EMORY TRANSPLANT CENTER
2007 ANNUAL REPORT

Submitted by:
Christian P. Larsen, MD, D Phil
Director, Emory Transplant Center and
Carlos and Marguerite Mason Professor of Surgery
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I. Emory Transplant Center
Mission and Vision

MISSION STATEMENT

The Emory Transplant Center is committed to providing and improving access to quality clinical care and support services for patients with organ failure, and to developing new transplant therapies to prevent or delay organ failure through basic, translational, and clinical research.

VISION STATEMENT

The Emory Transplant Center will be the leader in the field of transplantation in the United States as defined by clinical volume, transplant outcomes, and research endeavors.
II. A Word from the Director

The Emory Transplant Center continues to mark extraordinary accomplishments in both the clinical and academic arenas, and as is our hallmark, in the integration of the two. We are entering the next phase of the implementation of the Emory Transplant Center organizational integration, bringing together our core transplant faculty into a new section of The Emory Clinic. Our adult clinical transplant programs are thriving, and at the same time, Emory Transplant Physicians and Surgeons continue to perform pediatric transplants at Children’s Healthcare of Atlanta (CHOA), which as of May 2007 is tied for the 5th largest pediatric transplant center in the US, ranking in the Top 5 for the seventh consecutive year. For the past three years, CHOA has ranked among the Top 4 pediatric kidney transplant programs in the country. The CHOA liver transplant program has been one of the top 10 busiest in the US for the last 10 years, with one of the highest graft and patient survival rates with no deaths on the wait list of patients with chronic liver disease.

On the academic side, our program continues to show strong growth, despite declining federal funding trends. Our total program funding is now over $12.25 million (FY 07), an impressive increase of more than 50% since FY 04 ($8.1 million). This vitality stems from the unique strength of the Emory Transplant Center - the translation of quality scientific research to patient care, facilitated by unparalleled collaborations, and faculty and staff recruitment, retention and development. We finish this year with a period of exceptional recruitment, including the addition of Dr. Allan Kirk as the Center's first Scientific Director. Dr. Kirk joins us as the 57th Eminent Scholar of the Georgia Research Alliance. The Emory Transplant Center has grown to encompass 37 faculty, all working towards an ever-increasing level of success.

As we move ahead towards Vision 2012, Emory University is investing in a small number of specialty areas – including transplant – with the goal of launching each to world-renowned excellence. The Emory Transplant Center is already on track towards recognized leadership through our expanding clinical and research programs. Our surgeons, nephrologists, pulmonologists, immunologists, pediatricians, nurses and many others work together clinically and academically to address the most pressing unmet needs in our field, coalesced around our central theme of developing new approaches to overcome the debilitating problems created by the toxicities of the drugs we use to prevent rejection.

The achievements of the Emory Transplant Center are a shining example of what can happen when a diverse and dedicated team pursues a common goal of transforming health and healing. New challenges and numerous opportunities await us in the year ahead. I applaud the remarkable and collaborative work of all of the members of the Emory Transplant Center and am pleased and proud to present the outcome of our work for fiscal year 2007 in this Annual Report.

Christian P. Larsen, MD, D Phil
III. KEY CENTER STATISTICS

The Emory Transplant Center is one of the most advanced and comprehensive transplant centers in the Southeast, bringing together Emory University’s transplantation programs in heart, lung, liver, kidney, pancreas and islet. The Center is active in full-service patient care and support services, as well as in groundbreaking research.

- The Center has been a leader in fostering inter-departmental, multi-disciplinary grants from both federal sources (like the NIH) and private foundations. Center research funding continues to grow and for FY06-07 totals $12,252,939 exclusive of philanthropic support (see Research Funding, page 45).

- The Center has 37 faculty who include basic scientists and clinical researchers across departments ranging from surgery to medicine to pediatrics (see Faculty Listing and Highlights, page 16).

- In 2007, the Emory Transplant Center supported Children’s Healthcare of Atlanta in ranking in the Top 5 pediatric transplant programs in the United States.

TOTAL NUMBER OF TRANSPLANTS PERFORMED PER PROGRAM SINCE INCEPTION

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>TOTAL # OF TRANSPLANTS PERFORMED*</th>
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<tr>
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<td>Kidney</td>
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<td>199</td>
</tr>
<tr>
<td>Pancreas or Kidney-Pancreas</td>
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*Note: January, 1988 – May, 2007 (Adult and Pediatric) as reported on www.optn.org
### TOTAL NUMBER OF TRANSPLANTS PERFORMED IN FY 2006 AND FY 2007*

<table>
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<tr>
<th>PROGRAM</th>
<th># ADULT AND PEDIATRIC TRANSPLANTS, FY 2006</th>
<th>ACTUAL # ADULT AND PEDIATRIC TRANSPLANTS, FY 2007 (through July**)</th>
<th>PROJECTED # ADULT AND PEDIATRIC TRANSPLANTS, FY 2007</th>
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<tr>
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<td><strong>347</strong></td>
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* As reported on [www.optn.org](http://www.optn.org)

**Note: Fiscal Year (FY) 2007: September 1, 2006 – August 31, 2007

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**Collaboration: Savannah Outpatient Transplant Clinic**

The Kidney/Pancreas and Liver Transplant Clinics held monthly at St. Joseph's/Candler Hospital in Savannah have continued to grow over the last year. The Liver clinics have had to limit the number of appointments the team can accommodate due to the popularity of the location of the clinic. The team sees at least 40 patients every other month at the Candler site. The Kidney/Pancreas clinics meet every other month opposite the Liver clinics. Since this is the first year the Kidney/Pancreas team has held clinics in this location, their volumes have been ramping up and they are now seeing between 15 and 20 patients per clinic. The Kidney/Pancreas team also offers their patients an education class held by the transplant outreach coordinator. By offering this class in the Savannah area, it allows patients from the area to obtain the required educational piece of the transplant process without having to travel to Atlanta. Providing these clinics in the Candler location allows Emory the opportunity to remove the distance barrier to the Atlanta transplant center and improve patient access to transplant care.
IV. RESEARCH PROGRAM GROWTH AND HIGHLIGHTS

The breadth and scope of the work of the Emory Transplant Center spans basic science, immunology research, clinical practice and trials, and social and public health studies. A central theme of the Center is its interdisciplinary structure, and a major focus is creating an environment that promotes natural synergies and a multi-disciplinary approach to transplantation. The strength of the program can be seen in its continued growth: from just over $8 million to over $12.25 million over four years, an increase of more than 50%.

As can be seen above, from FY 04 to FY 05, the overall program's direct dollars decreased slightly. However, given the make-up of the direct dollars awarded, the indirect costs increased significantly, resulting in a slight increase in overall funding. The increased indirects were related to an increase in dollars from NIH, from 54% of total funding in FY 04 to 63% in FY 05 (see below). The Center participates in numerous NIH grants ranging from R01s to P01s to U19s and others. Despite a small decrease in the number of NIH awards in FY07, the Center maintains a healthy 58% of its funding from NIH. While the overall research program of the Center is well-funded by NIH, it also is well diversified in its total program funding, as can be seen below.
Despite challenging times, our researchers continue to be successful in attracting funding for their work to transform health and healing. Highlights of that work, and the faculty who lead it, follow.
**Vision 2012: Transforming Health and Healing**

By the year 2012, the Woodruff Health Sciences Center will be recognized as one of the top ten academic health sciences centers and will be leading change in health care through its education, research and patient care programs. The WHSC is redefining the term "center," making new investments in a number of specialty areas, including transplant, with the goal of launching each to national leadership. These new centers will be integrating research innovations that will help patients and creating models for patient-centered care that others throughout the country can follow. The Emory Transplant Center has been named one of the first Centers to receive initial funding. We will be assessed annually on our ability to do the following: 1) create new models in which interprofessional and interdisciplinary teams work together to provide patient-centered care, 2) power the clinical models by innovative research that differentiates Emory from other academic health sciences centers, and 3) integrate system-wide priorities and themes, including patient quality and safety, bioinformatics and predictive health.

