM-dependent Pathway”
- 06/07 Phagocyte Gordon Research Conference, Smithfield, RI. “Leukocyte Integrin Signaling Pathways”
- 06/07 FASEB Summer Research Conference, Aspen, CO. Signal Transduction in the Immune System. “Signaling in Innate Immune Cells” Overall meeting organizer

REGIONAL AND OTHER PRESENTATIONS (last 2 years only)

- 1/04 UCSF Mission Bay Research Series -- research presentation
- 3/04 UCSF Program in Immunology “Immune Complexes in the Joints and Lungs” – review talk
- 3/04 UCSF Department of Cellular Molecular Pharmacology – research presentation
- 5/04 UCSF BioMedical Sciences Faculty Seminar Series – research presentation
- 11/04 UCSF Program in Immunology Annual retreat – research presentation

- 2/05 UCSF Lung Biology Center – research presentation
- 2/05 UCSF Hematopoietic Malignancies Group, Cancer Center – research presentation
- 7/05 UCSF Department of Medicine – Division Nephrology – research presentation
- 10/05 UCSF Biomedical Sciences Graduate Program, Lake Tahoe Retreat – research presentation
- 11/05 UCSF Program in Immunology “New adapter proteins in phagocytosis” – review talk
- 1/06 UCSF Molecular Medicine Program – research presentation
- 5/06 UCSF Department of Cellular Molecular Pharmacology – research presentation
- 10/06 UCSF Neonatal Brain Disorders/Brain and Spinal Cord Injury Center – research presentation

TEACHING AND MENTORING**DIDACTIC TEACHING (last 2 years only)**

<u>Duration</u>	<u>Quarter</u>	<u>Class name</u>
1996 – 2006	Fall	Microbiology and Immunology I-3 block <u>Medical School 2nd Year Microbiology</u> Laboratory/Discussion Group Leader (35 students). Total hours: 60
1997 – current	Fall	Microbiology 204 <u>Graduate Basic/Clinical Immunology</u> 2 nd year BMS/PIBS/Pharm. Chem. Graduate Students Lecturer/Discussion Group Leader (30 students). Total hours: 20
1996 – current	Winter	Biomedical Sciences 225A <u>Introductory Immunology/Cell Biology.</u> 1 st year BMS Graduate Students. Lecturer/Discussion Group Leader (20 students). Total hours: 10
2004 – current	Fall	Biomedical Sciences 260 <u>Graduate Cell Biology</u> 1 st year BMS/MSTP Graduate Students. Discussion Group Leader (10 students). Total hours: 20
2000 – current	Fall / Spring	Dept. of Medicine, Heme/Onc Lecture Series for residents/fellows “Flow cytometry” (10 - 20 residents) total hours: 10
2001 – current	Fall/ Spring	Dept. of Laboratory Medicine, Hematology Core Course for residents “Flow cytometry” (10 – 20 residents) total hours: 10
2003 – current	Spring	Medicine 170.09 Current Topics in Medical Science 1 st /2 nd year Medical Students. Small Group Lecturer (30 students) Total hours: 10
2006	Spring	Microbiology 209 <u>Advanced Topics Graduate Microbiology</u> Course Director: 30 students, Small Group Lectures, Journal Papers Total hours: 60

LABORATORY TEACHING

1996 - current	PIBS/BMS/Molecular Medicine Faculty/Student Journal Clubs: Faculty coach and presenter: Total hours: 20
1996 - current	Research Laboratory. Daily meetings/supervision post-doctoral fellows and students. Total hours: 200

CLINICAL TEACHING

1996 - current	Daily supervision/signout with Laboratory Medicine residents Immunology rotation. Small group lectures to Medicine/AP/CP residents Total hours 40
1996 - current	Weekly flow cytometry case conference with Laboratory Medicine Residents. Total hours 20

PIBS/BMS GRADUATE STUDENT COMMITTEES

Oral Examination Committees: (last 5 years only)

	<u>Student</u>	<u>Thesis Advisor</u>
2001	Rebecca Blank	Dr. Jim McKerrow (Pathology)
2002	Rayna Takaki	Dr. Lewis Lanier (Microbiology/Immunology)
2002	Emil Palacios	Dr. Art Weiss (Medicine/Micro/Immunology)
2003	Danni Belonick	Dr. Zena Werb (Anatomy)
2003	Vikas Gupta (Chair)	Dr. Art Weiss (Medicine/Micro/Immunology)
2003	Chris Allen	Dr. Jason Cyster (Microbiology/Immunology)
2004	Susan Levin	Dr. Art Weiss (Medicine/Micro/Immunology)
2004	Tiffany Reese	Dr. Richard Locksley (Medicine/Micro/Immunology)
2005	Larry Shioh	Dr. Jason Cyster (Microbiology/Immunology)
2006	Elizabeth Szyleyko (Chair)	Dr. Jim McKerrow (Pathology)
2006	Kelly Haston (Chair)	Dr. Renee Reijo (OB/Gyn)
2006	Cathleen Collins (Chair)	Dr. Eric Brown (Medicine)
2006	Julia Gilden (Chair)	Dr. Max Krummel (Pathology)

Thesis Committees: (last 5 years only)

2000 - 2002	Jonathan Snow	Dr. Mark Goldsmith (Gladstone Institute/Medicine)
2003 – current	Emil Palacios	Dr. Arthur Weiss (Medicine/Micro/Immunology)
2003 – 2005	Aaron Tward (Chair)	Dr. J. Michael Bishop (Microbiology/Immunology)
2003 – current	Piam Vacharotayangul (Chair)	Dr. Tony DeFranco (Microbiology/Immunology)
2004 – current	Tiffany Reese	Dr. Richard Locksley (Medicine/Micro/Immunology)

MEDICAL STUDENT COMMITTEES: M.D. with THESIS

1997 Patrick Suen (Chair)	Dr. Clifford Lowell (Lab Medicine), Advisor
1997 Ginard Henry (Chair)	Dr. Harlan Ives (Medicine), Advisor
2001 Tamiko Katsumoto	Dr. Kevin Shannon (Medicine), Advisor

