

# *Infectious Diseases*

**Fred R. Sattler, M.D.**  
Professor and Chief

**Erika Anaya**  
Division Administrator

**Luis Mendez**  
Research Program and Budget Manager

# Infectious Diseases

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The Division of Infectious Diseases aims to 1) advance the frontier of medical science through clinical and translational research in infectious diseases, 2) promote excellence in the education of medical students, house officers and clinical fellows, and 3) deliver compassionate, evidence-based, state-of-the-art care to a large, diverse, multicultural community of Southern California.

## OVERVIEW OF ACHIEVEMENTS

**Research:** The Division continues to provide scientific leadership in a wide range of research. The Division maintains consistent funding for ongoing investigations relating to both HIV and other areas of infectious diseases. The Division has had an important and productive role in large, multicenter collaborative research groups that emphasize development of treatment and prevention modalities for HIV infection and complications associated with antiretroviral therapy and the underlying disease.

Our NIH-supported AIDS Clinical Trials Unit (CTU Fred R. Sattler, M.D., Principal Investigator) is a major focus of research in the Division. The CTU received a notice of grant award in June 2007 that it would be fully funded for an additional seven years. The USC CTU has been one of the most productive units in the United States over the past two decades. During this 22-year span, the CTU has performed at a very high level and has been second in enrollment of total research subjects in AIDS Clinical Trial Group (ACTG) studies and is the leading site in the continental U.S. for enrolling minorities. Moreover, key personnel on the grant at USC hold a number of important scientific and administrative leadership positions in the ACTG, including the Executive Committee (Dr. Fred Sattler), Optimization of Antiretroviral Therapies (Dr. Michael Dube), Translational Research and Drug Development (TRADD) Committee (Dr. Stan Louie, School of Pharmacy) and the Underrepresented Populations Committee (Dr. Alejandro Sanchez). In addition, Dr. Robert Larsen is co-chair of a large international study of Cryptococcal meningitis. These key positions have enabled faculty from our Division to contribute to and facilitate the scientific agenda and productivity of this world-leading HIV collaborative treatment group.

The Division remains an active member of the California Collaborative Treatment Group (CCTG), which is in its 22nd year and is funded by the State of California University-Wide AIDS Program with monetary backing from the California State Legislature. Dr. Larsen continues to provide a leading role for USC in this effort and is Principal Investigator for the USC site.

Dr. Larsen is the Principal Investigator for an NIH investigator-initiated grant to test novel methods to determine the susceptibility of *Cryptococcus neoformans* to antifungal drugs alone and in combination.

Under the principal leadership of Dr. Brenda Jones, USC has been a leading performance site in the Centers for Disease Control and Prevention-funded multicenter collaborations studying therapeutics and prevention of tuberculosis (Tuberculosis Trials Consortium). Dr. Jones also received a 5-year NIH subcontract with the University of California San Diego through October 2008 to establish a National TB Curriculum Center.

Dr. Anne Anglim has served as the local Principal Investigator of the GeoSentinel Global Surveillance Network sponsored by the CDC and the International Society of Tropical Medicine to determine surveillance and to track emerging patterns (prevalence and incidence) of important microbial pathogens acquired by travelers. GeoSentinel is constituted by an international network of 41 (16 in the U.S.) travel and tropical medicine clinics (one of which is located at USC) to detect geographic and temporal trends in infectious complications and other morbidities in travelers, immigrants and refugees. She works with other faculty and clinical fellows in the ID Division to provide regular reports of sentinel infections amongst these populations at LAC+USC Medical Center and USC University Hospital.

Finally, Dr. Sattler is Principal Investigator of a National Institute of Aging multicenter clinical and translational investigation to assess the effects of the hypothalamic-pituitary gonadal and hypothalamic-pituitary-IGF-1 axes in regulating muscle protein synthesis and breakdown in older persons at risk for sarcopenia and frailty. This study is funded by the National Institute of Aging and deemed by a panel reporting to the Institute of Medicine as one of five important national studies that will provide the basis and financial justification for the conduct of a large multicenter study (under Dr. Sattler's guidance USC will participate in the planned study) to determine the safety of testosterone replacement therapy for prostate and cardiovascular health in older men.

These faculty and others also conduct additional investigator-initiated mechanistic and clinical research outside the structure of these multicenter trials and are funded by the NIH and other peer-reviewed funding agencies.

## MAJOR PATIENT CARE SERVICE RESPONSIBILITIES

**Rand Schrader HIV Clinic:** The Infectious Diseases Division maintains responsibility for the medical operations of the Rand Schrader HIV Clinic, operated under the auspices of the Los Angeles County-University of Southern California (LAC+USC) Medical Center. Dr. Joseph Cadden serves as the Medical Director of the Clinic and is responsible for the day-to-day operations of the Clinic in consultation with Dr. Sattler. This modern free-standing, 3-story, 33,000-square-foot facility is dedicated to the comprehensive care of persons infected with HIV and features faculty physicians from the Division and other specialties in the Department of Medicine as well as other departments who serve as consultants to provide specialty care, primary care providers, supervisors of physician extenders, and attending physicians for interns, residents, and fellows. Approximately 50 USC faculty members work in the clinic each week to provide comprehensive state-of-the-art care for patients afflicted with HIV.

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Patients are referred to the Rand Schrader HIV Clinic from the LAC+USC Medical Center, as well as from outside clinics, agencies and providers. The Clinic is open for morning and afternoon sessions Monday through Friday, with an additional Tuesday evening session, and reports approximately 3,000 monthly patient visits. This Clinic serves as a critical conduit with the Los Angeles County Department of Health for tracking patients also infected with tuberculosis.

In addition to HIV-AIDS primary care, the outpatient Infectious Diseases Referral Clinic holds a morning session each week in the Rand Schrader Clinic Building. Infectious Diseases faculty and fellows, as well as internal medicine housestaff and medical students rotating on the Infectious Diseases Consult Service, staff this clinic each week.

**Hospital Infection Control:** Dr. Paul Holtom serves as the Hospital Epidemiologist of LAC+USC Medical Center, USC/Norris Cancer Hospital, and USC University Hospital. He also chairs the respective infection control committees at those facilities.