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**NIH Kidney Transplant Chief Joins ETC as Georgia Research Alliance Eminent Scholar**

Allan D. Kirk, MD, PhD, has joined the Emory University School of Medicine as Scientific Director of the Emory Transplant Center and as a Georgia Research Alliance (GRA) Eminent Scholar. Dr. Kirk previously served as the chief of the Transplantation Branch at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health. He is the founding director of the NIH Intramural Organ Transplant Program. Dr. Kirk will serve as a kidney/pancreas transplant surgeon at Emory University Hospital and at Children's Healthcare of Atlanta, with a primary appointment in Emory's Department of Surgery and a secondary appointment in the Department of Pediatrics to facilitate novel transplant therapies for children. Dr. Kirk is the 57th scientist attracted to Georgia research universities by the GRA and the ninth to join Emory as a GRA Eminent Scholar – a national model for attracting world-class scientific talent to the state.

An internationally recognized surgical scientist and authority on transplant immunology, Dr. Kirk has conducted groundbreaking translational research in an effort to achieve immune tolerance of organ and tissue transplants without the use of toxic immunosuppressant drugs. While at the NIH, he served as principal investigator on ten clinical trials leading to notable clinical breakthroughs, including the first trial to investigate a co-stimulation inhibitor in human transplantation, and the first trial to investigate the drug alemtuzumab in transplantation in North America. Blocking co-stimulation inhibitors is a strategy to keep the immune system from rejecting transplanted organs. His work has supported the introduction of several novel drug regimens into clinical trials. He has been awarded two Bench-to-Bedside Awards by the NIH Clinical Center. Under Dr. Kirk's leadership, the NIH developed into an influential kidney transplant research center that has added major new scientific information to the field. Clinically, the NIH center maintained exceptional results with graft and patient survival rates exceeding those typical for kidney transplantation in the United States.
Immune Tolerance and Costimulation Blockade

The Center has a strong track record in both scientific research and clinical practice – and in their connection. Emory is at the forefront of transplant immunology research, investigating innovative strategies to stop rejection of transplanted organs. With the aid of significant grant funding, researchers Drs. Larsen, Pearson, Newell and Kirk are working to establish true immune tolerance among transplant recipients. This research strives to free patients from the toxic side effects of daily immunosuppressant medicines and achieve permanent, long-term acceptance of organs.

Drs. Larsen and Pearson are receiving significant funding from NIH to study transplant tolerance in non-human primates. Projects under this grant will explore costimulation blockade, chimerism, and tolerance across MHC disparity, as well as the effect of adoptive cellular therapies to enhance tolerance and protective immunity.

The work of up-and-coming emerging faculty like Dr. Kean includes the study of transplantation tolerance as it applies to non-malignant hematologic disease, including sickle cell disease and beta-thalassemia; the study of the effect of natural killer cells on transplantation tolerance in both bone marrow and solid organ transplantation; and the translation of murine studies on transplantation tolerance to primate preclinical models, in particular, bone marrow transplantation in the non-human primate, the Rhesus Macaque. Dr. Rigby’s work within the Center focuses on understanding the immunologic mechanisms involved with Type 1 diabetes mellitus. His team plans to use this understanding to prevent disease and/or achieve tolerance for curative islet transplants. He received a Junior Faculty Award from the American Diabetes Association to study anergy and regulation in costimulation-blockade induced tolerance in autoimmune diabetes.

Dr. Newell continues to investigate the individual clinical and biological characteristics that contribute to the induction and maintenance of clinical tolerance. More than 50 years after the first successful clinical organ transplant, transplantation tolerance in humans remains a rare, unpredictable, and poorly understood phenomenon. Dr. Newell is playing a leading role in the Immune Tolerance Network, the largest, the most comprehensive study of its kind to date, which has revealed unexpected and important insights into differences between tolerant kidney transplant recipients and other groups. These insights may hint at mechanisms of tolerance and eventually provide a useful tool to help identify tolerant patients.

Drs. Larsen and Pearson have a strong track record of bringing research to the patient – their research in costimulation blockade has been brought from basic research in the early 1990s through the primate center and into highly successful clinical trials in humans, led by Emory.
**Cancer, Immunology and Systemic Lupus Erythematosus**

*Drs. Mittler* (Surgery) and *Spencer* (Pediatrics), with the aid of significant NIH grant funding, are working toward development of highly effective novel approaches for treating neuroblastoma, melanoma, or sarcoma with a commitment to rapidly translate these approaches from basic research to clinical testing. Using monoclonal antibodies to the 4-1BB (CD137) T cell costimulatory receptor in mouse models of cancer, Dr. Mittler and his colleagues have demonstrated eradication of poorly immunogenic tumors in anti-4-1BB treated mice. This work has led to multiple publications and the award of three US patents to Dr. Mittler and his colleagues, the most recent being April, 2007. The pharmaceutical company, Bristol-Myers Squibb where Dr. Mittler began his work using anti-4-1BB mAbs has now successfully completed a Phase I clinical trial in melanoma patients using these antibodies and as a result, these studies are scheduled to move into a Phase II clinical trial later this year.

Emory University has the largest systemic lupus erythematosus (SLE) patient population in the Southeastern United States. Apart from his interest in cancer therapy, *Dr. Mittler* is equally committed to providing more effective and safer approaches for treating patients with autoimmune diseases such as SLE, RA and Crohn’s Disease. The same monoclonal antibodies reactive with the 4-1BB T cell costimulatory receptor used for eradicating established tumors have been shown to be efficacious in reversing disease progression in SLE and Rheumatoid Arthritis (RA). These studies have met with unparalleled success. Dr. Mittler’s team is actively working on humanizing monoclonal antibodies reactive with human 4-1BB receptors. They are particularly committed to testing these reagents in clinical trials for treating SLE.

**Andrew J. McKelvey Lung Transplantation Center**

The mission of the Andrew J. McKelvey Lung Transplantation Center at Emory University School of Medicine, led by *Dr. Lawrence*, is to improve the outcomes following lung transplantation and promote the development of novel medical treatments for complex lung disorders, especially interstitial and pulmonary vascular lung diseases. This has been accomplished by the recruitment of both laboratory investigators and clinicians as members of the McKelvey Center. Research supported by the McKelvey Center ranges from basic studies into the mechanisms of obliterative bronchiolitis following lung transplantation, to multi-center clinical trials of new immunosuppressant medications for lung transplantation and new drugs for the treatment of pulmonary hypertension.

**Heart Failure and Transplant Program**

Under the direction of *Dr. Smith*, Emory has a robust heart failure program with busy offices at Emory and Crawford Long Hospitals. We have over 5,000 heart failure patient visits per year and see approximately 50 new patients each month who have congestive heart failure.
**The Atlanta Cardiomyopathy Consortium (TACC)**

TACC is a unique initiative undertaken by the Emory University to bring together the various academic and community cardiology practices in Atlanta together in a collaborative relationship to study: a) the natural history of heart failure, b) develop a serial (every 6-month collection) bio-bank of DNA, serum, plasma, and urine, c) assess changes in biomarkers and gene expression overtime and how it impacts on treatment and outcomes, d) apply and assess novel therapies for heart failure, and e) assess the social, behavioral, and psychological determinants of heart failure care and outcomes.

The current plans are to enroll a representative sample of men and women, whites/blacks/other minorities, heart failure patients with reduced and preserved heart contraction, and those who are younger and older. The patients will be enrolled from Emory University Hospital, Emory Crawford Long Hospital, Grady Memorial Hospital, and the Atlanta VA Medical Center.

**Clinical Trials:** All the therapies which we know today improve outcomes for patients with heart failure were experimental at one time and all new discoveries have to undergo scientific evaluation for both benefits and risks through clinical trials. The Center for Heart Failure and Transplantation has a robust clinical trials program which includes assessment of newer drugs, devices including left ventricular assist devices, telemonitoring and tele-management, and assessing novel ways of improving patients' healthcare behaviors.

**Genomics and Gene Bank:** Emory University cardiology division has a robust program in human genomics and genetics including assessment of patients with heart failure, coronary artery disease, peripheral vascular disease, and also familial cardiovascular diseases. The TACC initiative is expected to enhance the genomic aspect of heart failure research at Emory University.

**Telemonitoring and Telemanagement:** With the increasing burden of heart failure in the population, it is not realistically possible that there will be enough man-power in terms of cardiologists, lets side heart failure specialists, to take care of all the patients in United States. Responding to this urgent need to develop and study the technological advances in capturing data on heart failure patients through remote monitoring, Emory University is developing and studying systems to manage these patients more effectively based on the data collected through telemonitoring and to triage patients flow in order to manage the overall population more effectively while managing more intense time and resources to the patients who need it the most. The Center for Heat Failure Therapy is involved in several multi-center projects studying this important aspect of care.

