The following report on the Department’s research activities was prepared by the research committee and presented to Dean Alderson in May 2008.

**Executive Summary**

The Department of Internal Medicine has developed and maintained strong research programs with national and international visibility and recognition. Some of the strongest programs are housed in the Divisions of Cardiology and Geriatric Medicine, the Saint Louis University Liver Center, and the Center for Vaccine Development.

The work done in these programs has strongly influenced American medicine over the last 2 decades. This is illustrated in the attached report on publications from the faculty of the Department of Internal Medicine which presents an analysis of the impact that key members of the Department have had. In addition, we list examples of our publications from the last 5 years in *The New England Journal of Medicine*, *JAMA*, and other high impact journals.

A summary of research being conducted by the Division of Cardiology, the Division of Geriatrics, the Saint Louis University Liver Center, SLUCOR, and the Center for Vaccine Development is presented.

Other attachments include a summary of a proposal to create a Center for Excellence in Translational Vaccine Immunobiology Research that has been submitted to the Provost for consideration and represents an example of how research within the Department of Internal Medicine can be leveraged across the School and University. We include a University press release regarding the renewal of the NIH funded Vaccine Center. Combined, the Department of Internal Medicine has a portfolio of more than $50 million in research funds that have been awarded for the next several years. A summary of that funding is presented.

### Impact of Department of Internal Medicine Publications

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Departamental Research Activities

High Impact Publications
2003-2008

The New England Journal of Medicine


DEPARTMENTAL RESEARCH ACTIVITIES

The Journal of the American Medical Association


The Journal of Biological Chemistry


Nature Medicine


Nature Neuroscience


Science


DEPARTMENTAL RESEARCH ACTIVITIES

Annals of Internal Medicine


Proceedings of the National Academy of Sciences USA


Lancet


Lancet Neurology


Cardiology Research

The cardiology section has well established National and International Core laboratories that contribute outcomes research to NIH clinical trials and industry in the areas of electrocardiography, echocardiography, ventricular function assessment and ACS classification. Current multicenter NIH funded trials include BARI-2D, a trial investigating the role of coronary revascularization and optimal diabetes management on death and MI, the AIM-HIGH trial investigating the impact of HDL elevating therapy in subjects with low LDL cholesterol on the outcomes of death, MI and stroke, WARCEF, a trial that examines various anticoagulation regimens in atrial fibrillation and effectiveness in reducing embolic stroke, and FOCUS, a trial examining what cut-point to blood transfuse patients after hip fracture surgery. The focus of selected industry sponsored trials are to examine (1) novel oral antithrombotic agents to reduce stent thrombosis and ACS, (2) treatment strategies to improve QOL in heart failure, (3) perfusion and contrast imaging agents that enhance resolution (4) pacemaker...
device studies to improve QOL and survival (5) gene therapy to improve LV function and (6) small animal studies as part of the SLU cardiovascular research institute.

Research in the Division of Geriatrics

The research in geriatrics is multidisciplinary and translational. It includes the research efforts of the Geriatrics Research Educational and Clinical Center (GRECC) at the VA and of outlying nursing homes. Efforts include development of clinical assessment tools, industry sponsored research including that designed or initiated by SLU researchers, and national and international studies on basic and clinical research. SLU geriatric research is integrated with other SLU research entities such as SLUCORE, the Department of Pharmacology & Physiology and the Department of Psychiatry. Research from geriatrics has resulted in several patents and one biotech start up company, the latter testing a novel class of drug in the reversal of Alzheimer's disease. Examples of major projects or grants from Geriatrics include the African-American Inner City initiative, a multi-year, NIH-funded study of health outcomes measures in inner city St. Louis; effects of testosterone treatment on health outcomes in aging males; relations of proinflammatory markers to functional status in nursing home populations and studies of nutritional status in older persons. Basic science projects funded at the R01 or VA merit review level include the role of calcium and vitamin D in the pathophysiology of aging, mechanisms of nitrosamines in prostatic cancer, mechanisms of HIV and prion entry into the central nervous system, role of blood-brain barrier efflux systems in mediating Alzheimer's disease and alcohol withdrawal seizures, development of CNS active drugs in the treatment of Alzheimer's disease and obesity, mechanisms of alcohol in the induction of cognitive deficits. Over the 19 years since its inception the division has consistently been among one of the best funded divisions in the Department of Medicine. Dr. Morley is among the top 10 cited scientists in geriatrics in the world and the only active clinician on this list. Dr. Banks is also highly cited. In addition, the program has had a large Bureau of Health Professionals grant for 17 years to provide and study geriatric education. Two in the division have Federal Grants for young faculty development.

Saint Louis University Liver Center

The Saint Louis University Liver Center continues to be a viable entity with over 40 members, regular conferences and a funding source for clinical and basic investigation within the University. Both clinical and basic research activities are active. The GI/Hepatology Clinical Studies Unit sees between 125 and 130 clinical research patients each month for ongoing research protocols and in FY ’07 and ’08, we had over 40 active clinical industry funded protocols. Members of this multidisciplinary Liver Center were either principal investigator or co-investigator on 39 NIH, VA or Foundation grants in FY ’07 and ’08. Over five years of fundraising events, The Friends of the Saint Louis University Liver Center organization has raised $1.6 million to support research and education for the Saint Louis University Liver Center. A total of eleven Liver Center grants have been awarded over the past three years through an RFA process. These directed research grants were established to provide bridge funding to Liver Center investigators while they work toward developing their projects, gathering preliminary data allowing them to submit NIH grant applications and publish their results. The 11 grants that were awarded total $360,000. These bridge funds generated seven NIH, VA and foundation awards totaling $5,543,550, which represents more than a 17 fold return on investment. More than 120 original papers, chapters, reviews and editorials were published by Liver Center members in FY07-08.