## Faculty

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<b>Anne M. Anglim, M.D.</b>	Assistant Professor of Clinical Medicine
<b>Joseph J. Cadden, M.D.</b>	Assistant Professor of Clinical Medicine Medical Director, Rand Schrader HIV Clinic
<b>P. Jan Geiseler, M.D.</b>	Associate Professor of Clinical Medicine
<b>Paul D. Holtom, M.D.</b>	Associate Professor of Clinical Medicine and Orthopedics Director, Jeanette Wilkins Memorial Microbiology Laboratory
<b>Brenda E. Jones, M.D.</b>	Associate Professor of Clinical Medicine
<b>Jens J. Kort, M.D., Ph.D.</b>	Associate Professor of Clinical Medicine Associate Medical Director, Rand Schrader HIV Clinic
<b>Robert A. Larsen, M.D.</b>	Associate Professor of Medicine Vice Chair, USC Institutional Review Board Research Subject Advocate, USC General Clinical Research Center (GCRC)
<b>In Memory of: John Leedom, M.D. 1933-2008</b>	Emeritus Professor of Medicine
<b>James Mosley, M.D.</b>	Emeritus Professor of Medicine
<b>Fred R. Sattler, M.D.</b>	Professor of Medicine and Biokinesiology Chief, Division of Infectious Diseases Senior Associate Dean of Faculty Affairs, Keck School of Medicine Associate Program Director, GCRC

### NEW FACULTY

<b>Michael P. Dube, M.D</b>	Professor of Clinical Medicine
<b>Alejandro Sanchez, M.D</b>	Assistant Professor of Clinical Medicine

## Faculty Honors

### MEMBERSHIP IN DISTINGUISHED SOCIETIES

**Paul D. Holtom, M.D.**

Alpha Omega Alpha

**Brenda E. Jones, M.D.**

Western Society for Clinical Investigation

**John M. Leedom, M.D.**

Alpha Omega Alpha

Western Association of Physicians

Western Society for Clinical Investigation

**Fred R. Sattler, M.D.**

Western Society for Clinical Investigation, Counselor

### MEMBERSHIP IN PROFESSIONAL SOCIETIES

**Anne M. Anglim, M.D., M.S.**

American College of Physicians

American Medical Association

American Society for Microbiology

American Society for Tropical Medicine and Hygiene

Infectious Diseases Society of America

Society for Healthcare Epidemiology of America

Wilderness Medical Society

**Joseph J. Cadden, M.D.**

American Academy of HIV Medicine

American Medical Association

**Michael P. Dubé, M.D.**

American College of Physicians

American Society for Microbiology

Infectious Diseases Society of America

**P. Jan Geiseler, M.D.**

American College of Physicians

American Federation for Clinical Research

American Society for Microbiology

Infectious Diseases Society of America

**Paul D. Holtom, M.D.**

American College of Physicians

American Society for Microbiology

American Society of Tropical Medicine and Hygiene

Gold Humanism Honor Society

Infectious Diseases Society of America

Musculoskeletal Infection Society

Society for Healthcare Epidemiology of America

**Brenda E. Jones, M.D.**

American Lung Association

American Thoracic Society

**Jens J. Kort, M.D., Ph.D.**

American Association of Immunologists

American Society for Microbiology

Infectious Diseases Society of America

Society for Neuroscience

**Robert A. Larsen, M.D.**

American Society of Microbiology

Infectious Diseases Society of America

**Alejandro Sanchez, M.D.**

American Academy of HIV Medicine

American College of Physicians

American Society for Tropical Medicine and Hygiene

California Latino Medical Association

Infectious Diseases Society of America

**Fred R. Sattler, M.D.**

American College of Physicians

American College of Sports Medicine

American Federation for Medical Research

American Physiological Society

American Society of Microbiology

Endocrine Society

Infectious Diseases Society of America

### INVITED LECTURES

**Anne M. Anglim, M.D.**

New strategies in the diagnosis and treatment of elusive pathogens.

Grand Rounds, Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, CA, 10/26/2007.

Evaluation of fever in the returning traveler. Grand Rounds, Department of Medicine, Loma Linda University, Loma Linda, CA, 1/23/2008.

**Michael P. Dubé, M.D.**

Management strategies for the dysmorphic complications of HIV.

USA HIV Update Course, International AIDS Society, Chicago, IL, 5/19/2008.

**Fred R. Sattler, M.D.**

Hormonal regulators of muscle and metabolism in aging (HORMA) study. Body Composition and Muscle Performance Outcomes, Experimental Biology, San Diego, CA, 4/9/2008.

Pathogenesis and treatment of lipodystrophy: what physicians need to know. USA Continuing Medical Education Course, International AIDS Society, Washington, D.C., 5/2008.

### EDITORSHIPS/EDITORIAL BOARDS

**Anne M. Anglim, M.D.**

Current Opinion in Organ Transplantation, Infectious Diseases  
Special Issue, Guest Editor

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**OFFICES/COMMITTEE MEMBERSHIPS HELD IN  
NATIONAL/REGIONAL PROFESSIONAL & OTHER  
SOCIETIES**

**Michael P. Dubé, M.D.**

American Heart Association and American Academy of HIV  
Medicine Initiative to Decrease Cardiovascular Risk and  
Increase Quality of Care for Patients Living with HIV/  
AIDS Writing Group, Chair

**Paul D. Holtom, M.D.**

American Academy of Orthopaedic Surgeons  
Infections Committee, Consultant  
United States Pharmacopeia  
Infectious Diseases Expert Committee  
USC Keck School of Medicine Representative

**Brenda E. Jones, M.D.**

American Lung Association  
Tuberculosis Control Technical Advisory Group  
Barlow Respiratory Research Center  
Board of Directors  
Los Angeles Tuberculosis Control and Elimination  
Professional Advisory Council

**Alejandro Sanchez, M.D.**

Office of AIDS Programs and Policy, Los Angeles County  
Standards of Care Committee

**Fred R. Sattler, M.D.**

Western Society for Clinical Investigation, Counselor

**NATIONAL INSTITUTES OF HEALTH STUDY SECTIONS/  
NOTEWORTHY GOVERNMENT ACTIVITIES**

**Michael P. Dubé, M.D.**

National Institutes of Health  
National Institute of Allergy and Infectious Diseases, AIDS  
Division  
AIDS Clinical Trials Group  
Optimization of Antiretroviral Therapy  
Committee

**Jens J. Kort, M.D., Ph.D.**

National Institutes of Health  
National Institute of Allergy and Infectious Diseases, AIDS  
Division  
Adult AIDS Clinical Trials Group  
Entry Inhibitor Study Team, Vice-Chair

**Robert Larsen, M.D.**

National Institutes of Health  
National Institute of Allergy and Infectious Diseases, AIDS  
Division  
AIDS Clinical Trials Group  
A5241 Protocol Team, Co-Chair

**Fred R. Sattler, M.D.**

Department of Defense and Veterans Association Study Sections  
Ad Hoc Member  
Food and Drug Administration  
Anti-Infective Committee, Ad Hoc Consultant  
National Institutes of Health  
General Clinical Research Centers Program Branch,  
Site Visitor  
National Center for Research Resources, Ad Hoc Member  
National Institute of Allergy and Infectious Diseases,  
AIDS Division  
Adult AIDS Clinical Trials Group  
Executive Committee  
A5241 Protocol Team

**Alejandro Sanchez, M.D.**

National Institutes of Health  
National Institute of Allergy and Infectious Diseases, AIDS  
Division  
AIDS Clinical Trials Group  
Under-Represented Populations Committee

**SPECIAL/INTERNATIONAL ACTIVITIES**

**Anne M. Anglim, M.D.**

International Society for Travel Medicine

**Joseph J. Cadden, M.D.**

International AIDS Society

**Brenda E. Jones, M.D.**

International Union Against Tuberculosis and Lung Disease

**Alejandro Sanchez, M.D.**

International AIDS Society  
International Society of Infectious Diseases

**AWARDS/HONORS**

**Paul D. Holtom, M.D.**

Arnold P. Gold Foundation  
Leonard Tow Humanism in Medicine Award

**SERVICE ON UNIVERSITY, SCHOOL, HOSPITAL  
AND DEPARTMENTAL COMMITTEES**

**Anne M. Anglim, M.D.**

USC University Hospital  
Lung Transplantation Evaluation Committee  
USC University Hospital/Norris Cancer Center  
Infection Control Committee  
Pharmacy and Therapeutics Committee  
Department of Medicine  
Practice and Operations Development Committee