**Risk Prediction:** Currently funded research is looking at the discrimination, calibration, validity, and bias of the various heart failure risk prediction models with respect to timing to event analysis. Risk for poor outcomes prediction is essential for patients with heart failure as the timing and need for transplant or mechanical cardiac support is intricately dependent on accurate outcomes prediction.

**Role of Novel Biomarkers:** The center for heart failure therapy has a funded robust program to assess the utility of novel biomarkers in heart failure disease progression and outcomes.
Protective Immunity Project

*Dr. Larsen* and other investigators at the Emory Transplant Center in collaboration with *Dr. Ahmed* and the Emory Vaccine Center, the Rollins School of Public Health, and Affymetrix, Inc., through a contract from NIH, are studying immune function and biodefense in recipients of organ transplants in preclinical and clinical settings. Such knowledge will be critical to strategies for enhancing desirable immune responses while not precipitating rejection.

Juvenile Diabetes Research Foundation Center for Islet Transplantation

The Emory Transplant Center is positioned to be a world leader in the search for a cure for type 1 diabetes. A primary strategy is targeted toward building upon the clinical islet cell transplant program. The long-term success of the Center’s work, which includes the goal of eliminating insulin therapy for type 1 diabetes, would revolutionize the face of diabetes treatment. *Drs. Larsen, Weber, Pearson, Chaikof, and Gangappa* lead a Center grant from the Juvenile Diabetes Research Foundation to continue the Emory Transplant Center JDRF Center for Islet Transplantation.

Endocrine Replacement through Transplantation of Porcine Pancreatic Islets

*Dr. Larsen* received funding from the JDRF to explore translational strategies for porcine islet xenotransplantation in non-human primates. A critical part of this work is being led by *Dr. Avila* whose research has been focused on improving organ storage and islet isolation techniques in order to increase islet availability and quality for transplantation. Now, an interdisciplinary group of surgeons, basic researchers and technologists is trying to physiologically and genetically characterize neonatal pig islets (NPI’s) for transplantation into human patients suffering from type I Diabetes Mellitus (T1DM). The recent surge in studies examining xenogeneic sources for islet transplantation in both mouse and non-human primate models demonstrate that the transplant community is entering into a new phase in the effort to utilize porcine donors as a source for islet replacement therapy in the treatment of humans with T1DM. The focus must now include research to obtain critical data in non-human primate models needed to make decisions regarding the design of potential clinical trials using xenogeneic islet tissue in humans. One of the goals is to provide genetic characterization of this tissue, in parallel with islet potency and safety studies currently performed at the ETC. This project uses the expertise of the islet isolation laboratory personnel for the development of procedures to obtain, study and improve NPI for transplantation. In addition, it uses the collaboration of surgeons/researchers for transplantation and follow-up of non-human primates treated with this tissue, using tolerogenic and immunomodulatory protocols currently developed at the ETC.
**Vaccine Induced Immunity in the Young and Aged**

Dr. Mittler is leading a component of a five-year study to generate human anthrax toxin neutralizing monoclonal antibodies. The purpose behind this proposal is two-fold. The first is proof of concept of the approach used to achieve this objective, and the second is to provide to the U.S. Government a source of anthrax toxin neutralizing antibodies that could be administered to the general, non-vaccinated (Anthrax) public in the event of a terrorist attack in which *Bacillus anthracis* spores were released as an aerosol. In such a situation untreated individuals would suffer a fatality rate exceeding 97%. While antibiotics help curtail infection and allow the immune system to contain it, the use of antibiotics must be started early in the infection to be of value, whereas administration of toxin neutralizing antibodies can be given later. Because early symptoms of *Bacillus anthracis* infection resemble those of a common respiratory virus it is unlikely, that initially, infected individuals will seek immediate medical attention and thus the use of antibiotic treatment will come too late. The first objective of this study has been accomplished and the second phase is beginning. During this period we will be testing the efficacy of these antibodies for protecting *Bacillus anthracis* infected rodents from fatal toxemia. Later studies will be carried out in which non-human primates are infected by *Bacillus anthracis* spore inhalation and at later time points given anti-toxin monoclonal antibodies. If these studies are successful the reagent will be produced commercially for human use.

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**Educational Conferences and Inter-group Lab Meetings**

The Center hosted numerous outside speakers at its weekly Noon Conference, coordinated by Dr. Newell, including transplant surgery and medicine leaders in fields from adult renal transplant, pulmonary medicine, pathology, and pediatric cardiology. Average attendance is over 75 including representatives from the kidney, liver, heart and lung groups, the HLA lab, pathology, nursing and the Transplant Center.

The Center also fosters exchange through regular joint meetings among the labs of Drs. Ahmed, Larsen, Pearson, Mittler, Newell and Kirk. Current research (ongoing or recently completed) is presented in an informal setting allowing for discussion and suggestions. This setting has resulted in ideas and comments from colleagues being integrated into the research. In addition, a new research meeting series brings together the labs of Drs. Larsen, Pearson, Ahmed, Chaikof and Weber to discuss new and ongoing major collaborative research projects and grants such as the JDRF Center and the Protective Immunity Project.
**Other Center Research Highlights**

- **Dr. Pearson** is leading an NIH Training Grant, one of the few in the country in transplantation.

- **Dr. Mittler** is testing the efficacy of altered vaccination route and dose regimens for protection against anthrax in humans and non-human primates and to correlate a number of immunological and inflammatory parameters with vaccination. Using his expertise in the study of how T cells undergo activation, Dr. Mittler is currently studying ways of amplifying primary and memory T cell-mediated immunity following vaccination against viral and bacterial infection in immunocompromised subjects. Examples of such individuals include those with the autoimmune disease systemic lupus erythematosus, and in the young, and aged.

- **Dr. Newell** is leading a single-center study of early conversion to efalizumab maintenance therapy in primary renal transplant recipients.

- **Dr. Larsen** was honored as the recipient of the 2007 Thomas E. Starzl Prize in Surgery and Immunology in March 2007 at the University of Pittsburgh.

- **Dr. Perryman** is collaborating with the Rollins School of Public Health at Emory University to increase organ donation rates.

- **Dr. Pearson** is participating in a multi-site study to evaluate the safety and efficacy of solid organ transplantation in people with HIV disease.

- **Dr. Mittler** is working to define the cellular and biochemical events that are involved in the successful induction of anti-tumor immunity to established poorly immunogenic tumors following anti-4-1BB treatment, a process that activates tumor-specific T cells.
V. FACULTY LISTING AND HIGHLIGHTS

The Emory Transplant Center thrives on the synergy of its numerous faculty, who span basic science and clinical investigation. The Center’s faculty includes:

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Departmental Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christian P. Larsen, MD, D Phil, FACS</td>
<td>Director, Emory Transplant Center, Vice Chair for Research – Department of Surgery, and Carlos and Marguerite Mason Professor of Surgery</td>
<td>Department of Surgery, Division of Transplantation, Emory University School of Medicine</td>
</tr>
<tr>
<td>Jose G. Avila, MD, PhD</td>
<td>Assistant Professor</td>
<td>Department of Surgery, Division of Transplantation, Emory University School of Medicine</td>
</tr>
<tr>
<td>Wendy M Book MD</td>
<td>Assistant Professor</td>
<td>Department of Cardiology, Emory University School of Medicine</td>
</tr>
<tr>
<td>Patrick H. Bowen, MD</td>
<td>Assistant Professor</td>
<td>Department of Medicine, Division of Endocrinology, Emory University School of Medicine</td>
</tr>
<tr>
<td>Javed Butler, MD</td>
<td>Associate Professor</td>
<td>Department of Cardiology, Emory University School of Medicine</td>
</tr>
<tr>
<td>Carlos Fasola, MD, FACS</td>
<td>Assistant Professor</td>
<td>Department of Surgery, Emory University School of Medicine</td>
</tr>
<tr>
<td>Seth Force, MD</td>
<td>Director, Lung Transplant Program; Assistant Professor and McKelvey Scholar</td>
<td>Department of Surgery, Division of Cardiothoracic Surgery, Emory University School of Medicine</td>
</tr>
<tr>
<td>Shiv Gangappa, DVM, PhD</td>
<td>Assistant Professor</td>
<td>Department of Surgery, Emory University School of Medicine</td>
</tr>
<tr>
<td>Antonio Guasch, MD</td>
<td>Medical Director, Renal Transplant and Kidney-Pancreas Transplant and Associate Professor</td>
<td>Department of Medicine, Renal Division, Emory University School of Medicine</td>
</tr>
<tr>
<td>Thomas G. Heffron, MD, FACS</td>
<td>Carlos and Marguerite Mason Chair for Liver Transplantation, Director of Liver Transplantation, and Associate Professor</td>
<td>Department of Surgery, Division of Transplantation, Emory University School of Medicine</td>
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<tr>
<td>Harsh Kapoor, MD, FRCP, FACP, FACG</td>
<td>Clinical Assistant Professor</td>
<td>Department of Medicine, Division of Digestive Diseases, Emory University School of Medicine</td>
</tr>
<tr>
<td>Name</td>
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<tr>
<td>Neal Iwakoshi, PhD</td>
<td>Assistant Professor</td>
<td>Department of Surgery, Division of Transplantation, Emory University School of Medicine</td>
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<tr>
<td>Hetal Karsan, MD</td>
<td>Assistant Professor</td>
<td>Department of Medicine, Division of Digestive Diseases, Emory University School of Medicine</td>
</tr>
<tr>
<td>Leslie S. Kean, MD, PhD</td>
<td>Assistant Professor of Pediatrics, Burroughs Wellcome Fellow, and McKelvey Scholar</td>
<td>Department of Pediatrics, Division of Hematology/ Oncology/ Bone Marrow Transplantation, Emory University School of Medicine</td>
</tr>
<tr>
<td>Allan D. Kirk, MD, PhD, FACS</td>
<td>Professor of Surgery and Pediatrics, Emory Transplant Center Scientific Director, Georgia Research Alliance Eminent Scholar, and McKelvey Scholar</td>
<td>Department of Surgery, Division of Transplantation, Emory University School of Medicine</td>
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<tr>
<td>Kenneth E. Kokko, MD, PhD</td>
<td>Assistant Professor</td>
<td>Department of Medicine, Renal Division, Emory University School of Medicine</td>
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<td>S. Raja Laskar, MD</td>
<td>Assistant Professor</td>
<td>Division of Cardiology, Emory University School of Medicine</td>
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<td>E. Clinton Lawrence, MD</td>
<td>Director, Andrew J. McKelvey Lung Transplantation Center and Augustus J. McKelvey Professor of Medicine</td>
<td>Department of Medicine/Pulmonary, Emory University School of Medicine</td>
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<td>Jerre F. Lutz, MD</td>
<td>Associate Professor</td>
<td>Department of Medicine, Division of Cardiology, Emory School of Medicine</td>
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<tr>
<td>Robert S. Mittler, PhD</td>
<td>Associate Professor</td>
<td>Department of Surgery, Division of Transplantation, and Emory Vaccine Center, Emory University School of Medicine</td>
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<tr>
<td>Ana L. Mora, MD</td>
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<td>Assistant Professor of Medicine, and Associate Director McKelvey Lung Transplant Center</td>
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<td>Surgical Director, Heart Transplant Program and Associate Professor</td>
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Collin J. Weber, MD, DM Sci, FACS  

William McGarity Professor of Surgery  
Department of Surgery, General and Endocrine Surgery, Emory University School of Medicine

In addition, the Center is supported by several staff in administration:

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<th>Name</th>
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<tr>
<td>Heather Holley Hamby, MPH</td>
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<td>Lisa M. Carlson, MPH, CHES</td>
<td>Academic Program Director and Adjunct Associate Professor</td>
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<td>Cynthia L. Devroy, MBA</td>
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<td>Katharine M. Foster</td>
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<tr>
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<td>Gina White</td>
<td>Program Coordinator</td>
<td>Emory Transplant Center</td>
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FACULTY RESEARCH HIGHLIGHTS

Jose G. Avila, MD, PhD

Dr. Avila is an Assistant Professor in the Department of Surgery and the Scientific Director of the Emory Transplant Center (ETC) Cell and Tissue Processing Laboratory. Dr. Avila’s research has been focused on improving organ storage and islet isolation techniques in order to increase islet availability and quality for transplantation. Now, with the aid of an interdisciplinary group conformed by surgeons, basic researchers and technologists he is trying to physiologically and genetically characterize neonatal pig islets (NPI’s) for transplantation into human patients suffering from type I Diabetes Mellitus (T1DM). The recent surge in studies examining xenogeneic sources for islet transplantation in both mouse and non-human primate models demonstrate that the transplant community is entering into a new phase in the effort to utilize porcine donors as a source for islet replacement therapy in the treatment of humans with T1DM. The focus must now include research to obtain critical data in non-human primate models needed to make decisions regarding the design of potential clinical trials using xenogeneic islet tissue in humans. One of our goals is to provide genetic characterization of this tissue, in parallel with islet potency and safety studies currently performed at the ETC. This project uses the expertise of the islet isolation laboratory personnel for the development of procedures to obtain, study and improve NPI for transplantation. In addition, it uses the collaboration of surgeons/researchers for transplantation and follow-up of non-human primates treated with this tissue, using tolerogenic and immunomodulatory protocols currently developed at the ETC.

Recent Publications (2006-2007)


Wendy M. Book, MD

Dr. Book is an assistant professor in the Department of Cardiology at Emory University School of Medicine.
Patrick H. Bowen, MD

Dr. Bowen is Section Head of Endocrinology and Diabetes for Emory Healthcare and the Emory Clinic, and is an Assistant Professor in the Division of Endocrinology at Emory University School of Medicine. His clinical interests focus on management of type 1 and type 2 diabetes mellitus, insulin pump therapy, and islet cell transplantation for type 1 diabetes.

Carlos Fasola, MD, FACS

Dr. Carlos Fasola is an abdominal transplant surgeon who graduated from the Universidad de Chile Medical School, in Santiago, Chile. He trained at the University of Minnesota, where he did his General Surgery Residency, transplant research, and a multi-organ transplant fellowship. In 2003, he joined Dr. Thomas Heffron as a transplant surgery fellow for additional training and experience in split, reduced-size, and living-donor liver transplantation for both adults and children. He joins the faculty of the Emory Department of Surgery as a liver transplant surgeon at Emory University Hospital and Children’s Healthcare of Atlanta.

Seth Force, MD

Dr. Force is the Surgical Director of the Adult Lung Transplant Program, and a McKelvey Scholar in Lung Transplantation. He plays an active role in the residency program and serves as an Assistant Professor in the Department of Surgery Division of Cardiothoracic Surgery.

Recent Publications (2006 – 2007)


Shiv Gangappa, DVM, PhD

Dr. Gangappa’s work focuses on the investigation of novel immunotherapeutic strategies for transplantation tolerance in non-human primate and murine models; and mechanisms of viral latency and antiviral immunity in costimulation blockade-induced transplantation tolerance.
Most transplant recipients harbor latent infections of several human herpesviruses, which is not surprising given their wide distribution. If the recipient is seronegative for CMV, EBV, HHV-6, or KSHV, the individual is still at risk of infection from donor organs. Infections with any of these herpesviruses can threaten the survival of both the patient and the graft. EBV, KSHV, and HHV-6 have been considered etiologic agents or cofactors for several malignancies. Between 14% and 28% of kidney transplant recipients with a reactivation of KSHV may develop Kaposi’s sarcoma and the disease can be very aggressive in transplant recipients, with a mortality rate of 34% within 3 years of diagnosis. One of the limitations in studying the mechanisms by which herpes viruses affect allograft survival is the lack of a suitable small animal model owing to their species specificity. A murine herpesvirus, gamma-herpesvirus 68 is genetically related to human gamma-herpesviruses and infects laboratory strains of mice, and therefore serves as a good small animal model to study effects of latent infection on transplant tolerance. Dr. Gangappa’s work in this animal model suggests that latent infection in allograft recipients interferes with tolerance induction. The results from this project were featured in the “What’s Hot, What’s New” plenary summary of important new work at the 2007 American Transplant Congress at San Francisco. Ongoing work is aimed at defining mechanisms by which viral and host factors interfere with tolerance induction, and utilize this knowledge to overcome the tolerance resistance barrier and improve strategies for allograft tolerance.