STUDENTS/POST-DOCTORAL FELLOWS SUPERVISEDFellows:Status

1995 - 1998	Fanying Meng, M.D.-Ph.D. (Univ. Virginia)	Staff Scientist - Telik Corp.
1995 - 2001	Mark Frohlich, M.D. (Harvard)	Medical Director, Xycte Pharm.
1996 - 1998	Vivien Chan, Ph.D. (U.C.S.F.)	Staff Scientist - Chiron Corp.
1997 - 1999	Christine Burke, Ph.D. (Yale)	Co-founder: LabVelocity.com
1998 - 2004	Shalini Pereira, Ph.D. (Univ. Rochester)	Specialist, UCSF HLA Lab.
1998 - 2000	Laura Corral, Ph.D. (U.C. Berkeley)	Scientist – Abgenix Corp.
1999	Jean-Max Pasquet (Oxford University, UK)	Hôpital du Haut-Lévêque, FR.
1999 - 2003	Attila Moscai, M.D.-Ph.D. (Semmelweis U. Hungary)	Asst. Professor, Semmelweis
1999 – 2000	Andrew Horvai, M.D.-Ph.D. (Univ. of San Diego)	Resident, Pathology
2001 – current	Hong Zhang, Ph.D. (Univ. Calif. Davis)	
2001 – 2002	Fumiko Higashikawa, Ph.D. (Univ. of Florida)	Asst. Professor, U. Hiroshima
2002 – 2005	Ching Liang-Chu, Ph.D. (Tawian University)	Asst Professor, Nat. U. Taiwan
2003 – current	Clare Abram, Ph.D. (University of Manchester)	
2005 – current	Patrizia Scapini, Ph.D. (University of Verona)	
2005 – current	Allison Miller, Ph.D. (University of Michigan)	

Students:Status

1995 - 1996	Patrick Suen (UCSF Med Student)	Orthopaedics – Stanford
1996 - 1998	Rebecca Holmes (Undergrad)	Yale Univ. Sch. Med.
1997 - 1998	Ambie Yesus (Undergrad)	Duke Univ. Sch. Med.
1998 - 1999	Gloria Fann (Undergrad)	Univ. Washington Sch. Med.
1999	Lynn Quekk (Visiting Grad. Student)	Oxford University, UK
1999	Elena Cavegion (Visiting Grad. Student)	Univ. Verona, Italy.
2000 – 2001	Slivia Ciedel (Undergrad)	UCSD Grad School
2001 – 2004	Zoltan Jankus (Visiting Grad Student)	Semmelweis Univ., Hungary
2004 – current	Jessica Van Ziffle (UCSF – BMS Graduate Student)	
2006 – current	Michelle Toft (UCSF – BMS Graduate Student)	

TEACHING AWARDS

1999	Nominated Medical School Class 2001 – “Excellence in Small Group Teaching”
1999	Nominated Department Laboratory Medicine Residents -- Teaching Award
2000	Nominated Medical School Class 2002 – “Excellence in Small Group Teaching”
2001	Nominated Medical School Class 2003 – Three Awards: “Excellence in Small Group Teaching” “Major Faculty Contribution to Teaching” “An Outstanding Lecturer”
2002	Awarded, Medical School Class of 2002 – Excellence: Pre-clinical/Small Group Teaching Awarded by the Dean of the Medical School at the 2002 Graduation ceremony.
2006	Nominated Medical School Class 2008 – “Excellence in Small Group Teaching”
2006	Nominated by UCSF School of Medicine for Kaiser Award for Excellence in Teaching

SUMMARY OF TEACHING DUTIES -- TOTAL HOURS

2004-2005	420 total hours of teaching (including preparation) Didactic teaching hours: 140 hours Laboratory teaching hours: 220 hours Clinical teaching hours: 60 hours
2005-2006	480 total hours of teaching (including preparation) Didactic teaching hours: 200 hours Laboratory teaching hours: 220 hours Clinical teaching hours: 60 hours
ANTICIPATED	
2006 – 2007	420 total hours of teaching (including preparation)

SERVICE

UNIVERSITY SERVICE

DEPARTMENTAL SERVICE

1995-present: Residents Teaching Committee
 1996-present: Advancements and Promotions Committee
 1997-present: Residency Applicant Interviewer
 1998: Faculty Search Committee -- Clinical Hematology
 1999-2001: Department Laboratory Medicine/Pathology – Grand Rounds Organizer
 2001-2003: Hematology Section – Faculty Search Committee
 2004: Immunology Section – Chair Faculty Search Committee

SCHOOL, CAMPUS, AND SYSTEMWIDE SERVICE

1996-2004: UCSF Biomedical Sciences (BMS) Graduate Program
 Graduate School: **Admissions Committee**
 1998: Advisory Member, Gladstone Foundation Director -- Faculty Search Committee
 1999: Dept. of Pediatrics: Faculty Search Committee -- Bone Marrow Stem Cell Program
 2000: Dept. of Pathology: Immunology Faculty Search Committee
 2000: Dean's Office. Planning committee, Parnassus Services Building, Animal Care
 2000: Medical Student Faculty Network – Faculty Representative
 2001-2002: UCSF School of Medicine – Medical School **Admissions Committee**
 2002-2006: **Associate Director, UCSF Medical Scientist Training Program (MSTP)**
 This is the main M.D-Ph.D. program at UCSF. It is sponsored by an NIH grant (now in its 25th year). Responsibilities include mentoring of student issues, interviewing/admissions for new MSTP applicants, organization of annual retreat, participation in grant renewal.
 2003: Dept. of Medicine: Hematology/Oncology Faculty Search Committee
 2003: UCSF Academic Affairs – Committee on Advancements/Promotions – ad hoc reviewer
 2003-present: Molecular Medicine – Residency selection committee
 2005: Dept. of Ophthalmology – Immunology Faculty Search Committee
 2006: Dept. of Pediatrics – Chair, Hematology/Oncology Faculty Search Committee

GOVERNMENT SERVICE

2002 – 2004: NIH: Allergy and Immunology Study Section (ALY) – ad hoc reviewer
 NIH: Special Emphasis Study Section – panel member
 NIH: NHLBI, Special Emphasis Study Section – PO1 reviewer
 2004 – 2009: NIH: Innate Immunity and Inflammation (III) Study Section – regular member
 2007: NIH: NIAID, Special Emphasis Study Section – PO1 reviewer

SERVICE TO PROFESSIONAL SOCIETIES

2000 – 2004: American Association of Immunologists: Block Chair Organizer for National Meeting. Reviewing abstracts for oral/poster presentation, organization of meeting sessions on immune stem cells/growth factors/cell development.
 2004: American Society of Hematology: Organizer for National Meeting. Reviewing abstracts for oral/poster presentation, organization of meeting sessions on hematopoietic cytokines and signal transduction
 2002 – 2005: Wellcome Trust, UK. Programme Grant Applications – adhoc reviewer
 2007: FASEB Summer Research Conference, Aspen, CO. “Signal Transduction in the Immune System” Elected as meeting co-organizer.