**Michael P. Dubé, M.D.**

Keck School of Medicine  
General Clinical Research Center, Research Subject  
Advocate

# Infectious Diseases

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**P. Jan Geiseler, M.D.**

USC University Hospital  
Infection Control Committee, Chairman

**Paul D. Holtom, M.D.**

Association of Physicians of Los Angeles County Hospital  
Board of Directors  
LAC+USC Medical Center  
Comprehensive Antimicrobial Utilization Subcommittee,  
Co-Chair  
Infection Control Committee, Secretary  
Medical Executive Committee  
Pharmacy and Therapeutics Committee, Chair  
USC/Norris Comprehensive Cancer Hospital  
Infection Control Committee, Chair  
Pharmacy and Therapeutics Committee  
USC University Hospital  
Antibiotic Usage Subcommittee, Chair  
Infection Control Committee  
Pharmacy and Therapeutics Committee

**Brenda E. Jones, M.D.**

Department of Medicine  
Education Committee  
Keck School of Medicine  
Curriculum Revision (Respiratory Section)  
Infectious Diseases Education Officer  
General Clinical Research Center  
Local Advisory Committee  
Institutional Review Board

**Jens J. Kort, M.D., Ph.D.**

Keck School of Medicine  
General Clinical Research Center, Advisor

**Robert A. Larsen, M.D.**

Department of Medicine  
Resident Selection Committee  
Keck School of Medicine  
General Clinical Research Center, Research Subject  
Advocate  
LAC+USC Medical Center  
Institutional Review Board, Vice Chair

**Alejandro Sanchez, M.D.**

General Clinical Research Center  
Local Advisory Committee  
LAC+USC Medical Center  
Quality Assurance and Quality Improvement Committee,  
Chair  
Keck School of Medicine  
Admissions Committee

**Fred R. Sattler, M.D.**

Department of Medicine  
Research Advisory Committee  
Keck School of Medicine  
Graduate Student Ph.D. Committees  
LAC+USC Medical Center  
Comprehensive Antimicrobial Utilization Subcommittee

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## Clinical Activities

The Division of Infectious Diseases (ID) provides care and consultation in all the major venues served by the Department of Medicine.

**LAC+USC Medical Center:** The Division continues to provide a very active consultation service, seeing approximately 2,000 new consultations each year. These patients are followed in the hospital seven days per week and in the Rand Schrader Clinic when appropriate. The Division is also responsible for the medical operations of the Rand Schrader HIV Clinic. The AIDS Clinic features our faculty as primary care providers and supervisors of physician assistants, and as attending physicians for interns, residents and fellows. Currently, there are 2,800-3,100 HIV seropositive patients who receive their primary care in the Clinic. Finally, we also operate an outpatient Infectious Diseases Clinic weekly, which is staffed by our faculty, fellows and residents. The Infectious Diseases Clinic records approximately 800 visits annually.

**USC/Norris Comprehensive Cancer Center and USC University Hospital (UH):** Because of the complexity of cases seen at these two hospitals, Drs. Geiseler, Anglim, Cadden, and Holtom frequently follow sizable case loads at the same time, including consultative inpatient (both teaching and private services) and outpatient services, which include a new home intravenous antibiotic program. Each month one of the ID fellows works with one of the attendings on the USC UH Teaching Service. There are approximately 600-800 new patient consultations per year at those institutions. Dr. Peter Sim, a former graduate of the USC ID Training Program and Clinical Assistant Professor of Medicine, attends at Norris and USC University hospitals and provides weekend coverage with the ID fellows at these facilities.

**Healthcare Consultation Center II (HCC II):** Drs. Anglim, Cadden, Geiseler, and Holtom have regularly scheduled weekly clinic sessions for infectious diseases patients at HCC II. These clinics generate more than 300 visits per year. Dr. Holtom also continues to work in the Orthopedic Clinic with Dr. Patzakis and other orthopedic surgeons, seeing patients with chronic osteomyelitis and prosthetic joint infections in consultation or after discharge from USC UH. During FY07, Dr. Sattler and members of the Division began planning for a daily Travel Medicine Clinic for outgoing persons in need of prophylaxis and immunizations and for returning travelers with new signs and symptoms.

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## SERVICE AND ADMINISTRATION

The Division of Infectious Diseases staffs the HIV (Rand Schrader, 5P21) Clinic at LAC+USC Medical Center. The Clinic is open for morning and afternoon sessions Monday through Friday, as well as a Tuesday evening session, where approximately 40,000-50,000 patient visits occur each year. Dr. Cadden serves as Medical Director of the Clinic. Members of the Division also supervise fellows in their weekly HIV continuity and research clinics, mentor medical residents and physician assistant students rotating through the Clinic, and attend a weekly Infectious Diseases Clinic held in 5P21, which is coordinated by Dr. Larsen for patients with and without HIV. Dr. Larsen also serves as Vice Chair of the USC Institutional Review Board and as the Research Subject Advocate for the USC GCRC.

Dr. Fred Sattler, Chief of Infectious Diseases, completed his service as Senior Associate Dean for Faculty Affairs for the Keck School of Medicine on December 31, 2007, but continues as Associate Program Director for the USC General Clinical Research Center in LAC+USC Medical Center. Dr. Sattler was appointed by the Vice Provost for Research to serve as Director of the Center for Human Studies in the new Clinical and Translational Science Institute.

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## Educational Activities

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### CLINICAL FELLOWS

#### **FIRST YEAR**

James Kim, M.D.  
Mario Perez, D.O.

#### **SECOND YEAR**

Chris Miller, M.D.  
Eddy Sattah, M.D.

### TEACHING AND EDUCATION

**Clinical Training:** Faculty of the Division are heavily involved in the education of physician assistants, students, residents and clinical fellows. Four clinical fellows in Infectious Diseases receive clinical training in a two-year ACGME-accredited training program on the inpatient services at the LAC+USC Medical Center, USC/Norris Comprehensive Cancer Center and Hospital, and USC University Hospital, and for outpatient care in HCC II and the Rand Schrader HIV Clinic. In addition, faculty of the Division mentor and supervise three to four house officers (PGL 2 and 3 residents) and two to three USC and occasionally external medical students per month on the Infectious Diseases consultation services. In the Rand Schrader HIV Clinic, the faculty, in association with members of the Department of Family Medicine, operate an educational program (Pacific AIDS Educational Training Center grant) sponsored by HRSA for community physicians, physician assistants, nurse practitioners and nurses involved in the primary care of patients with HIV. Faculty of the Division also participate in the Keck School of Medicine annual postgraduate education program.

**Conferences:** A number of didactic and interactive conferences are provided each week and are facilitated by Infectious Diseases faculty. Clinical fellows also present cases, discuss journal articles and provide disease overviews at a number of the conferences. Student and resident trainees rotating on the LAC+USC Medical Center consult service also attend these conferences.