Dr. Gangappa is a member of the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS), and is a reviewer for the journals *Microbes and Infection* and *American Journal of Transplantation*. He was awarded the AST Basic Science Faculty Development award for 2007-2009 at the American Transplant Congress in San Francisco in May, 2007.

**Recent Publications (2006-2007)**


Antonio Guasch, MD

Dr. Guasch’s research interests are related to the pathophysiology of glomerular damage in humans. He uses a combined physiological-structural approach to understand how the glomerulus is injured and the what the mechanisms of progressive renal insufficiency are in both the native and transplanted kidney. Using clearance techniques and glomerular sieving of polydisperse dextrans, he has developed techniques to analyze glomerular hemodynamics and the filtering properties of the glomerular capillary wall. By applying histomorphometric techniques to kidney biopsies, he can quantitate the ultrastructural pathological changes and correlate them with the physiological alterations. He has applied these methods to the study of the glomerular damage caused by sickle cell anemia, chronic renal allograft rejection, and diabetic nephropathy. He is also interested in evaluating new therapies in patients with glomerulonephritis.

Thomas G. Heffron, MD, FACS

Dr. Heffron is the Carlos and Marguerite Mason Chair for Liver Transplantation and is the Director of Liver Transplantation, practicing at both Emory University Hospital and Children’s Healthcare of Atlanta at Egleston. His work focuses on innovative surgical techniques involved in liver transplantation with his overall research geared toward expertise in surgical techniques applicable to living donor liver transplantation. Specifically: 1) The aim of the research of Dr. Heffron’s team is to develop animal models for hand-assisted laparoscopic liver resection. They are attempting to define a logical sequence of operative steps that will result in the safe resection of a liver segment. To that end, they are utilizing novel laparoscopic instruments in a series of acute large animal experiments. 2) Other surgical research of the team is centered around novel approaches using left lateral segments for adult transplantation. Other themes involved in their research are associated with our molecular labs which are involved with opportunistic viral infections associated with solid organ transplantation. Most recent work has been with long chain polymerase chain reaction (PCR), genomics and drug resistance of cytomegalovirus.

Recent Publications (2006-2007)
Dr. Karsan is a graduate of Indiana University in Bloomington and the Indiana University School of Medicine in Indianapolis. He completed both his Internship and Residency in Internal Medicine at Boston University Medical Center and also spent time as Chief Medical Resident. Following his Residency, he completed Fellowships in both Gastroenterology and Hepatology at the UCLA Medical Center in Los Angeles. While at UCLA, he was nominated for Teaching Fellow of the Year by the Department of Internal Medicine and received awards from the American Gastroenterology Association and the American Society of Transplantation.

He has a vast array of experience in managing patients before, during and after liver transplantation as a UNOS-certified Transplant Hepatologist. He initially joined Emory University in 2005 and currently serves as an Assistant Professor with Emory University School of Medicine.

He has been an invited speaker at various conferences, including the recent international combined Portal Hypertension Single Topic Conference in June 2007 by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL). He is a current member of the Portal Hypertension Special Interest Group for the AASLD.

In addition, he has been featured as a medical expert on WebMD and in print, television and radio interviews. He is also actively involved in clinical research.

Recent Publications (2006-2007)


Dr. Harsh Kapoor completed his residency in Internal Medicine and his Gastroenterology fellowship at Dalhousie University in Halifax, Nova Scotia, Canada, prior to completion of a fellowship in Hepatobiliary disease in Sydney, Nova Scotia. From 1999 until 2000, he was on staff at Dalhousie University, where he received the best teacher award. In 2001 he moved to Atlanta to practice Gastroenterology and
Transplantation tolerance, defined as long-term allograft acceptance by an immunocompetent recipient in the absence of immunosuppression, remains an elusive goal of clinical transplantation. The Emory Transplant Center has been at the center of research that has focused on understanding mechanisms leading to transplantation tolerance, with the ultimate goal of translating knowledge of these mechanisms to clinical transplantation. Over the past several years, our group and others have developed strategies targeting the CD40 and CD28 T cell costimulation pathways to control allograft rejection in murine models. By providing costimulation blockade in the peri-transplant period, existing donor-reactive T cells receive “signal one” (supplied by donor cells and antigens) in the absence of “signal two” and are preferentially deleted. This leads to robust, long-term tolerance when normal mice are transplanted under the protection of costimulation blockade. However, when more immunologically complex systems are transplanted with these same techniques, true immunologic tolerance is more difficult to achieve. My work is focused on four specific questions, all related to transplantation tolerance, and its acquisition in immunologically complex model systems:

1. In a highly immunologically active model of a non-malignant hematologic disease (sickle cell disease) what are the major barriers to the acquisition of transplantation tolerance?
2. How do natural killer cells impact the acquisition of transplantation tolerance, and can control of natural-killer alloreactivity produce transplantation tolerance in otherwise resistant models?
3. In the non-human primate model, what are the major barriers to the acquisition of transplantation tolerance, and can we combine blockade of the costimulation pathway with adoptive cellular therapies to achieve robust donor specific tolerance?
4. During bone marrow transplantation in a rhesus macaque model, what are the barriers to tolerance that result in graft-versus host disease, and can these underlying immune barriers be overcome by a costimulation-blockade based immunomodulation strategy?

Recent Publications (2006 – 2007)


Allan D. Kirk, MD, PhD, FACS

When patients receive an organ transplant they must take immunosuppressive medications for life to prevent rejection. These drugs are incompletely effective and cause significant morbidity. Dr. Kirk’s research is directed toward understanding transplant rejection and translating this understanding into less morbid therapies for transplant recipients. His group uses in vitro and animal models to develop transplant strategies and then investigates them in clinical trials.

Dr. Kirk has successfully targeted several costimulatory molecules with monoclonal antibodies in primates and is evaluating multiple anti-CD154 approaches pre-clinically. He is interested in the expression of CD154 on platelets and its implications for immune activation and thrombosis. While at the NIH, he initiated several clinical trials using monoclonal or polyclonal antibodies to achieve transient lymphocyte depletion substantially reducing the need for immunosuppression in humans. His group has shown that monocytes play a key role in post-depletional immune responses and are evaluating the signals influencing human monocytes during lymphopenia. He also has determined that memory T-cells are disproportionately spared during depletion in humans and is studying how this affects the post-transplant need for immunosuppression. In addition to developing new therapeutics for use in transplantation, Dr. Kirk has developed several novel means to more precisely monitor transplant recipients. Improved therapeutics and more precise monitoring techniques will facilitate tailor-made immune therapies and improve patient outcomes.

Dr. Kirk received his M.D. from Duke University School of Medicine in 1987 and his PhD in immunology from Duke in 1992. He completed a general surgery residency at Duke in 1995 and a multi-organ transplantation fellowship at the University of Wisconsin in 1995. He is a Diplomat of the American Board of
Surgery and a Fellow of the American College of Surgeons. He has authored 83 original scientific manuscripts and 50 invited manuscripts on immunological pathways, published in leading scientific peer-reviewed journals. He has developed several novel methods related to immunosuppression resulting in seven patent applications. He has participated in more than 100 guest professorships, including those at Cambridge, Oxford, Columbia, Duke, Emory, Harvard, Johns Hopkins, Penn, and Yale, and numerous international lectureships.