SERVICE TO PROFESSIONAL PUBLICATIONS

1996-current: Editorial Board; *Clinical and Diagnostic Immunology*. Published by American Society for Microbiology

1995-current

Ad hoc Journal Reviewer: Am. J. Physiology, Blood, Cytometry, EMBO J., Gene, Hepatology, Immunity, J. Biol. Chem., J. Cell Biology, J. Cell. Immunol., J. Exp. Medicine, J. Immunol., Leukocyte Biol., J. Am. Med. Assoc., Molecular Medicine, Mol. Cell. Biol., Nature Medicine, Oncogene, P.N.A.S., Science

RESEARCH AND CREATIVE ACTIVITIES

Original Research (Peer Reviewed):

- 1) **Lowell, C.A.**, Bogenhagen, D., Clayton, D.A. (1978). S₁ Nuclease-specific nicking of mitochondrial DNA containing displacement loops. *Analytical Biochemistry* 91: 521 - 531.
- 2) Bogenhagen, D., **Lowell, C.A.**, Clayton, D.A. (1981). Mechanism of mitochondrial DNA replication in mouse L-cells: replication of unicircular dimer molecules. *J. Mol. Biol.* 148: 77 - 93.
- 3) Stearman, R.S., **Lowell, C.A.**, Pearson, W.R., John F. Morrow (1982). Regulation of synthesis of Amyloid A-Related Protein. *Annals of N.Y. Academy of Science* 389: 106 - 115.
- 4) Stearman, R.S., **Lowell, C.A.**, Peltzman, C.G., Morrow, J.F. (1986). The sequence and structure of a new serum amyloid A gene. *Nucleic Acids Research* 14: 797 - 809.
- 5) **Lowell, C.A.**, Stearman, R.S., Morrow, J.F. (1986). Transcriptional regulation of serum amyloid A gene expression. *J. Biol. Chem.* 261: 8453 - 8461.
- 6) **Lowell, C.A.**, Potter, D.A., Stearman, R.S., Morrow, J.F. (1986). Structure of the murine serum amyloid A gene family: gene conversion. *J. Biol. Chem.* 261: 8442 - 8452.
- 7) Shirey, R.S., Morton, S., Lawton, S.B., **Lowell, C.A.**, Kickler, T.S., Ness, P.M. (1988). Fenoprofen-induced immune hemolysis. *Am. J. Clin. Pathol.* 89: 410-414.
- 8) **Lowell, C.A.**, Klickstein, L.B., Carter, R.H., Mitchell, J.A., Fearon, D.T., Ahearn, J.M. (1989). Mapping of the Epstein-Barr virus and C3dg binding sites to a common domain on complement receptor type 2. *J. Exp. Med.* 170: 1931 - 1946.
- 9) **Lowell, C.A.**, Soriano, P., Varmus, H.E. (1994). Functional overlap in the *src*-gene family: inactivation of *hck* and *fgr* impairs natural immunity. *Genes and Development* 8: 387-398.
- 10) **Lowell, C.A.**, Niwa, M., Soriano, P., Varmus, H. E. (1996). Deficiency of the Hck and Src tyrosine kinases results in extreme levels of extramedullary hematopoiesis. *Blood* 87: 1780-1792.
- 11) **Lowell, C.A.**, Fumagalli, L., Berton, G. (1996). Deficiency of Src-family kinases p59/61^{*hck*} and p58c-^{*fgr*} results in defective adhesion-dependent neutrophil functions. *J. Cell Biol.* 133: 895-910.
- 12) Schwartzberg, P.L., Xing, L., Hoffmann, O., **Lowell, C.A.**, Garrett, L., Lee, E., Boyce, B.F., Varmus, H.E. (1997) Rescue of osteoclast function by transgenic expression of kinase-deficient Src in *src*^{-/-} mutant mice. *Genes and Development* 11: 2835-2844.
- 13) Crowley, M.T., Costello, P.S., Fitzer-Attas, C.J., Turner, M., Meng, F., **Lowell, C.A.**, Tybulewicz, V.L., DeFranco, A.L. (1997) A critical role for Syk in signal transduction and phagocytosis mediated by the Fc receptors on macrophages. *J. Exp. Med.* 186: 1027-1039.
- 14) Franceschi, L.D., Fumagalli, L., Olivieri, O., Corrocher, R., **Lowell, C.A.**, Berton, G. (1997) Deficiency of Src-Family kinases Fgr and Hck results in activation of erythrocyte K/Cl co-transport. *J. Clin. Invest.* 99: 220-227.
- 15) Meng, F.M., **Lowell, C.A.** (1997) LPS-Induced macrophage activation and signal transduction in the absence of Src-family kinases Hck, Fgr and Lyn. *J. Exp. Med.* 185: 1661-1670.
- 16) Chan, V.W.F., Meng, F., Soriano, P., DeFranco, A.L., **Lowell, C.A.** (1997) Characterization of the B-lymphocyte populations in Lyn-deficient Mice and the role of Lyn in signal initiation and downregulation. *Immunity*, 7: 69-71.
- 17) Jodus, M.R., Williams, C.C., Avina, M.D., Ly, M., Kim, S., Liu, Y., Narasaki, R., **Lowell, C.A.**, Wepsic, T. (1998) Macrophages kill T9 glioma tumor cells bearing the membrane isoform of macrophage colony stimulating factor through a phagocytosis-dependent pathway. *J. Immunol.* 160: 361-368.
- 18) Chan, V.W.F., Mecklenbräuker, I., Texido, G., Leitges, M., Carsetti, R., **Lowell, C.A.**, Rajewsky, K., Miyake, K., Tarakhovsky, A. (1998) The molecular mechanism of B cell activation by *toll*-like receptor