**Infectious Diseases Core Curriculum Lecture Series** is held weekly (Monday mornings 8:00-9:00) and is a vital component of the didactic portion of the total educational program. This series covers a large number of distinct and important topics over a 2-year cycle, encompassing the essential principles for the practice of infectious diseases. These lectures are generally given by the Infectious Diseases faculty. Each fellow is expected to give two lectures per year, which are facilitated by the Infectious Diseases faculty. The lectures also serve as a platform for hypotheses that may provide the underpinning for fellow and faculty investigations that expand the knowledge base in this ever-changing specialty.

The weekly **Infectious Diseases Case Conference** is held on Wednesday mornings from 8:30-9:30 and consists of the presentation of two clinical cases each week (usually one from the LAC+USC Medical Center Consult Service and one from the USC University Hospital Teaching Service), each selected by the fellows on the respective consultation services. The fellow may present the case or assign this learning experience to an internal medicine resident or medical student. The Pediatric Infectious Diseases Service selects at least one case per month for presentation at the Conference. The format consists of the case presentation, followed by a discussion of diagnostic and therapeutic issues by another fellow, selected by virtue of his or her unfamiliarity with the case. This lively conference usually has 30-40 attendees, including USC faculty, trainees, Rand Schrader Clinic providers, and community practitioners of both pediatric and adult infectious diseases.

**Infectious Diseases Grand Rounds** are held on the second Friday of every month with guest speakers selected and hosted by the Infectious Diseases faculty. These lectures are frequently delivered by visiting faculty of national stature in their respective areas of expertise.

# Infectious Diseases

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**Clinicopathologic Conference** occurs on the fourth Friday of each month. The clinical fellow on the LAC+USC Medical Center Consultation Service selects and organizes the conference with cases and topics chosen in conjunction with the Division Chief, Program Director and the attending for the month on the LAC+USC Medical Center Consultation Service. Faculty members from other specialties and subspecialties are invited to discuss significant diagnostic elements of and review pathologic slides, microbiologic specimens, radiographic imaging, retinal photographs, and/or their specialty contribution to the case patient's care. A member of the ID Division Faculty is asked to provide a wrap-up of salient diagnostic, management, or treatment issues at the end of the conference.

**Infectious Diseases Journal Club** is held monthly. Two articles are selected by the fellows as approved by an ID faculty facilitator for discussion and are presented for critical review at each of the sessions. A fellow is assigned as the primary discussant for each of the two articles, presenting a critical analysis of study hypotheses, study design, statistical methods, results, appropriateness of the authors' conclusions, and applicability of the results. The emphasis is on critical review of all aspects of the reported studies for potential flaws in the design or analysis and introduction of potential bias that could affect the conclusions drawn.

**Combined Pulmonary-Infectious Diseases Teaching Conference** is held once a month on the third Tuesday from 8:30-9:30 a.m. Similar to Infectious Diseases Case Conference, the format consists of preparation and presentation of two cases as unknowns, one selected by the Infectious Disease fellow assigned to the conference, and the other presented by the Pulmonary fellow. Faculty from the Infectious Diseases and Pulmonary/Critical Care Divisions attend the conference and participate in the case discussions. A short review of the relevant current literature generally follows each case presentation.

A series of three **HIV Conferences** are held at the Rand Schrader Clinic, facilitated by Infectious Diseases faculty based at the clinic. This stimulating sequence of discussions alternates among the following themes each month:

- HIV Management and Resistance Conference
- Primary Case in HIV Medicine (e.g., management of hypertension, CAD, diabetes)
- HIV Co-Infections (e.g., tuberculosis, hepatitis B or C, human papilloma virus)

These conferences are facilitated by Dr. Cadden, Medical Director of the Rand Schrader Clinic, Dr. Jens Kort, and Dr. Michael Dube, Associate Medical Director. The conferences are attended by faculty from the ID Division, Rand Schrader Clinic physicians, general internists from the Department of Medicine, faculty psychiatrists, physician assistants, social workers and a number of clinic nurses. The ID fellows along with students and house officers rotating on the ID service are required to attend these teaching activities.

**Intercity Infectious Diseases Rounds:** This is a long-standing 2-hour monthly meeting of academic infectious diseases specialty, trainees, and allied health professionals that rotates amongst the different participant hospitals (USC, Harbor-UCLA, Harbor City Kaiser, St. Mary's Medical Center, Long Beach VA, Torrance Memorial Hospital). The format of the conference is for the host institution fellows to present interesting and instructive cases (usually 4-5) in infectious diseases as unknowns. The guest faculty are then asked to provide a differential diagnosis, diagnostic workup, and treatment plan. This is followed by a review of the microbiology, histopathology, special imaging, etc., and then a short didactic presentation by the fellow describing salient features or important aspects of the case.

**Combined Adult-Pediatric Infectious Diseases Research Conference:** A new bimonthly conference (established this year by Drs. Kort and Sattler) on current clinical and translational research topics of USC adult and pediatric Infectious Diseases faculty and affiliated institutions such as the City of Hope National Medical Center. This conference is also integrated into the ACGME-teaching curriculum for the ID fellows.

## Research Activities

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The Division of Infectious Diseases published 23 papers in peer-reviewed journals during the 2007-2008 fiscal year and another two are in press. Four publications are highlighted below.

Burman W, Weis S, Vernon A, Khan A, Benator D, **Jones B**, Silva C, King B, Lahart C, Mangura B, Weiner M, El-Sadr W, and the Tuberculosis Trials Consortium: Frequency, severity and duration of immune reconstitution events in HIV-related tuberculosis. *Int J Tuberc Lung Dis* 11:1282-1289, 2007.

Setting: Patients were enrolled in a prospective trial of rifabutin-based tuberculosis (TB) treatment for human immunodeficiency virus related TB. Antiretroviral therapy (ART) was encouraged but not required. Objective: To evaluate the frequency, risk factors and duration of immune reconstitution events. Design: Patients were prospectively evaluated for immune reconstitution events, and all adverse event reports were reviewed to identify possible unrecognized events. Results: Of 169 patients, 25 (15%) developed immune reconstitution events related to TB. All 25 were among the 137 patients who received ART during TB treatment, so the frequency in this subgroup was 18% (25/137). Risk factors for an immune reconstitution event in multivariate analysis were Black race, the presence of extra-pulmonary TB, and a shorter interval from initiation of TB treatment to initiation of ART. The most common clinical manifestations were fever (64%), new or worsening adenopathy (52%), and worsening pulmonary infiltrates (40%). Twelve patients (48%) were hospitalized for a median of seven days, six underwent surgery and 11 had needle aspiration. The median duration of events was 60 days (range 11-442). Conclusion: Immune reconstitution events were common among patients receiving ART during TB treatment, produced substantial morbidity and had a median duration of two months.