Recent Publications (2006 - 2007)


Kenneth E. Kokko, MD, PhD

Emory University maintains an active collaborative research group in the area of transplant immunobiology. Dr. Kokko is associated with the transplant immunology laboratory and studies the effects that conventional immunosuppression has on the ability of a subject to maintain protective immunologic memory to antigen presentation. At a basic science level, Dr. Kokko has explored the regulatory role of an inflammatory cytokine, interleukin-15, on the maintenance of T lymphocyte memory to a transplanted organ. In collaboration with Dr. Chris Larsen, Dr. Kokko is studying the effects of immunosuppression on the protective immunity to various viral pathogens such as BK polyoma, influenza and vaccinia. In collaboration with Dr. Kenneth Newell, Dr. Kokko is studying the utility of novel immunologic assays as a predictor of which patients can undergo immunosuppressive reduction safely. Dr. Kokko serves on the evaluation committee for renal transplantation and is a member of the renal transplant leadership group.
Dr. Larsen is an expert in transplantation surgery, immunology and immunotherapy. With the aid of significant grant funding, his research with Drs. Pearson, Newell and Kirk works to establish true immune tolerance among transplant recipients. This research strives to free patients from the toxic side effects of daily immunosuppressant medicines and achieve permanent, long-term acceptance of organs. Areas of primary research focus in his laboratory include: (1) understanding the fundamental mechanisms involved in the T cell response to transplant tissues, specifically the role of costimulatory pathways in T cell activation, and (2) the mechanisms involved in immunologic tolerance to self and transplanted tissues. Drs. Larsen and Pearson have a strong track record of bringing research to the patient – their research in co-stimulation blockade has been brought from basic research in the early 1990s through the primate center and into highly successful clinical trials in humans led by Emory to apply these strategies to the development of a clinically relevant means to achieving hematopoietic chimerism as a route to clinical transplantation tolerance. Among his many appointments, Dr. Larsen is Professor and holder of the Carlos and Marguerite Mason Chair, Director of Emory Transplant Center, Vice Chairman of Research-Surgery, and Director of Mason Transplantation Biology Research Center. In recognition of Dr. Larsen's "outstanding contributions and preeminence in the field of transplantation", he was honored as the recipient of the 2007 Thomas E. Starzl Prize in Surgery and Immunology in March 2007 at the University of Pittsburgh.

Recent Publications (2006 - 2007)


S. Raja Laskar, MD

Dr. Laskar is a graduate of Emory University School of Medicine. His internal medicine and cardiology training was at the University of Texas Southwestern. He joined the Emory and the Center for Heart Failure Therapy in 2004. He is actively involved in the numerous clinical trials involving heart failure, mechanical circulatory support, and heart transplantation.
E. Clinton Lawrence, MD

E. Clinton Lawrence, a native Texan, received his BA from the University of Texas at Austin and MD from the University of Texas-SOUTHWESTERN Medical School, both in 1973. After a residency in Internal Medicine at the University of California-San Francisco, Dr. Lawrence performed immunology research at the National Cancer Institute, National Institutes of Heath, where he developed an interest in the lungs' immune system. He then pursued pulmonary subspecialty training at Baylor College of Medicine after which he joined the faculty, establishing and directing first the Rockwell-McKelvey Pulmonary Immunology Laboratory, followed by the heart-lung and lung transplantation programs. After a brief period as co-medical director of lung transplantation at Stanford University School of Medicine, Dr. Lawrence was recruited to Emory in 1993 as Professor of Medicine and Medical Director of Lung Transplantation. In 2001, Dr. Lawrence was appointed Director of the newly established Andrew J. McKelvey Lung Transplantation Center at Emory University School of Medicine. The focus of his research is to determine the mechanisms of acute and chronic rejection following lung transplantation and to develop alternative medical treatments for end-stage lung diseases. He has authored more than 80 original articles and book chapters.

Recent Publications (2005 - 2006)


Robert S. Mittler, Ph.D

The focus of Dr. Mittler’s individual research program is the study of mouse and human T-cell costimulation pathways that are essential for productive T-cell responses to foreign antigens. In this context, they hope to learn how to artificially regulate immune responses in humans, either to enhance the response in situations of immunodeficiency and tumorigenesis or to selectively diminish the response to organ transplantation or in autoimmune diseases. They have focused upon T-cell activation regulated by the PD-1 receptor, a negative regulator of T cell activation, and the 4-1BB receptor an activator of T cells. PD-1 is a member of the CD28 family but unlike the CD28 T cell costimulatory receptor, its function is to counterbalance immune
activation by turning it down. By blocking this signaling pathway, in conjunction with anti-4-1BB immunotherapy Dr. Mittler’s team hopes to enhance the establishment of anti-tumor immunity to refractive, advanced neuroblastoma and Ewing’s sarcoma, two of the most common and fatal childhood cancers. They further believe that this therapeutic strategy will lead to stronger and more durable immune responses to chronic viral infection. The CD137 receptor (AKA 4-1BB) is an activation inducible member of the Tumor Necrosis Factor Receptor Superfamily (TNFR). A key finding has been that in the mouse, CD137 receptors are preferentially used to activate CD8+ T-cells even though both CD4 and CD8 positive T cells express them. Dr. Mittler’s team collaborating with Drs. Chris Larsen and Tom Pearson was also the first to show that administration of monoclonal anti-CD137 antibodies into mice receiving skin or cardiac allografts rejected their grafts much more rapidly than mice injected with a control mAb. In Drs. Newell and Mittler showed that blockade of the CD137 signaling pathway in mouse small intestine allografts led to graft acceptance. Chris Gilson, a PhD candidate in the Larsen/Pearson lab is now working with Dr Mittler’s group to see whether controlled use of CD137 blocking or activating agents (fusion proteins and mAbs) can replicate the findings of Newell and Mittler in skin allograft transplants. Dr. Mittler’s lab were also the first to show that anti-CD137 mAbs proved remarkably effective in completely eradicating established poorly immunogenic tumors in mice. Subsequently Dr. Mittler’s group provided the first long-term comprehensive study that showed that anti-CD137 treatment reversed the course of established SLE and RA in mice and that the treated lupus mice that normally die before one year of age survived for over two years, the normal lifespan of a mouse. Collectively, these studies have led to the U.S. Patent office to award Dr Mittler and his collaborators three U.S. patents for the use of agents that bind to and affect CD137 function. The last of these was awarded in May 2007.

Recent Publications (2006 - 2007)


Dr. Mora joined the Division of Pulmonary, Allergy and Critical Care at the Emory School of Medicine in summer 2002, to investigate mechanisms of immunopathogenesis in Idiopathic Pulmonary Fibrosis (IPF). IPF is a progressive, fibrotic, interstitial lung disease of unknown etiology. No proven effective treatment is available, other than lung transplantation. Spontaneous remissions do not occur and death due to respiratory failure usually ensues within three to five years of diagnosis. Dr. Mora’s clinical evidence shows that more than 95% of IPF patients have chronic pulmonary infection with one or more herpesviruses. To determine the potential for developing chronic pulmonary herpesvirus infection as an animal model of IPF, Dr. Mora’s team sought information on the pathophysiologic effects of a herpesvirus infection in animals. MHV-68 is a natural pathogen of rodents that is closely related to the human gamma herpesviruses, HHV-8 and EBV. Their studies indicated that chronic lung infection with MHV68 of IFNγR/- mice causes epithelial damage and inflammatory responses that evolve into progressive pulmonary fibrosis. The histopathological features of the pulmonary disease in their experimental model coincide with many of the patterns that are described in the lungs of IPF patients. These changes in the lung were accompanied by derangement in alveolar Type II cells which has been reported in some families with familial IPF. Currently we are using this animal model to determine molecular mechanisms involved in disrepair of the injured lung and to define future treatments for IPF.
Recent Publications (2006-2007)


David Neujahr, MD

Dr. Neujahr has joined the Transplant Center after finishing a fellowship in Pulmonary diseases at the University of Pennsylvania. Dr. Neujahr is engaged in a longitudinal study of the immune system in patients following lung transplantation. The goals of the research are to identify patients who are at risk of accelerated graft loss through the use of novel immune monitoring strategies. This research takes advantage of the unique opportunity to collect immune cells which have migrated into the lung allograft using fiberoptic bronchoscopy.

Kenneth A. Newell, MD, PhD, FACS

Basic: Clinical evidence such as inferior graft survival and increased rates of rejection demonstrate that intestinal allografts are uniquely immunogenic. Our laboratory has shown that this is at least in part due to a strong immune response mediated by CD8+ T cells. Importantly, some biologic therapies that inhibit CD4+ T cell function do not impair CD8+ T cell function to the same degree. We have therefore explored alternative strategies for inhibiting CD8+ T cell function including detailed investigation of several TNF receptor superfamily molecules including CD154, membrane lymphotoxin, 4-1BB, and LIGHT. These experiments suggest potential targets of intervening in the immune response to intestinal allografts but also provide more basic insights into the behavior of CD8+ T cells that may be applicable to other disease processes such as autoimmunity and immunity to viral infections and tumors. Recently we have expanded our studies to include an examination of tissue specific factors that may contribute to differences in the nature of the immune response to different organs. The intestine posses a
unique immunologic microenvironment which includes organized secondary lymphoid tissues, specialized immune cell populations, and unique chemokines and integrins to regulate cell trafficking. Our data demonstrate that the secondary lymphoid organs within the transplanted intestine contribute to the process of intestinal allograft rejection and may contribute to the unique immunogenicity of transplanted intestines.