- protein RP-105. *J. Exp. Med.* 188: 93-101.
- 19) Satterthwaite, A.B., **Lowell, C.A.**, Khan, W.N., Sideras, P., Alt, F.W., Witte, O.N. (1998) Independent and opposing roles for Btk and Lyn in B and myeloid signaling pathways. *J. Exp. Med.* 188: 833-844.
 - 20) Chan, V.W.F., **Lowell, C.A.**, DeFranco, A.L. (1998) Defective negative regulation of antigen receptor signaling in Lyn-deficient B lymphocytes. *Current Biology* 8: 545-553.
 - 21) **Lowell, C.A.**, Berton, G. (1998) Resistance to endotoxic shock and reduced neutrophil migration in mice deficient for the Src-family kinases Hck and Fgr. *Proc. Natl. Acad. Sci. (USA)* 95: 7580-7584.
 - 22) Meng, F., **Lowell, C.A.** (1998) A $\beta 1$ integrin signaling pathway involving Src-Family kinases, Cbl, and PI-3 Kinase is required for macrophage spreading and migration. *EMBO J.* 17: 4391-4403.
 - 23) Mócsai, A., Ligeti, E., **Lowell, C.A.**, Berton, G. (1999) Adhesion-dependent degranulation of neutrophils requires the Src-family kinases Fgr and Hck. *J. Immunol.* 162: 1120-1126.
 - 24) Brady, K.A., Atwater, S.K., **Lowell, C.A.** (1999) Flow cytometric detection of CD10 (cALLA) on peripheral blood B lymphocytes of neonates. *British J. Haematology* 107: 712-715.
 - 25) Suen, P.W., Ilic, D., Cavegion, E., Berton, G., Damsky, C.H., **Lowell, C.A.** (1999) Impaired integrin-mediated signal transduction and altered cytoskeletal structure in Hck/Fgr deficient macrophages. *J. Cell Science* 112: 4067-4078.
 - 26) Gresham, H., Dale, B.M., Potter, J.W., Chang, P.S., Vines, C.M., **Lowell, C.A.**, Lagenaur, C.F., Willman, C.L. (2000) Negative regulation of phagocytosis in murine macrophages by the Src kinase family member, c-Fgr. *J. Exp. Med.* 191: 515-528.
 - 27) Weinstein, S.L., Finn, A.J., Dave, S., Meng, F., **Lowell, C.A.**, Sanghera, J.S., DeFranco, A.L. (2000) Phosphatidylinositol 3-kinase and mTOR mediate lipopolysaccharide-stimulated nitric oxide production in macrophages via interferon- γ . *J. Leuk. Biol.* 67: 405-414.
 - 28) Fitzer-Attas, C.J., Lowry, M., Crowley, M.T., Finn, A.J., Meng, F., DeFranco, A.L., **Lowell, C.A.** (2000) Fc γ receptor-mediated phagocytosis in macrophages lacking the Src-family tyrosine kinases Hck, Fgr, and Lyn. *J. Exp. Med.* 191: 669-681.
 - 29) Mócsai, A., Jákus, Z., Vántus, T., Berton, G., **Lowell, C.A.**, Ligeti, E. (2000) Kinase Pathways in chemoattractant-induced degranulation of neutrophils: the role of p38 MAP kinase activated by Src family kinases. *J. Immunol.* 164: 4321-4331.
 - 30) Satterthwaite, A.B., Willis, F., Kanchanastit, P., Fruman, D., Cantley, L.C., Helgason, C.D., Humphries, R.K., **Lowell, C.A.**, Simon, M., Leitges, M., Tarakhovsky, A., Tedder, T.F., Lesche, R., Wu, H., Witte, O.N. (2000) A sensitized genetic System for the analysis of murine B Lymphocyte signal transduction pathways dependent on Bruton's tyrosine kinase. *Proc. Natl. Acad. Sci. (USA)* 97: 6687-6692.
 - 31) Kawakami, Y., Kitaura, J., Hartman, S.E., **Lowell, C.A.**, Siraganian, R.P., Kawakami, T. (2000) Regulation of protein kinase C β I by two protein-tyrosine kinases, Btk and Syk. *Proc. Natl. Acad. Sci. (USA)* 97: 7423-7428.
 - 32) Kawakami, Y., Kitaura, J., Satterthwaite, A.B., Kato, R.M., Asai, K., Hartman, S.E., Maeda-Yamamoto, M., **Lowell, C.A.**, Rawlings, D.J., Witte, O.N., Kawakami, T. (2000) Redundant and opposing functions of two tyrosine Kinases, Btk and Lyn, in mast cell activation. *J. Immunol.* 165: 1210-1219.
 - 33) Fujimoto, M., Fujimoto, Y., Poe, J.C., Jansen, P.J., **Lowell, C.A.**, DeFranco, A.L., Tedder, T.F. (2000) CD19 regulates Src-family protein tyrosine kinase activation in B lymphocytes through processive amplification. *Immunity* 13: 47-57.
 - 34) Pasquet, J., Quek, L., Pasquet, S., Poole, A., Matthews, J.R., **Lowell, C.A.**, Watson, S.P. (2000) Evidence for a role of SHP-1 in platelet activation by the collagen receptor GPVI. *J. Biol. Chem.* 275: 28526-28531.
 - 35) Quek, L.S., Pasquet, J., Hers, I., Cornall, R., Knight, G., Barnes, M., Hibbs, M.L., Dunn, A.R., **Lowell, C.A.**, Watson, S.P. (2000) Fyn and Lyn phosphorylate the Fc γ receptor β chain downstream of glycoprotein VI in murine platelets; Lyn also regulates a novel feedback pathway. *Blood* 96: 4246-4253.