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Best BM, Goicoechea M, Witt MD, Miller L, Daar ES, Diamond C, Tilles JG, Kemper CA, **Larsen R**, Holland DT, Sun S, Jain S, Wagner G, Capparelli EV, McCutchan JA, Haubrich RH and the California Collaborative Treatment Group 578 Study Team (CCTG 578): A randomized controlled trial of therapeutic drug monitoring in treatment-naïve and experienced HIV-1-infected patients. *J Acq Immune Def Syndr* 46:433-442, 2007.

Objective: To improve the utility of therapeutic drug monitoring (TDM) by defining the proportion of patients with and predictors of above or below target protease inhibitor (PI) or nonnucleoside reverse transcriptase inhibitor (NNRTI) concentrations. Methods: This 48-week, multicenter, open-label clinical trial randomized patients to TDM versus standard of care (SOC). Serial pharmacokinetics, including a week-2 3-sample sparse collection, and expert committee TDM recommendations were given to TDM-arm patients' providers. Results: Seventy-four (39%) of 190 patients had week-2 concentrations outside of targets and 122 (64%) of 190 had nontarget exposure at least once over 48 weeks. Providers accepted 75% of TDM recommendations. Among patients with below-target concentrations, more TDM-arm than SOC-arm patients achieved targets (65% vs. 45%;  $P = 0.09$ ). Increased body weight and efavirenz or lopinavir/ritonavir use were significant predictors of nontarget concentrations. Patients at target and patients who achieved targets after TDM-directed dose modifications trended toward greater viral load reductions at week 48 than patients with below-target exposures (HIV RNA reductions: 2.4, 2.3, and 1.9 log<sub>10</sub> copies/mL, respectively;  $P = 0.09$ ). Conclusions: Most patients had non-target PI and/or NNRTI concentrations over 48 weeks. TDM recommendations were well accepted and improved exposure. Patients below TDM targets trended toward worse virologic response.

Allison DC, Miller T, **Holtom P**, Patzakis MJ, Zalavras CG: Microbiology of upper extremity soft tissue abscesses in injecting drug abusers. *Clin Orthop Relat Res* 461:9-13, 2007.

Drug injection often results in upper extremity soft tissue infections. We determined the bacteriology of soft tissue abscesses in substance abusers who inject drugs to provide guidelines for empiric antibiotic therapy. We retrospectively studied 855 patients (638 men and 217 women; mean age, 41.5 years) with a history of injecting illicit drugs and a diagnosis of an upper extremity soft tissue abscess. In the 694 patients with positive cultures the most common organism was *Staphylococcus aureus*, identified in 359 of 694 patients (52%). An increase in the incidence of oxacillin-resistant *S. aureus* over time was observed. Oxacillin-resistant *S. aureus* comprised 5% of *S. aureus* infections in 1999, 50% in 2001, 56% in 2003, and 82% in 2005. Microaerophilic streptococci were present in 37% of culture-positive cases and other anaerobes in 10%. Infections were monomicrobial in 366 of 694 patients (53%) and polymicrobial in 328 of 694 patients (47%). *S. aureus* is the most common pathogen in soft tissue abscesses in injecting drug abusers with an increasing incidence of oxacillin-resistant *S. aureus*. In addition to surgical decompression of abscesses, broad-spectrum empiric antibiotic therapy is necessary.

Vercillo M, Patzakis MJ, **Holtom P**, Zalavras CG: Linezolid in the treatment of implant-related chronic osteomyelitis. *Clin Orthop Relat Res* 461:40-43, 2007.

New antibiotics have been developed targeting resistant microorganisms; however, limited information is available on their use in implant-related chronic osteomyelitis. We evaluated the infection control rate of linezolid in treating these challenging infections and delineate indications for its use. We retrospectively reviewed 22 consecutive adult patients with chronic implant-related osteomyelitis, treated with linezolid in addition to surgical debridement and implant removal. Osteomyelitis was associated with fracture fixation implants ( $n = 18$ ) or arthroplasty implants ( $n = 4$ ). Methicillin-resistant *Staphylococcus aureus* (MRSA) was the most common pathogen (10 of 22 patients). Fourteen patients had one or more comorbidity, including intravenous drug abuse in four patients. Indications for linezolid use included preference for oral administration in 13 patients, presence of vancomycin-resistant enterococcus (VRE) in five patients, and development of allergic reactions to vancomycin in four patients. Fourteen patients were followed for a minimum of six months (mean, 22 months; range, 6-34 months) with no recurrence of infection. Linezolid is a reasonable alternative for treating chronic implant-related osteomyelitis. Our treatment protocol, including linezolid, achieved control of infection in all patients despite the challenging nature of these infections due to patient comorbidities and resistant organisms.

## **OVERVIEW**

**AIDS Clinical Trials Group Grant:** The Division of Infectious Diseases continues to provide scientific leadership and to obtain funding in a wide range of clinical research in both HIV and non-HIV disciplines. Dr. Robert Larsen serves as co-chair of A5225, Dr. Fred Sattler is a member of the protocol team for A5241, Dr. Brenda Jones served as member of the TB Working Group and Dr. Jens Kort served on the Phase IIIB concept proposal team of CCR5 Inhibitor (PR507).

Our NIH-supported ACTG Clinical Trials Unit and Clinical Research Site is one of the major components of the research efforts of the Division. The current grant is in its 22nd year of funding. Over the past decade USC was one of the top performing sites in the United States and led accrual of number of different high-priority studies and ranked at the top of more than 50 different ACTG Clinical Trials Units, in the categories of total accrual of research subjects. The Unit has consistently been at the top of the list for enrollment of underprivileged minorities and has also been successful in enrolling women. We believe the inclusion of ethnic minorities and women is of great importance based on genetic differences that predispose them to different risks for drug-related toxicities and disease complications.

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**NIH National TB Curriculum Consortium and TB Trials Consortium:** Dr. Brenda Jones has established liaisons with public health clinics in Southern California caring for large numbers of patients with tuberculosis (TB). She serves as the Principal Investigator at USC for the NIH National TB Curriculum Consortium (2003-2008) and the TB Trials Consortium (TBTC) [200-93-0693], an investigator-driven consortium funded by the CDC and modeled after the ACTG. She is working with other investigators planning future collaborative efforts between the TBTC and the ACTG to address the treatment and prevention of HIV-related TB.

Dr. Jones and her TB research staff have been highly efficient in enrolling > 360 patients into TBTC studies in the last five years. Dr. Jones is committed to making major contributions to ACTG Network studies such as ACTG 5221. She is also working with Dr. Neil Kaplowitz, Chief of the Gastrointestinal and Liver Diseases Division, to define genetic markers that predispose patients to serious adverse effects of medications like the ansamycin rifalazil to be studied by the ACTG Network. Finally, she is exploring feasibility studies to evaluate use of an INFg assay and nucleic acid amplification methods for diagnosis and management of TB in HIV co-infected patients. Thus, Dr. Jones' contributions will be invaluable in the design and conduct of future nationwide studies of tuberculosis.

**California Collaborative Treatment Group and California NeuroAIDS Tissue Network Grants:** The Infectious Diseases Division is also a member of the California Collaborative Treatment Group (CCTG, Robert Larsen, M.D., USC Principal Investigator) of the University-wide AIDS Program of the University of California, also in its 20th year, and the NIMH study evaluating neurocognitive effects of HIV (California NeuroAIDS Tissue Network, Robert Larsen, M.D., USC Principal Investigator), which was successfully re-competed for an additional five years of funding.