In collaboration with Drs. Christian Larsen and Aron Lukacher we have undertaken studies designed to understand the immune response to polyoma BK virus (BKV) following transplantation. BKV is a common, usually asymptomatic virus that persists in the renal tubular cells of healthy individuals. Over the last decade BKV has emerged as a major pathogen leading to dysfunction and failure of transplanted kidneys. However, little is understood about the mechanisms responsible for the control of BKV following renal transplantation. Making use of unique microsurgical models in mice and immunologic reagents available through the ETC we have submitted an R01 application to the NIH to further investigate BKV-induced nephropathy and evaluate new therapeutic approaches.

Clinical: Outcomes of transplantation have continued to improve dramatically over the last three decades. This is at least in part due to the development of more and better immunosuppressive agents. However, the long-term reliance upon drugs that globally suppress the immune system is associated with numerous deleterious side effects. For this reason, immunosuppressive drug minimization or withdrawal is now an important focus of the transplant community. Two NIH funded projects seek to address this issue. In the first funded project we are studying patients who have maintained excellent graft function despite no longer taking immunosuppressive drugs. This small cohort is recruited from around the world for the purpose of gathering patient data and clinical material to evaluate potential assays predictive of “tolerance”. The results obtained will be compared to several other groups of transplant recipients. A second set of NIH-sponsored trials is intended to develop and validate assays for the purpose of guiding decisions about immunosuppressive drug management. This project is a collaboration among investigators at the Cleveland Clinic, Case Western Reserve, the University of Manitoba, Brigham and Womens’ Hospital (Harvard), the University of California San Francisco, Yale University, and Emory University. It is comprised of a number of sub-studies aimed at developing assays to monitor both the cellular and humoral response to organ allografts and then to use these assays prospectively to manage immunosuppressive medications following kidney, heart, and lung transplantation.

A second major factor contributing to the dysfunction and premature loss of transplanted kidneys is the continued dependence upon nephrotoxic immunosuppressive drugs to prevent rejection. In an investigator-initiated single center study we will examine the potential of efalizumab, an antibody specific for LFA-1 which has been shown to be immunosuppressive and is FDA approved for the treatment of psoriasis, to replace nephrotoxic calcineurin inhibitors following transplantation. This study will also make use of new strategies to monitor the immune response following transplantation that are under development at the ETC.
Recent Publications (2006 – 2007)


Andres Pelaez, MD

Dr. Pelaez has established a protocol to analyze the relationship between chronic alcohol ingestion in lung transplant donors with the incidence of primary graft dysfunction in lung transplant recipients. He aims to test the hypothesis that alcohol use renders the donated lungs susceptible to oxidative injury, thereby triggering a cascade of events which leads to graft loss. By understanding the redox capacity of donated lungs, clinicians would have a better way of predicting which patients are at risk of adverse events.
T cells play a central and critical role in the rejection of transplanted organs. Dr. Pearson’s research has focused on better understanding the critical factors for T cell activation and function and the development of novel strategies to block the rejection response. These investigations have involved the development and assessment of novel immunomodulatory strategies in rodent models and pertinent pre-clinical testing in non-human primates. These investigations, on the whole of the costimulatory pathways and the alloimmune response, have the ultimate goal of developing a clinically relevant strategy to induce permanent long-term tolerance to transplanted organs in humans.

Recent Publications (2006 - 2007)


The focus of Dr. Perryman’s research is on the bio-psychosocial, economic and access issues related to organ transplantation and donation, including 1) the development of clinical practice models to improve organ donation rates in acute care settings; 2) the study of donation decision making within the African American family relative to both living and deceased donation, and 3) access of African-Americans to wait listing and transplantation. Currently, Dr. Perryman is the co-primary investigator on a five-year qualitative study of the African-American family in the donation decision-making process, being conducted with colleagues in the Rollins School of Public Health (RSPH) of Emory University with funding by NIDDK. Through the analysis of qualitative data generated from family focus groups and individual family member interviews, culturally-sensitive interventional education materials have been developed and are being tested in randomly selected study sites to determine their effectiveness over time when compared with standard materials currently used in the African-American community. Dr. Perryman’s other research focus, again being conducted with colleagues from RSPH compares donation, listing and transplantation rates of African-Americans in Georgia to states nationally and in the southeastern over a ten-year period of time. Upon completion of the quantitative analyses, a qualitative study has been initiated to conduct interviews; review of selection criteria, processes, practices, and, perform content analyses of educational materials of four transplant centers within the high ranking states with comparison of Georgia transplant center. Additionally, in Georgia interviews of nephrologists, dialysis clinic staff, African-Americans on dialysis and their families are underway to identify those variables which may negatively influence transplantation of African Americans and to develop interventions to improve Georgia’s rates of donation, listing and transplantation with the African American end-stage renal disease population.
Dr. Ramirez recently received an NIH KO8 award to study the effects of TGFbeta on the intracellular signaling molecules PPARgamma and Smad3. Using a mouse model of lung transplant, Dr. Ramirez has shown that increased levels of TGFbeta lead to increased Smad3 phosphorylation and subsequent increased in matrix genes responsible for chronic airway remodeling such as seen in bronchiolitis obliterans. Augmentation of PPARgamma using PPARgamma agonists represents a novel way to decrease Smad3 activation and uncouple the link between TGFbeta and chronic rejection.

As an investigator at the Emory Transplant Center, Dr Rigby primarily studies the immunopathogenesis and prevention of Type 1 diabetes mellitus. Type 1 diabetes mellitus is an autoimmune disease which targets the destruction of the pancreatic beta cells. The Emory Transplant Center is on the forefront of better understanding mechanisms of unwanted immunity, primarily using transplant models. As the cellular mechanisms of transplant rejection and autoimmunity likely have significant overlap, progress in both of these fields helps each other. They directly come together in the study of islet cell transplantation as a cure for T1DM. Islet transplantation is a research focus of Dr. Rigby as well as a clinical investigation focus for Emory Transplant Center. Dr. Rigby’s lab uses animal and cellular models to understand the immunopathogenesis of T1DM such as to identify mechanisms that can be (1) interrupted to prevent disease or (2) modified to allow for immune tolerance induction and therefore allow for immunosuppressive-free islet transplantation. Specifically we are using the NOD mouse model, transgenic diabetogenic T cells, and adoptive transfer systems to identify pathways involved with cellular activation of pathogenic T cells. Other studies are using well-defined reagents to interrupt select T cell activation and survival signals to prevent primary disease or disease recurrence after islet transplantation. In addition, Dr. Rigby is assisting in the Transplant Center in the evaluation of patients receiving islet transplants for Type 1 diabetes and studies in non-human primates optimizing islet transplantation with the goal to make islet transplantation more efficacious and generalizable therapy. With these combined efforts we hope to translate “basic” research on diabetes to clinical benefit.

Recent Publications (2006 – 2007)
Rigby, MR, Alison M. Trexler, AM, Pearson, TC, Larsen, CP. CD28/CD154 blockade prevents autoimmune diabetes by inducing nondeletional tolerance following effector T cell inhibition and regulatory T cell expansion. (Submitted)
Preissig, CM, Hansen, I, Roerig, PL, Rigby, MR. Hyperglycemia is common, can be safely and effectively managed using a protocolized approach, and treatment appears to improve survival in pediatric critical care. (Submitted)


Mauricio Rojas, MD

Dr. Rojas joined Emory University in 2002 as an Assistant Professor in the Division of Pulmonary, Allergy and Critical Care Medicine at Emory University and as a Scholar of the McKelvey Lung Transplantation Center where he has been involved in the develop of novel therapies for lung disease, which includes the use of gene therapy, protein therapy and cell therapy. The results of his research efforts have been published in numerous scientific journals including The Journal of Infection Disease, Parasite Immunology, Vaccine, The European Journal of Immunology, The Journal of Immunology, Lancet, Biochemical and Biophysics Research Communication, Journal of Peptide Research, Nature Biotechnology, Journal of Biological Chemistry, Autoimmunity, American Journal of Physiology and Lung Cell Molecular Physiology, American Journal of Respiratory Cell, Molecular Biology, Gastroenterology, American Journal Respiratory and Critical Care Medicine. In addition, Dr Rojas serve as reviewer for several journals including: TiPS, Critical Care Medicine, American Journal of Respiratory and Critical Care Medicine, American Journal of Physiology Lung Cellular and Molecular Physiology and Inflammation Research, Cytotherapy and international editor of the Journal of Clinical Rehabilitative Tissue Engineering Research.