- 36) Yu, C., Yen, B., **Lowell, C.A.**, DeFranco, A.L. (2001) Lupus-like autoimmune disease in mice lacking the Src-family kinases Fyn and Lyn. *Current Biology* 11: 34-38.
- 37) Pereira, S., Zhou, M., Mócsai, **Lowell, C.A.** (2001) Resting murine neutrophils express functional $\alpha 4$ integrins which signal through Src-family kinases. *J. Immunol.* 166: 4115-4123.
- 38) O'Laughlin, B., Radosevic, N, Taylor, M., DeBerry, C., Metcalf, D., Zhou, M., **Lowell, C.A.**, Linnekin, D. (2001) Lyn is required for normal SCF-induced proliferation and chemotaxis of primary hematopoietic cells. *Blood* 98: 343-350.
- 39) Hasegawa, M., Fujimoto, M., Poe, J.C., Steeber, D.A., **Lowell, C.A.**, Tedder, T.F. (2001) A CD19-dependent signaling pathway regulates autoimmunity in Lyn-deficient mice. *J Immunol.* 167: 2469-2478.
- 40) Hanna Z., Weng, X., Kay, D.G., Poudrier, J., **Lowell, C.**, Jolicoeur, P. (2001) The Pathogenicity of Human Immunodeficiency Virus (hiv) type 1 *nef* in *cd4c/HIV* transgenic mice is abolished by mutation of its SH3-binding domain, and disease development is delayed in the absence of Hck. *J Virol.* 75: 9378-9392.
- 41) Vines, C.M., Potter, J.W., Geahlen, R.L., Costello, P.L., Tybulewicz, V.L., **Lowell, C.A.**, Chang, P.W., Gresham, H., Willman, C.L. (2001) Inhibition of $\alpha 2$ integrin receptor and Syk kinase signaling in monocytes by the Src family kinase Fgr. *Immunity* 15: 507-519.
- 42) Dan, Q., Sanchez, R., Delgado, C., Wepsic, H.T., Morgan, K., Chen, Y., Jeffes, E., **Lowell, C.A.**, Morgan, T.R., Jadus, M.R. (2001) Non-immunogenic murine hepatocellular carcinoma Hepa1-6 cells expressing the membrane form of macrophage colony stimulating factor are rejected *in vivo* and lead to CD8+ T-cell immunity against the parental tumor. *Molecular Therapy* 4: 427-437.
- 43) Majeed, M. Cavegion, E., **Lowell, C.A.**, Berton, G. (2001) Role of Src kinases and Syk in Fc receptor-mediated phagocytosis and phagosome-lysosome fusion *J. Leuk. Biol.* 70: 801-811.
- 44) Stafford, S., **Lowell, C.A.**, Sur, S., Alam, R. (2002) Lyn tyrosine kinase is important for IL-5-stimulated eosinophil differentiation. *J. Immunol.* 168: 1978-1983.
- 45) Cho, M.J., Pestina, T.I., Steward, S.A., **Lowell, C.A.**, Jackson, C.W., Gartner, T.K. (2002) Role of the Src-Family kinase Lyn in TxA₂ production, adenosine diphosphate secretion, Akt phosphorylation and irreversible aggregation in platelets stimulated with α -thrombin. *Blood* 99: 2442-2447.
- 46) Oberfell, A., Eto, K., Mócsai, A., Buensuceso, C., Moores, S.L., Brugge, J.S., **Lowell, C.A.**, Shattil, S.J. (2002) Coordinate interactions of Csk, Src, and Syk kinases with α IIb β 3 initiate integrin signaling to the cytoskeleton. *J. Cell Biol.* 157: 265-275.
- 47) Mócsai, A., Zhou, M., Meng, F., Tybulewicz, V.L., **Lowell, C.A.** (2002) Syk is required for integrin signaling in neutrophils. *Immunity* 16: 547-558.
- 48) Vicentini, L., Mazzi, P., Cavegion, E., Continolo, S., Fumagalli, L., Lapinet-Vera, J.A., **Lowell, C.A.**, Berton, G. (2002) Fgr deficiency results in defective eosinophil recruitment to the lung during allergic airway inflammation. *J Immunol.* 12: 6446-6454.
- 49) Zeng, M., Zhang, H., **Lowell, C.A.**, He, P. (2002) Tumor necrosis factor- α -induced leukocyte adhesion and microvessel permeability. *Am. J. Physiol. Heart Circ. Physiol.* 283: 2420-2430.
- 50) Abtahian F., Guerriero, A., Sebzda, E., Zhou, R., Mócsai, A., Myers, E.E., Jackson, D.G., Ferrari, V.A., Tybulewicz, V., **Lowell, C.A.**, Lepore, J.J., Koretzky, G.A., Kahn, M.L. (2003) Regulation of blood and lymphatic vascular separation by signaling proteins SLP-76 and Syk. *Science* 299: 247-251.
- 51) Mócsai, A., Zhang, H., Jakus, Z., Kitaura, J., Kawakami, T., **Lowell, C.A.** (2003) G-protein-coupled receptor signaling in Syk-deficient neutrophils and mast cells. *Blood* 101: 4155-4163.
- 52) Saijo, K., Schmedt, C., Su, I., Karasuyama, H., **Lowell, C.A.**, Reth, M., Adachi, T., Patke, A., Santana, A., Tarakhovsky, A. (2003) Essential role of Src-family protein tyrosine kinases in NF- κ B activation during B cell development. *Nature Immunol.*, 4:274-279.
- 53) Cavegion, E., Continolo, S., Pixley, F.J., Stanley, E.R., Bowtell, D.D., **Lowell, C.A.**, Berton, G. (2003)

Expression and tyrosine phosphorylation of Cbl regulates macrophage chemokinetic and chemotactic movement. *J Cell Physiol.* **195**:276-289.

- 54) Chen, H., Mócsai, A., Zhang, H., Ding, R.X., Morisaki, H., White, M., Rothfork, J.M., Heiser, P., Colucci-Guyon, E., **Lowell, C.A.**, Gresham, H.D., Allen, P.M., Brown, E.J. (2003) Role for plastin in host defense distinguishes integrin signaling from cell adhesion and spreading. *Immunity* **19**:95-104.
- 55) Pereira, S., **Lowell, C.A.** (2003) The Lyn tyrosine kinase negatively regulates neutrophil integrin signaling. *J. Immunol.* **171**:1319-1327.
- 56) Whyburn, L.R., Halcomb, K.E., Contreras, C.M., **Lowell, C.A.**, Witte, O.N., Satterthwaite, A.B. (2003) Reduced dosage of Bruton's tyrosine kinase uncouples B-cell hyperresponsiveness from autoimmunity in *lyn*^{-/-} mice. *J. Immunol.*, **171**:1850-1558.
- 57) Kitaura, J., Song, J., Tsai, M., Asai, K., Maeda-Yamamoto, M., Mocsai, A., Kawakami, Y., Liu, F.T., **Lowell, C.A.**, Barisas, B.G., Galli, S.J., Kawakami, T. (2003) Evidence that IgE molecules mediate a spectrum of effects on mast cell survival and activation via aggregation of the Fc RI. *Proc. Natl. Acad. Sci. (USA)* **100**: 12911-12916.
- 58) Hernandez-Hansen, V., Mackay, G.A., **Lowell, C.A.**, Wilson, B.S., Oliver, J.M. (2004) The Src kinase Lyn is a negative regulator of mast cell proliferation. *J. Leuk. Biol.* **75**:141-153.
- 59) Newbrough, S.A., Mócsai, A., Clemens, R.A., Wu, J.N., Silverman, M.A., Singer, A.L., **Lowell, C.A.**, Koretzky, G.A. (2003) SLP-76 regulates Fc receptor and integrin signaling in neutrophils. *Immunity* **19**:761-769
- 60) Scapini, P., Morini, M., Tecchio, C., Minghelli, S., Di Carlo, E., Tanghetti, E., Albin, A., **Lowell, C.A.**, Berton, G., Noonan, D.M., Cassatella, M.A. (2004) CXCL1/macrophage inflammatory protein-2-induced angiogenesis in vivo is mediated by neutrophil-derived vascular endothelial growth factor-A. *J. Immunol.* **172**:5034-5040.
- 61) Mócsai, A., Humphrey, M.B., Van Ziffle, J.A., Hu, Y., Burghardt, A., Spusta, S.C., Majumdar, S., Lanier, L.L., **Lowell, C.A.**, Nakamura, M.C. (2004) The immunomodulatory adapter proteins DAP12 and FcR γ -chain regulate development of functional osteoclasts through the Syk tyrosine kinase. *Proc. Natl. Acad. Sci. (USA)* **101**:6158-6163.
- 62) Hernandez-Hansen, V., Smith, A.J., Surviladze, Z., Chigaev, A., Mazel, T., Kalesnikoff, J., **Lowell, C.A.**, Krystal, G., Sklar, L.A., Wilson, B.S., Oliver, J.M. (2004) Dysregulated Fc RI signaling and altered Fyn and SHIP activities in Lyn-deficient mast cells. *J Immunol.* **173**:100-112.
- 63) Chou, W.H., Choi, D.S., Zhang, H., Mu, D., McMahon, T., Kharazia, V.N., **Lowell, C.A.**, Ferriero, D.M., Messing, R.O. (2004) Neutrophil protein kinase C as a mediator of stroke-reperfusion injury. *J. Clin. Invest.* **114**:49-56.
- 64) Jakus, Z., Berton, G., Ligeti, E., **Lowell, C.A.**, Mócsai, A. (2004) Responses of neutrophils to anti-integrin antibodies depends on costimulation through low affinity Fc Rs: full activation requires both integrin and non-integrin signals. *J. Immunol.*, **173**, 2068-2077.
- 65) Tassiulas, I., Hu, X., Ho, H., Kashyap, Y., Paik, P., Hu, Y., **Lowell, C.A.**, Ivashkiv LB. (2004) Amplification of IFN γ -induced STAT1 activation and inflammatory function by Syk and ITAM-containing adaptors. *Nature Immunol.* **5**,1181-1189.
- 66) Kitaura, J., Xiao, W., Maeda-Yamamoto, M., Kawakami, Y., **Lowell, C.A.**, Kawakami, T. (2004) Early divergence of Fc receptor I signals for receptor up-regulation and internalization from degranulation, cytokine production, and survival. *J Immunol.*, **173**, 4317-4323.
- 67) Pereira, S., Zhang, H., Takai, T., **Lowell, C.A.** (2004) The inhibitory receptor PIR-B negatively regulates neutrophil and macrophage integrin signaling. *J. Immunol.*, **173**, 5757-5765.
- 68) Continolo, S., Baruzzi, A., Majeed, M., Cavegion, E., Fumagalli, L., **Lowell, C.A.**, Berton, G. (2005) The proto-oncogene Fgr regulates cell migration and this requires its plasma membrane localization. *Exp Cell Res.* **302**:253-269.