**Scientific Contributions:** Our participation in these collaborative research groups has emphasized development of treatment and prevention modalities for HIV and its complications. For example:

**Dr. Brenda Jones** has 15 years of experience in clinical research of tuberculosis (TB) and, as indicated above, she now serves as the PI at USC for the NIH National TB Curriculum Consortium (2003-2008) and CDC TB Trials Consortium (TBTC) [200-93-0693]. She has served as an active member of the ACTG Mycobacterial-Bacterial Study Group and was a major force in enrolling patients for ACTG 177, 222 and 309. Dr. Jones is working with collaborators at the CDC who are planning important studies with the ACTG to develop more effective and safer strategies for prevention and treatment of TB-HIV co-infected patients such as ACTG studies A5221 (a strategy of immediate versus deferred initiation of antiretroviral therapy for HIV infected persons treated for tuberculosis) and A5233, which Dr. Jones will be implementing at USC.

Dr. Jones has been mentoring our ID fellow, Dr. Martin Sattah, to utilize the infrastructure that she has developed over the last two decades to continually be a leading performance site for the CDC TB studies for which she has enrolled >360 subjects in the last five years. She and Dr. Sattah have initiated a pilot study on the use of the interferon gamma release assay (T-SPOT.TB) in HIV infected patients with active tuberculosis. Dr. Jones is expected to be equally productive in enrolling subjects in ACTG 5221 and 5233 and other upcoming ACTG and CCTG TB studies.

**Dr. Michael P. Dubé** serves on the ACTG Optimization of Antiretroviral Therapy (OpART) Committee and is a member of the A5257s metabolic and cardiovascular complications study team, currently in active protocol development. Previously, he was protocol chair for the ACTG metabolic study A5005s, which has yielded a total of nine publications (four in the past year), including seven as first or senior author. Several of these have set the standard for current and future metabolic studies in this field. Dr. Dubé was also the protocol chair for a multicenter ACTG study of extended-release niacin and has served as a protocol member on a variety of other ACTG studies.

Dr. Dubé mentored Dr. Samir Gupta during his K23 work at Indiana University on renal and cardiovascular complications of HIV disease, yielding four peer-reviewed publications as senior author. Dr. Gupta was recently awarded his first R01 as Principal Investigator and Dr. Dubé will serve as Co-Investigator on this project at USC.

**Dr. Robert Larsen** is currently the protocol vice chair for ACTG study A5225, an investigation drawn from the concept sheet he proposed in April 2004. Previously, Dr. Larsen was a key member of clinical trials in the ACTG responsible for the licensure of fluconazole and itraconazole for HIV-associated cryptococcosis and histoplasmosis. His pioneering work with combination therapies for cryptococcal meningitis set the stage for the ACTG 159 trial, which evaluated high doses of amphotericin B alone and combined with flucytosine as induction therapy for cryptococcal meningitis. He contributed to the protocol strategy for the management of intracranial hypertension for ACTG 202. Further, he is vice chair for the Bacterial and Mycoses Study Group (BAMSG) evaluation of the safety and activity of amphotericin B alone or combined with fluconazole for treatment of AIDS-associated cryptococcal meningitis. Finally, he has been the lead investigator of the California NeuroAIDS Tissue Network neurosyphilis study at USC. Dr. Larsen manages our weekly Fungal/ID Clinic in the Rand Schrader Clinic. His enthusiasm for conducting quality clinical research is immediately contagious to students, residents, fellows and staff who work with him in the Clinic. This is an ideal setting for accrual of sizable numbers of subjects for ACTG, CCTG, MSG and NeuroAIDS Network studies.

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**Dr. Fred Sattler** continued his research programs to study metabolic complications of HIV infection and its treatment, including HIV-associated wasting and lipodystrophy, dyslipidemias and alterations in glucose tolerance. He was PI for an NIDDK R01 grant to study metabolic-hormonal-dysregulation in HIV (R01 DK 49308) to investigate mechanisms that adversely affect muscle physiology and fat metabolism in HIV-positive patients with or at risk for wasting and lipoatrophy. As an outgrowth of those studies, Dr. Sattler was awarded a large multicenter R01 (Hormonal Regulators of Muscle and Metabolism in Aging, AG18169) to determine the molecular and regulatory effects of endogenous anabolic hormones on net muscle protein (actin and myosin) anabolic balance and the effects of these hormones on regional fat (hepatic, visceral and intramyocellular lipid), insulin sensitivity and lipid metabolism in older persons with muscle wasting and central obesity, a model similar to that occurring in HIV. Dr. Sattler is also conducting an investigator-initiated study to determine the effects of testosterone replacement in hypogonadal men with abdominal obesity and insulin resistance to assess whether his recently observed indirect evidence of benefits in insulin sensitivity during replacement doses with this androgen is due to decreases in visceral adipose tissue, hepatic fat or intramyocellular lipid using 2-stage hyperinsulinemic euglycemic clamps and magnetic resonance spectroscopy.

**Dr. Anne Anglim** was appointed by the Centers for Disease Control (CDC) and Prevention and became the first Principal Investigator of the USC GeoSentinel site on March 1, 2007, for the Keck School of Medicine. GeoSentinel is a cooperative project of the International Society for Travel Medicine (ISTM) and the CDC that provides worldwide surveillance for travel-related morbidity identified from a U.S. and international network of travel and tropical medicine clinics. The network was initiated in 1995 and now has 42 active sites. GeoSentinel is based on the concept that these sentinel clinics are ideally situated to effectively detect geographic and temporal trends in morbidity among travelers, immigrants and refugees by the active aggregation of final diagnoses in these mobile populations.

#### **FACULTY RESEARCH AREAS**

**Anne M. Anglim, M.D.**

Nosocomial Infections  
Antimicrobial Resistance  
Environmental Acquisition Factors in Infectious Diseases

**Joseph J. Cadden, M.D.**

Social Support Services for Patients with HIV  
Sociological Effects on Family Members or Children When Mother or Female Caregiver is HIV Positive  
Blocking Chemokine Receptors in Patients with HIV  
New HIV Therapies

**Michael P. Dubé, M.D.**

Metabolic, Cardiovascular, and Anthropometric Complications of HIV and Antiretroviral Therapy

**P. Jan Geiseler, M.D.**

Clinical Evaluation of New HIV Drugs  
Antiretroviral Therapy for HIV-1

**Paul D. Holtom, M.D.**

Bone and Joint Infections  
Hospital Epidemiology

**Brenda E. Jones, M.D.**

Development of a Tuberculosis Curriculum  
New Methods for the Treatment and Prevention of Tuberculosis  
Tuberculosis and HIV Infection  
Diagnostics for Tuberculosis  
Biomarkers for Tuberculosis Treatment Response  
Vitamin D Receptor Gene Expression Profile Analysis in Tuberculosis Patients