Recent Publications (2006 – 2007)


Holguin F., Rojas M and Hart M. The peroxisome proliferator activated receptor gamma (PPAR[gamma]) ligand, rosiglitazone, modulates bronchoalveolar lavage levels of leptin, adiponectin and inflammatory cytokines in lean and obese mice. *in press LUNG194R2*

### Andrew L. Smith, MD

Andrew L. Smith received a B.S. from Davidson College in 1980 and his M.D. from Emory University School of Medicine in 1984. A year later, he completed an internship in internal medicine at Emory University Affiliated Hospitals. He did an internal medicine residency at Temple University Hospital, where he later was a Fellow in Clinical Pharmacology, and in 1990 he completed a Cardiology Fellow at Temple. In 1991, while a junior faculty cardiologist there, Dr. Smith interviewed an Emory cardiac transplant surgeon interested in a position at Temple. Shortly thereafter, Smith was recruited to Emory to be the medical director of the Heart Failure and Transplant Program; and in 1992 he established the Emory Center for Heart Failure Therapy, a specialized program for patients with advanced heart failure. The referral program, which implements the use of new drugs, medical devices, and educates patients in lifestyle management, has served as a model for other medical practices in Georgia. Smith’s research focus is on improving the outcomes of patients with cardiomyopathy and congestive heart failure, and also improving outcomes in patients before and after cardiac transplantation. To that end, he serves on a national steering committee whose goal is to improve outcomes of patients with heart failure through education of other healthcare professionals. His work continues to be supported by numerous grants. Smith is author or coauthor of numerous publications that include abstracts, journal articles, and book chapters. He is a manuscript reviewer for the *Journal of American College of Cardiology* and the *Journal of International Society of Heart & Lung Transplantation.*
He is the recipient of the J. Willis Hurst Excellence in Teaching Award (Cardiology Fellows’ Award) and the Woodruff Fund Clinical Teaching Support Award in Medicine.

James R. Spivey, MD

Dr. James Spivey comes to Emory as the new Medical Director of the Liver Transplant Program after 12 years with the Mayo Clinic where he served as a consultant in the division of Gastroenterology and Assistant Professor of the Mayo Medical School. Dr. Spivey moved to the Mayo Clinic in Jacksonville, FL where, in 1998, he helped begin their solid organ transplant programs. Dr. Spivey served as Chief of the Division of Transplant Medicine in the Department of Transplantation. He is a graduate of Tulane Medical School and completed his Hepatology fellowship at the University of Miami.

Andrei C. Steiber, MD, FACS

Dr. Steiber is an active participant in clinical research and focuses his time on the teaching of residents and fellows. He was recently awarded a Golden Apple award by the Chief Residents.

Paul L. Tso, MD, FACS

Dr. Paul Tso is a provider of surgical care for the kidney and pancreas transplant patients of The Emory Transplant Center. He also provides dialysis access for the renal failure patients in the community. His areas of interest include machine perfusion of kidneys and if it can be more broadly applied in our transplant center and OPO. Dr. Tso is an active mentor for third year medical students on surgery rotation and is active in resident education for Emory, Morehouse and Atlanta Medical Center residents.

Recent Publications (2006 – 2007)

J. David Vega, MD, FACS

Dr. Vega's major research themes include mechanical circulatory support, cardiac transplantation, organ preservation, immunosuppression and lung transplantation. He is Chair of the OPTN/UNOS Thoracic Organ Transplantation Committee and a member of the HRSA Advisory Committee on Organ
Transplantation, the OPTN/UNOS Heart Sequence Task Force, the ASTS Thoracic Organ Transplantation Committee, and the American College of Surgeons Advisory Council for Cardiothoracic Surgery.


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**Collin J. Weber, MD, DM Sci, FACS**

Dr. Weber’s research focus is pancreatic islet transplantation. The long-term goal is to develop techniques for safe and durable islet cell replacement for large numbers of patients with insulin dependent diabetes mellitus. For the past several years, this research has concentrated on the use of xenogeneic tissues as sources of donor islets and microencapsulation plus selective immune modulation of hosts as the means to accomplish cross species islet graft survival. A second focus of research is cause(s) of human parathyroid tumors and their functional characteristics. These studies have concentrated on secreted products of human parathyroid tumors including neuropeptides and cytokines and analyses of replication of parathyroid tumors of differing histopathology.

Researchers Dr. Weber and Dr. Susan Safley are studying transplantation of endocrine cells, such as pancreatic islets and parathyroid cells. Unlike whole organ transplants, cell transplants may be protected from host immune responses by use of microcapsules as immunoisolation barriers. To block islet xenograft rejection, diabetic NOD mice were given CTLA4-Ig (a soluble fusion protein that blocks B7/CD28
interactions) and/or MRI (a mAb that interferes with CD40/CD154 binding). Microencapsulated islets functioned (bg<250 mg/dl) 13 ± 2 days (n=38); MRI treatment (days 0, 2, 4, and 6) did not prolong survival (11 ± 1days) (n=8). CTLA4-Ig (every other day for 21 days) extended graft survival to 24 ± 3 days (p<0.002, n=29); MRI + CTLA4-Ig further prolonged function to 57 ± 5 days (p<0.001, n=14). In all groups, graft failure was accompanied by a profuse peritoneal cellular infiltrate of macrophages, neutrophils, eosinophils, CD4+ and CD8+ T cells, suggesting that failure was due to rejection. By contrast, chronic treatment with MR1 + CTLA4-Ig extended graft survival to 111 ± 12 days (p<0.002, n=9), over 200 days in some animals. The profile of PEC from these mice was similar to untransplanted control diabetic NODs and was not characteristic of immunologic rejection. Biopsies of 3 mice with functioning grafts (days 130, 144, and 169 post-transplant) revealed intact microcapsules containing healthy islets with no apparent host cellular reaction. These data show that islet microencapsulation plus costimulatory blockade of host immune responses promotes long-term to indefinite survival of porcine islet xenografts.

A second area of research involves studies of secreted products of parathyroid tumors. Parathyroid hormone (PTH) stimulates osteoblasts to produce the proinflammatory cytokine interleukin-6 (IL-6), causing bone resorption. In patients with primary hyperparathyroidism, elevated serum levels of IL-6 normalize after resection of parathyroid tumors. Since IL-6 is also expressed in normal parathyroids and in other endocrine cells (adrenal and islet), we hypothesized that parathyroid tumors might contribute directly to the elevated serum IL-6 levels in patients with hyperparathyroidism. Immunohistochemistry identified IL-6, PTH, and chromogranin-A (an endocrine and neuroendocrine tumor marker) in normal, adenomatous, and hyperplastic parathyroids. By immunofluorescence and confocal microscopy, IL-6 co-localized with PTH and with chromogranin-A in parathyroid cells. All cultured parathyroid tumors secreted IL-6 at levels markedly higher than optimally stimulated peripheral blood mononuclear cells. Supernates from cultured parathyroids stimulated proliferation of an IL-6-dependent cell line, and anti-IL-6 mAb abolished this stimulatory effect. IL-6 mRNA was documented in cultured parathyroid tumors, cultured normal parathyroids, fresh operative parathyroid tumors, and fresh operative normal specimens. In conclusion, these data show that parathyroid tumors and normal parathyroids contain, produce, and secrete IL-6. Our findings present a novel pathway by which human parathyroids may contribute markedly to IL-6 production and elevation of serum IL-6 levels in patients with hyperparathyroidism. The physiologic relevance of IL-6 production by human parathyroids remains to be determined, but IL-6 secretion by parathyroid tumors may contribute to bone loss and to other multi-system complaints observed in these patients.
VI. RESEARCH FUNDING

The following table provides a breakdown of our funding.

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The Center has been the fortunate recipient of significant private and foundation funding not reflected in the totals above or the specific investigator awards below. For FY 06-07, these gifts total $10,900,000.
# VII. CONTACT INFORMATION

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<thead>
<tr>
<th>CONTACT</th>
<th>PHONE AND EMAIL</th>
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