- 69) Kitaura, J., Kinoshita, T., Matsumoto, M., Chung, S., Kawakami, Y., Leitges, M., Wu, D., **Lowell, C.A.**, Kawakami, T. (2005) IgE- and IgE/antigen-mediated mast cell migration in an autocrine/paracrine fashion. *Blood* 105: 3222-3229.
- 70) Lee, T.H., Wen, L., Montalvo, L., Esho, O., **Lowell, C.**, Reed, W., Busch, M.P. (2005) Minimal conditions of MHC compatibility and recipient immune compromise required to establish donor leukocyte persistence in a murine transfusion model. *Transfusion*, 45:301-314.
- 71) Zhang, H., Meng, F., Chu, C-L., Takai, T., **Lowell, C.A.** (2005) The Src-family kinases Hck and Fgr negatively regulate chemokine signaling in neutrophils and dendritic cells through the inhibitory receptor PIR-B. *Immunity*, 22:225-246.
- 72) Kitaura, J., Eto, K., Kinoshita, T., Kawakami, Y., Leitges, M., **Lowell, C.A.**, Kawakami, T. (2005) Regulation of highly cytokinergic IgE-induced mast cell adhesion by Src, Syk, Tec, and protein kinase C family kinases. *J Immunol.* 174:4495-4504
- 73) Hamerman, J.A., Tchao, N.K., **Lowell, C.A.**, Lanier, L.L. (2005) Enhanced Toll-like receptor responses in the absence of signaling adaptor DAP12. *Nature Immunol.* 6:579-586.
- 74) Underhill, D.M., Rossnagle, E., **Lowell, C.A.**, Simmons, R.M. (2005) Dectin-1 activates Syk tyrosine kinase in a dynamic subset of macrophages for reactive oxygen production. *Blood* 106:2543-2450.
- 75) Chu, C.L. and **Lowell, C.A.** (2005) The Lyn kinase differentially regulates dendritic cell generation and maturation. *J. Immunol.* 175:2880-2889.
- 76) Lee, J.Y., **Lowell, C.A.**, Lemay, D.G., Youn, H.S., Rhee, S.H., Sohn, K.H., Jang, B., Ye, J., Chung, J.H., Hwang, D.H. (2005) The regulation of the expression of inducible nitric oxide synthase by Src-family tyrosine kinases mediated through MyD88-independent signaling pathways of Toll-like receptor 4. *Biochem Pharmacol.* 70:1231-1240.
- 77) Xiao, W., Nishimoto, H., Hong, H., Kitaura, J., Nunomura, S., Maeda-Yamamoto, M., Kawakami, Y., **Lowell, C.A.**, Ra, C., Kawakami, T. (2005) Positive and negative regulation of mast cell activation by Lyn via the Fc RI. *J Immunol.* 175:6885-6892.
- 78) Hernandez-Hansen, V., Bard, J.D., Tarleton, C.A., Wilder, J.A., **Lowell, C.A.**, Wilson, B.S., Oliver, J.M. (2005) Increased expression of genes linked to Fc RI signaling and to cytokine and chemokine production in Lyn-deficient mast cells. *J. Immunol* 175:7880-7888.
- 79) Zhu, Q.S., Xia, L., Mills, G.B., **Lowell, C.A.**, Touw, I.P., Corey, S.J. (2006) G-CSF induced reactive oxygen species involves Lyn-PI 3-kinase-Akt and contributes to myeloid cell growth. *Blood* 107:1847-1856
- 80) Franceschi, L.D., Villa-Moruzzi, E., Biondani, A., Siciliano, A., Brugnara, C., Alper, S.L., **Lowell, C.A.**, Berton, G. (2006) Regulation of K-Cl cotransport by protein phosphatase-1 in mouse erythrocytes. *Pflügers Arch.* 451:760-768.
- 81) Sasanuma, H., Tatsuno, A., Hidano, S., Ohshima, K., Matsuzaki, Y., Hayashi, K., **Lowell, C.A.**, Kitamura, D., Goitsuka, R. (2006) Dual function for the adaptor MIST in IFN- γ production by NK and CD4+NKT cells regulated by the Src-kinase Fgr. *Blood* 107: 3647-3655.
- 82) Totani, L., Piccoli, A., Manarini, S., Federico, L., Pecce, R., Martelli, N., Cerletti, C., Piccardoni, P., **Lowell, C.A.**, Smyth, S.S., Berton, G., Evangelista, V. (2006) Src-family kinases mediate an outside-in signal necessary for α 2-integrins to achieve full activation and sustain firm adhesion of polymorphonuclear leukocytes tethered on E-selectin. *Biochem J.* 396:89-98.
- 83) Yu, M., **Lowell, C.A.**, Neel, B.G., Gu, H. (2006) Scaffolding adapter Grb2-associated binder 2 requires Syk to transmit signals from Fc RI. *J. Immunol.* 176:2421-2429.
- 84) Soriani, A., Moran, B., deVirgilio, M., Kawakami, T., Altman, A., **Lowell, C.**, Eto, K., Shattil, S.J. (2006) A role for PKC in outside-in signaling. *J. Thromb. Haemostasis* 4:648-6455.
- 85) Karur, V.G., **Lowell, C.A.**, Besmer, P., Agosti, V., Wojchowski, D.M. (2006) Lyn kinase promotes erythroblast expansion and late-stage development. *Blood.* 108:1524-1532.