**Jens J. Kort, M.D., Ph.D.**

Regulation of Cell Ion/Volume Homeostasis  
Pathogenesis of Human Immunodeficiency Virus (HIV) Infection  
Molecular Mechanism of HIV-Induced CD4 Lymphocyte Death  
Molecular Mechanism of AIDS Dementia Complex  
Pre-Clinical Development of Anti-HIV Agents  
Pharmacokinetic (PK) and Pharmacodynamics (PD) Studies of Anti-HIV Agents  
Cellular Transport, Toxicity and Interactions of HIV Drugs with Cell Metabolism/Function

# Infectious Diseases

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## **Robert A. Larsen, M.D.**

HIV and West Nile Viral Infections of Central Nervous System  
Diagnosis and Management of CNS Syphilis  
Treatments Strategies for Systemic Fungal Infections  
Fungal *in vitro* Susceptibility to New Antifungal Agents

## **Alejandro Sanchez, M.D.**

AIDS-Associated Cryptococcal *in vitro* Susceptibility Testing  
HIV-Associated Central Nervous Infections  
TB-HIV Coinfections  
Histoplasmosis in Non-Endemic Areas

## **Fred R. Sattler, M.D.**

Clinical Therapeutics and Pharmacokinetics of Antimicrobial and Antiviral Agents  
Pathogenesis and Treatment of Muscle Wasting in HIV  
Hormonal Regulators of Muscle and Metabolism in Persons Infected with HIV and the Elderly  
Understanding Disorders of Fat and Lipid Metabolism in HIV and Aging

## **SPECIAL BASIC AND TRANSLATIONAL RESEARCH ACTIVITIES**

### **Brenda E. Jones, M.D.**

Dr. Jones has developed collaboration relationships with faculty in the Department of Preventive Medicine and the Division of Gastrointestinal and Liver Diseases at USC. As a result, her future studies will include the use of a novel system to quantify levels of gamma interferon for the diagnosis of tuberculosis and studies to determine the genetic susceptibility and risks for isoniazid hepatotoxicity (i.e., pharmacogenomics).

### **Robert A. Larsen, M.D.**

Dr. Larsen continues his laboratory work on correlative studies involving a murine model of cryptococcal disease and an *in vitro* system to test fungal susceptibility.

### **Fred R. Sattler, M.D.**

Dr. Sattler continued with the seventh year of his multicenter R01 study as the overall project Principal Investigator to assess "Hormonal Regulators of Muscle and Metabolism in Aging." This study is investigating the effects of restoring testosterone and growth hormone individually and in combination to youthful levels on synthesis of myofibrillar proteins actin and myosin, muscle protein breakdown via activation of the ubiquitin-proteasome system and ligase (MuRF1, Atrogin 1,2 mRNA expression and protein synthesis), quantification of satellite cell activation in muscle cells and the effects of the local regulators IGF-1, IGFBP-4, MGF, mTOR, Akt, MyoD, myostatin, and follistatin on net myofibrillar protein balance.

## **SPECIAL CLINICAL RESEARCH ACTIVITIES**

### **Anne M. Anglim, M.D.**

Epidemiology of C. Difficile diarrhea and colitis; vancomycin-resistant enterococcal infections; catheter-related bloodstream infections; environmental factors influencing acquisition of infections; healthcare-acquired opportunistic infection prevention and surveillance of solid organ transplantation; travel-tropical disease.

### **Michael P. Dubé, M.D.**

Metabolic, cardiovascular, and anthropometric complications of HIV and antiretroviral therapy: Dr. Dubé will collaborate as Co-Investigator on an NHLBI-funded project R01 HL095149-01 (Gupta-PI) entitled HIV, Inflammation, and Endothelial Dysfunction. In the ACTG, he will serve as Co-Investigator on an ACTG study of Cardiovascular, Anthropometric, and Skeletal Effects of Antiretroviral Therapy. Locally, he is serving as PI for ACTG trials as well as trials in the California Collaborative Treatment Group.

### **P. Jan Geiseler, M.D.**

Antiretroviral therapy: Dr. Geiseler continued his work with and participation in studies to evaluate antiretroviral therapy utilizing new treatment medications and strategies in clinical trials being conducted by the AIDS Clinical Trials Group (ACTG) and California Collaborative Treatment Group for patients infected with HIV. Dr. Geiseler is currently the local PI for two ACTG trials. Trials A5175 and A5202 evaluate the efficacy of once daily protease inhibitor and once-daily non-nucleoside reverse transcriptase inhibitor-containing therapy in combination with nucleoside analogues.

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**Joseph J. Cadden, M.D.**

Dr. Cadden is involved in three research studies as either PI or co-PI. The first is an NIH-funded study in which he serves as co-PI and site PI at USC. This study is being conducted with Amy Wohl, Ph.D., Chief Epidemiologist in the HIV Epidemiology Program DHS, to evaluate and develop better social support services for HIV-positive persons. In addition, he is the site PI for a study with Eric Rich, Ph.D. from UCLA, which will evaluate the sociological effects on family members and children when the mother or female caregiver is HIV positive. Lastly is the GRACE study (Gender Race and Clinical Efficacy), which is designed to look at clinical outcomes primarily in women with advanced HIV disease and who are highly anti-retroviral experienced.

**Paul D. Holtom, M.D.**

Bone and soft tissue infections: Dr. Holtom is initiating new studies to investigate novel treatment strategies for bone and joint infections, in collaboration with Drs. Michael Patzakis, Charalampos Zalavras and others in the Department of Orthopaedic Surgery. These studies include new antimicrobials for skin and soft-tissue infections and the *in vitro* and *in vivo* studies on local antibiotic therapy and the elution of antibiotics from PMMA beads and spacers.

Epidemiologic Studies: Dr. Holtom is the Hospital Epidemiologist at LAC+USC Medical Center and is conducting several studies with two of the infectious diseases fellows on the epidemiology of *Staphylococcus aureus* and invasive candidal disease. Dr. Holtom remains the Director of the Jeanette Wilkins Memorial Microbiology Laboratory, which facilitates conduct of these studies.

**Brenda E. Jones, M.D.**

Dr. Jones is the USC Principal Investigator of a 10-year contract (September 1999-2009) sponsored by the Centers for Disease Control and Prevention (TBTC) on the natural history and treatment of tuberculosis. The USC study site, which includes Los Angeles County TB Control, is one of 27 international study sites. The purpose of the Consortium is to address the research needs for the treatment and prevention of tuberculosis. A high priority of research is for improved treatment of latent tuberculous infection. An important secondary goal of the Consortium is to contribute to the global control of tuberculosis in HIV-infected persons.

In October 2003, Drs. Jones (PI) and Patricio Escalante (Co-Investigator, Pulmonary Division) were awarded a five-year NIH subcontract with UCSD to establish a National TB Curriculum Center (NTCC). The NTCC will coordinate the activities of a multidisciplinary team to develop and implement curriculum, using state-of-the-art technology for education. The Consortium consists of 23 partner schools, of which USC is one of the five coordinating centers.

**Robert A. Larsen, M.D.**

Dr. Larsen's research is focused primarily toward understanding the mechanisms of pathogenesis and outcomes of central nervous system infections. He is also actively involved in other investigations including viral, fungal and bacterial pathogens.