- 86) Looney, M.R., Su, X., Van Ziffle, J.A., **Lowell, C.A.**, Matthay, M.A. (2006) Neutrophils and their Fc receptors are essential in a mouse model of transfusion-related acute lung injury. *J Clin Invest.* 116:1615-1623.
- 87) Mermel, C.H., McLemore, M.L., Liu, F., Pereira, S., Woloszynek, J., **Lowell, C. A.**, Link, D.C. (2006) Src-family kinases are important negative regulators of G-CSF dependent granulopoiesis. *Blood* 2006 Jun 13 [Epub ahead of print].
- 88) Giagulli, C., Ottoboni, L., Cavegion, E., Rossi, B., **Lowell, C.**, Constantin, G., Laudanna, C., Berton, G. (2006) The Src family kinases Hck and Fgr are dispensable for inside-out, chemoattractant-induced signaling regulating $\alpha 2$ integrin affinity and valency in neutrophils, but are required for $\alpha 2$ integrin-mediated outside-in signaling involved in sustained adhesion. *J Immunol.* 177:604-611.
- 89) Hirahashi, J., Mekala, D., Van Ziffle, J., Xiao, L., Saffaripour, S., Wagner, D.D., Shapiro, S.D., **Lowell, C.**, Mayadas, T.N. (2006) Mac-1 signaling via Src-Family and Syk kinases results in elastase-dependent thrombohemorrhagic vasculopathy. *Immunity.* 25: 271-283.
- 90) *Zhang, H., Ulrich, S.Y., Green, C.E., Chen, H., Saranto, M.R., Hu, Y., Wara, D., Simon, S.I., **Lowell, C.A.** (2006) Impaired integrin-dependent function in Wiskott-Aldrich Syndrome Protein-deficient murine and human neutrophils. *Immunity.* 25: 285-295.
* Selected for cover issue and mini-review.
- 91) Mócsai, A., Abram, C.L., Jakus, Z., Hu., Y., Lanier, L.L, **Lowell, C.A.**, (2006) Integrin signaling in neutrophils and macrophages uses adaptors containing immunoreceptor tyrosine-based activation motifs. *Nature Immunol.* 7, *in press*

Review Articles (Peer Reviewed):

- 92) Varmus, H.E., **Lowell, C.A.** (1994). Cancer genes and hematopoiesis. *Blood* 83: 5 - 9.
- 93) Berton, G., Yan, S.R., Fumagalli, L., **Lowell, C.A.** (1996) Neutrophil activation by adhesion: mechanisms and pathophysiological implications. *Int. J. Clin. and Lab. Res.* 26: 160-177.
- 94) **Lowell, C.A.**, Soriano, P. (1996). Knockouts of Src-family kinases: stiff Bones, wimpy T-cells and bad Memories. *Genes and Development.*, 10: 1845-1857.
- 95) DeFranco, A.L., Chan, V., **Lowell, C.A.** (1998) Positive and negative roles of the tyrosine kinase Lyn in B-cell function. *Semin. Immunol.*, 10, 299-308.
- 96) Berton, G., **Lowell, C.A.** (1999) Integrin signaling in neutrophils and macrophages. *J. Cell Signaling*, 11: 621-635.
- 97) **Lowell, C.A.** Berton, G. (1999) Integrin signal transduction in myeloid leukocytes. *J. Leukocyte Biology*, 65: 313-320.
- 98) **Lowell, C.A.** (2004) Src-family kinases: Rheostats of immune cell signaling. *Mol. Immunol.*, 41: 631-643.
- 99) Berton, G., Mocsai, A., **Lowell, C.A.** (2005) Src kinases and Syk: key regulators of phagocytic cell activation. *Trends Immunol.*, 26, 208-214.
- 100) **Lowell, C.A.** (2006) Beautiful blistering *Blood* 107: 849-850.
- 101) **Lowell, C.A.** (2006) Rewiring phagocytic signal transduction. *Immunity* 24: 243-245.

Book Chapters:

Lowell, C.A. (1997) "Formation of Immune Effector Cells" Chapter 1 in Medical Immunology, 9th edition. Stites, Terr and Parslow, Eds. Lange Medical Books, Norwalk, CT.

Lowell, C.A. (2001) Chapters 1, 14, 15, 19 in Medical Immunology, 10th edition. Parslow, Stites, Terr, and Imboden, Eds. Lange Medical Books/McGraw-Hill Medical Publishing, New York, NY

Significant Recent Publications:

*Zhang, H., Ulrich, S.Y., Green, C.E., Chen, H., Saranto, M.R., Hu, Y., Wara, D., Simon, S.I., **Lowell, C.A.** (2006) Impaired integrin-dependent function in Wiskott-Aldrich Syndrome Protein-deficient murine and human neutrophils. *Immunity*. 25: 285-295.

* Selected for cover issue and mini-review.

Responsible for the oversight of the post-doc conducting this work, for the vast majority of writing and editing of the manuscript. Wrote the initial grants that funded this work.

Zhang, H., Meng, F., Chu, C-L., Takai, T., **Lowell, C.A.** (2005) The Src-family kinases Hck and Fgr negatively regulate chemokine signaling in neutrophils and dendritic cells through the inhibitory receptor PIR-B. *Immunity*, 22:225-246.

Responsible for the oversight of the post-doc conducting this work, for the vast majority of writing and editing of the manuscript. Wrote the initial grants that funded this work.

Mócsai, A., Humphrey, M.B., Van Ziffle, J.A., Hu, Y., Burghardt, A., Spusta, S.C., Majumdar, S., Lanier, L.L., **Lowell, C.A.**, Nakamura, M.C. (2004) The immunomodulatory adapter proteins DAP12 and FcR γ -chain regulate development of functional osteoclasts through the Syk tyrosine kinase. *Proc. Natl. Acad. Sci. (USA)* 101:6158-6163.

Responsible for the joint oversight of the post-docs conducting this work. The majority of the work was done in our laboratory, with expert help from our collaborators (Humphrey/Nakamura). Responsible for all editing of the manuscript. Wrote the initial grants that funded the project. This project represented an extension into a new area (osteoclast biology) for our group.

Mócsai, A., Zhang, H., Jakus, Z., Kitaura, J., Kawakami, T., **Lowell, C.A.** (2003) G-protein-coupled receptor signaling in Syk-deficient neutrophils and mast cells. *Blood* 101: 4155-4163.

Responsible for the oversight of the post-docs conducting this work, for helping with initial drafts and all editing of the manuscript. Wrote the initial grants that funded this work.

Mócsai, A., Zhou, M., Meng, F., Tybulewicz, V.L., **Lowell, C.A.** (2002) Syk is required for integrin signaling in neutrophils. *Immunity* 16: 547-558.

Responsible for the oversight of the post-docs conducting this work, for helping with initial drafts and all editing of the manuscript. Wrote the initial grants that funded this work.