Fungal infections: Dr. Larsen is a member of the NIH-sponsored Bacterial and Mycoses Study Group (BAMSG). The BAMSG has initiated a trial of amphotericin B plus fluconazole in persons with AIDS and cryptococcal meningitis. Dr. Larsen is a co-chair of this study being conducted in the U.S. and Thailand. The NIH-sponsored Adult AIDS Cooperative Trials Group has developed and is implementing an international study of AIDS-associated cryptococcal meningitis with high doses of fluconazole (AACTG 5225). Dr. Larsen is vice-chair of this study, which will be conducted in the U.S., Peru, Brazil and South Africa. Both trial concepts were proposed by Dr. Larsen and based on prior clinical studies that he has conducted at USC.

Bacterial infections: Dr. Larsen continues to study neurosyphilis in persons co-infected with HIV, as a subproject of the California NeuroAIDS Tissue Network (CNTN). A novel diagnostic approach to identify central nervous system infection with syphilis is being tested with samples collected as part of the CNTN program.

Other activities: Dr. Larsen is the USC primary site investigator for the California Collaborative Treatment Group (CCTG). Dr. Larsen also served as a site investigator of a Center for Disease Control and Prevention (CDCP) study of clinic and drug adherence in persons with HIV infection receiving highly active anti-retroviral drug therapy.

**Fred R. Sattler, M.D.**

Metabolic abnormalities in HIV infection and aging: Dr. Sattler has for a number of years provided his scientific and administrative leadership in the NIAID AIDS Clinical Trials Group involving studies that have evaluated the pathophysiology and management of HIV-associated weight loss, changes in body fat, and metabolic complications. He has served as a chair, co-chair, vice-chair or protocol team member for a number of studies including ACTG 313, 329, 392, 892, 5079, 5112, 5116s, 5124s and 5125s, which are either in the phase of study maintenance or were recently completed (ACTG 313, 329, 392, 892) and the results are being analyzed and/or prepared for manuscripts.

As an outgrowth of studies of AIDS muscle wasting, Dr. Sattler conducted investigator-initiated pilot studies in the USC GCRC to evaluate the effects of anabolic androgens in elderly subjects with loss of skeletal muscle mass (sarcopenia) and muscle strength and thus at risk for frailty and who have gains in central fat and are at risk for the metabolic syndrome. These studies have demonstrated dose-dependent improvements in muscle mass, maximal voluntary strength and leg power, which are necessary constituents for physical function, independence, and quality of life during aging. In addition, study subjects have had a dose-related decrease in total and central fat.

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Based on the results of these studies, which have been presented at The Endocrine Society meetings, Dr. Sattler received funding from the National Institute of Aging (5-RO1-AG18169) to study the interactions of the growth hormone/IGF-1 and androgen axes in the molecular regulation of myofibrillar protein synthesis and breakdown and adipose tissue biology in elderly persons through use of stable isotope dilution methods. The translational effects of these interventions as measured by body composition (DEXA, MRI and total body water analysis by stable isotope biology), anthropometry, skeletal muscle strength, power, and physical function, maximal ventilatory capacity, and aerobic endurance are being measured in the USC GCRC. Dr. Sattler has also continued work on an investigator-initiated study on the GCRC to evaluate the role of androgen replacement to improve insulin sensitivity and other risk factors for the metabolic syndrome by carefully quantifying intra-abdominal adipose tissue stores, intramyocellular lipid, hepatic glucose output, and peripheral glucose disposal in older, hypogonadal men with central obesity and insulin resistance.

## Publications

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Type	Number Appeared	Number in Press	Number Submitted
Peer Reviewed Publications	23	2	4
Book and Book Chapters	1	2	0
Other Publications	3	0	0
Abstracts	7	0	2

## Federal and Agency Grants

Principal Investigator	Agency Name	Title of Account or Grant	Annual Direct	Annual Indirect	Total	Beg Date	End Date
Jones, Brenda	Center for Disease Control and Prevention	Tuberculosis Trials Consortium (TBTC)	\$ 497,689	\$ 197,017	\$ 694,706	9/23/99	9/22/09
Jones, Brenda	University of California, San Diego	Tuberculosis Curriculum Coordinating Center (TCCC)	112,673	9,802	122,475	9/30/03	9/29/08
Larsen, Robert	University of California, San Diego	California NeuroAIDS Tissue Network (CNTN)	148,266	81,923	230,189	6/17/03	3/31/08
Larsen, Robert	University of Alabama at Birmingham	Amphotericin B Alone or with Fluconazole in AIDS Associated Cryptococcal Meningitis	5,429	1,900	7,329	3/15/05	12/31/07
Sattler, Fred	National Institute on Aging	Hormonal Regulators of Muscle and Metabolism in Aging	81,211	7,424	88,635	9/1/02	8/31/09
Sattler, Fred	National Institute of Allergy and Infectious Diseases	University of Southern California AIDS Clinical Trials Unit	1,301,386	384,374	1,685,760	3/1/92	1/31/14
<b>TOTAL:</b>			<b>\$ 2,146,654</b>	<b>\$ 682,440</b>	<b>\$ 2,829,094</b>		

## Other Grants

Principal Investigator	Agency Name	Title of Account or Grant	Annual Direct	Annual Indirect	Total	Beg Date	End Date
Cadden, Joseph	Tibotec Therapeutics	Prezista/R by Gender and Race over a 48 Week Period	\$ 45,732	\$ 11,433	\$ 57,165	11/2/06	Present
Cadden, Joseph	Tibotec Therapeutics	Early Access of TMC125 with Antiretrovirals in HIV-1 Infected Subjects with Limited Treatment Options	4,680	1,170	5,850	9/4/07	Present
Holtom, Paul	Cubist Pharmaceuticals	Ceftobiprole Medocaril vs Ceftiaxone with and without Linezolid for Community-Acquired Pneumonia	158	39	197	10/19/04	Present
Larsen, Robert	Merck	L-000900612 with Optimized Background Therapy vs Optimized Background Therapy Alone for HIV	920	230	1,150	5/17/05	Present
Larsen, Robert	Gilead Sciences	GS-9137 with Other Antiretrovirals for HIV 1	12,809	3,202	16,011	5/14/07	Present
Larsen, Robert	Schering Corporation	Posaconazole vs Fluconazole in Coccidioidomycosis	10,289	2,572	12,861	6/27/07	Present
Larsen, Robert	University of Minnesota	Sub-Cutaneous Recombinant Human Interleukin-2 for HIV	11,200	2,800	14,000	5/11/04	Present
Larsen, Robert	Gilead Sciences	Tenofovir Disoproxil Fumarate and Emtricitabine with Efavirenz vs Combivir and Efavirenz for HIV	11,141	2,785	13,926	10/16/03	Present
Sanchez,, Alejandro	Glaxosmithkline	Atazanavir plus Ritonavir and ABC/3TC FDC followed by Atazanavir and ABC/3TC FDC or Maintenance of the Initial Regimen for HIV 1	31,719	7,930	39,649	6/13/07	Present
<b>TOTAL:</b>			<b>\$ 128,648</b>	<b>\$ 32,161</b>	<b>\$ 160,809</b>		