Research Program

Genetic Analysis of Signal Transduction in Hematopoietic Cells

My research group studies the role of cytoplasmic tyrosine kinases in signal transduction pathways within hematopoietic cells. We have focused on the Src-family kinases; in particular the Hck, Fgr and Lyn kinases, which are found in myeloid leukocytes and B-lymphocytes. Like all Src-family kinases, these proteins play critical roles in transducing signals from cell surface receptors to intracellular targets. Most recently, we have also begun to focus on the Syk tyrosine kinase, which operates in similar signaling pathways as the Src-family kinases. The diversity of signaling pathways in which these kinases have been implicated is very large, ranging from responses to innate immune stimuli (bacterial/viral products) to regulation of proliferative responses to cytokines or growth factors.

We have taken a genetic approach to study these kinases by generating mutant mice (using embryonic stem cell technology) that lack Hck, Fgr, and Lyn or using Syk-deficient animals generated by V. Tybulewicz (Cambridge, UK). Single mutant mice are interbred to generate double mutant or triple mutant mice, allowing us to address issues of redundancy of function. Mutant animals and primary cell cultures derived from the mice are then studied to determine which signaling pathways are affected. Our major finding has been that these kinases function in signaling pathways initiated by integrin-mediated cell adhesion. Integrins are heterodimeric cell surface proteins that mediate attachment of all cells to extracellular matrix protein (i.e., collagen, fibrinogen or fibronectin) coated surfaces. Integrin-dependent adhesion induces an intracellular signaling cascade leading to formation of focal contacts, cytoskeletal rearrangements and cell spreading. In leukocytes, these signaling pathways contribute to immune activation – neutrophils undergo respiratory burst and degranulation while lymphocytes proliferate and secrete cytokines or antibodies. Using *hck^{-/-}fgr^{-/-}* double mutant or *hck^{-/-}fgr^{-/-}lyn^{-/-}* triple mutant animals, we have found that integrin-dependent signaling responses are impaired in myeloid leukocytes lacking these kinases. The defective integrin signaling responses in *hck^{-/-}fgr^{-/-}* macrophages results in a dysformed cytoskeletal structure and poor cell motility. Biochemical analysis indicates that the kinases operate in a signaling pathway involving the Cbl adapter protein. We have also found that the Syk tyrosine kinase operates in this pathway, as deficiency of Syk completely impairs neutrophil integrin-mediated activation. Defects in these integrin signaling pathways also lead to impairments in osteoclast function in *syk^{-/-}* mice.

Deficiency of the Lyn tyrosine kinase has a paradoxical effect on B-lymphocyte function, in that *lyn^{-/-}* B-cells are hyper-reactive to antigenic stimulation *in vitro* and produce excessive levels of immunoglobulin *in vivo* leading to autoimmunity. This unanticipated finding was explained when we found that Lyn operates in a signaling pathway that normally down-modulates lymphocyte immune responses by activating tyrosine phosphatases which dampen intracellular signaling. Recent work suggests that Lyn performs a similar function in myeloid cells as well. This pathway involves the inhibitory receptor PIR-B, which is a natural substrate of the Lyn kinase. When Lyn phosphorylates PIR-B, this results in recruitment of tyrosine phosphatases that down modulate integrin and lymphocyte antigen signaling.

Future projects will include determination of how Syk and other intracellular molecules contribute to integrin signaling, with goal of learning exactly how these pathways lead to leukocyte activation. We are also studying the relative contribution of activating versus inhibitory signaling responses to immune cell function, especially with respect to leukocyte chemokine signaling responses. Ultimately, these studies will provide a better molecular understanding of leukocyte signal transduction, with the hope that therapeutic manipulation of these pathways can be achieved for the treatment of inflammatory, autoimmune and malignant disease.

RESEARCH AWARDS AND GRANTS

ACTIVE

NIH: Specialized Clinical Center for Research in Transfusion Biology, P50 HL081027-01
P.I. Pearl Toy, M.D., Department of Laboratory Medicine
C. Lowell – Project Leader: "Leukocyte Mediated Acute Lung Injury."
C. Lowell – Core B Leader: "Neutrophil Function Assays for Clinical Testing"
\$236,000/yr (direct costs for Dr. Lowell's project); \$115,000/yr (direct costs, Core B)
11/1/05 - 10/31/10

NIH: "Signaling by Cytoplasmic Tyrosine Kinases in Leukocytes" RO1 AI068150-06
P.I. Clifford Lowell, M.D.-Ph.D
\$200,000/yr 5/1/06 – 4/30/11

NIH: "Mechanisms of Leukocyte Integrin Signaling" RO1 AI065049-01
P.I. Clifford Lowell, M.D.-Ph.D
\$250,000/yr 7/1/05 – 6/30/10

NIH: "Proximal Signaling Events in Leukocyte Integrin Function" RO3 TW006831-02
P.I. Clifford Lowell, M.D.-Ph.D
\$35,000/yr 7/1/04 – 6/30/07

Leukemia/Lymphoma Society Scholar Award in Basic Research
P.I. Clifford Lowell, M.D.-Ph.D.
\$100,000/yr 7/1/01 – 6/30/06

American Society of Hematology Scholar Award: \$60,000/yr 7/1/97 - 6/30/99 (funds still active)

TRAINING GRANTS

NIH: "Basic Research in Hematology and Oncology" T32 DK007636-21
P.I. Y.W. Kan., Department of Laboratory Medicine
NIH: "Molecular and Cellular Immunology" T32 AI07334-15
P.I. Tony DeFranco, Department of Microbiology/Immunology
NIH: "Molecular Analysis of Tumor Viruses" T32 CA009043-29
P.I. J. Michael Bishop, Department of Microbiology/Immunology

Dr. Lowell is listed as a co-investigator on the above training grants and has had post-docs sponsored by each.

EXPIRED

U.S. Army Medical Research Branch 7/1/02 – 6/30/05 \$75,000/yr
NIH: SCOR Project, Transfusion Medicine P50 HL054476-10 P.I. Pearl Toy
Project #3 (C. Lowell), 1/1/96 – 12/31/05. \$216,000/yr.
Sandler Award Basic Science – 4/1/00 – 3/31/01 \$50,000
Stewart Family Trust Award – 7/1/00 – 6/30/01 \$37,500
Leukemia Research Foundation – 7/1/00 – 6/30/01 \$50,000
NIH: Program Project Grant, Mouse Models to Investigate the Hematologic System PO1 DK 50267-05
P.I. Y.W. Kan Project #3 (C. Lowell), 8/1/95 - 7/31/00. \$150,000/yr.
Howard Hughes Medical Institute Research Resources Program – 1996
Laboratory Renovations for Junior Faculty. \$100,000

UCSF Program in Biological Sciences -- 1996 \$50,000

UCSF Academic Senate/REAC programs -- 1997 \$50,000