SLUCOR

The Saint Louis University Center for Outcomes Research (SLUCOR) is striving to become a nationally known center known for excellence in translational research and graduate education. SLUCOR is home to 5 full time PhD and MD faculty, staff, doctoral and post-doctoral students with formal training in biostatistics, economics, epidemiology, outcomes assessment, informatics, psychology and medicine.

While collaborating on research in a broad range of clinical disciplines, SLUCOR’s primary research is focused in three outcome areas: 1) organ transplantation, 2) diabetes and 3) cardiovascular disease. Multidisciplinary research teams have been established in each of these areas, with organ transplantation, under the leadership of Dr. Mark Schnitzler, being the most advanced and best example. This multi-university team consists of more than 15 faculty (transplant surgeons, nephrologists, HLA lab directors, statisticians, economists and psychologists), the SLUCOR analytic team and PhD
DEPARTMENTAL RESEARCH ACTIVITIES

students. SLUCOR provides academic leadership for the group and serves as the data and analytic center for most of the studies, facilitating strong research collaboration. This team-based approach has provided an effective and efficient strategy for managing a relatively large number of studies and maximizing academic productivity. It can serve as a model for additional areas of clinical and translation research.

SLUCOR has methodological cores for data management, biostatistical/economic analyses, instrument development, data collection and budget/regulatory. It has recently completed the development of a computer-aided telephone interviewing center for an NIH funded grant. SLUCOR also has the internal capability for the development and deployment of large volume surveys via the internet, telephone interviewing and scannable forms. Without university support, however, these cores are not financially viable.

Across the past three years, SLUCOR has established formal relationships with some of the largest insurers, pharmacy benefit management companies, and registries in the United States which collectively provide access to clinical data on more millions of Americans. The data provides multiple years of clinical, laboratory, pharmacy and economic data to be linked at the individual patient level. Aggregated together, these data serve as a unique vehicle for studying disease, outcomes, and healthcare costs at a national level. This research bridges the clinical and public health components of translational research.

SLUCOR has the potential to serve as a formal research and training bridge between the School of Medicine and School of Public health – strengthening SLU’s potential for funded translational research. In 2005, SLUCOR launched a PhD program in Health Services Research in 2005. This program is designed to provide future scientists with extensive training in outcomes measurement, biostatistics and economic analyses, informatics, public policy and clinical medicine. This year, Dr. Burroughs assumed the role of co-director of all PhD programs in the School of Public Health.

SLUCOR has had several substantial barriers to its long-term success. 1) Initial efforts to serve as a biostatistical consulting service to the university were not financially viable without core university support which was not forthcoming. 2) SLUCOR did not receive the tuition support agreed to by the university in its first two years of the doctoral program, and 3) SLUCOR tenure-track faculty do not receive the hard-dollar salary support given by the university to tenure track faculty outside of the School of Medicine. Notwithstanding these barriers, SLUCOR has the potential to play a major role the development of translational research at SLU. It is positioned to serve as a formal bridge between medical and public health research, and can serve as a mechanism to get clinical faculty actively involved in funded research.

Center for Vaccine Development and Projected Goals

A comprehensive proposal detailing scientific plans to continue and expand the VTEU efforts was successfully submitted to NIH and a seven year award totaling $23 million was subsequently signed by Saint Louis University in November of 2007. Key features of the VTEU renewal and Vaccine Center include:

1) Respiratory virus vaccine development. Continuing efforts are focused on development and evaluation of avian influenza virus vaccines, human influenza vaccines, parainfluenza vaccines, and RSV vaccines. Our strength is respiratory vaccine development, and we propose to collaborate with industry to further develop our intellectual property of our patents on parainfluenza 3 vaccines (croup vaccine) for children.

2) Biodefense vaccine development. Previously our Vaccine Center played a key role in demonstrating that smallpox vaccine could be diluted 1:5 or 1:10 to expand and successfully vaccinate volunteers. This effectively expanded the available smallpox vaccine for the nation. Additional projects are ongoing with the development of more attenuated smallpox vaccines, including MVA. We are collaborating with Washington University and the MRCE for these studies.

3) Herpes virus vaccine projects. We are continuing to evaluate Herpes Simplex vaccine for the NIH as a gender-specific vaccine for young women. More than 8,000 participants are enrolled in the Herpevac Trial for Women. Saint Louis University is coordinating 50 other academic centers to evaluate this vaccine.

4) Collaborations between the Vaccine Center and the Immunobiology Division are strong. Dr. Dan Hoft has conducted a series of TB vaccine trials and related basic research in TB immunity which have been internationally recognized. This work has resulted in additional funding to support studies of new TB vaccines and strategies from the Gates Foundation, WHO and the NIH sponsored TBRU. Dr. Hoft has also successfully collaborated with the Vaccine Center studying regulatory T cell responses protective against smallpox and pandemic flu. The recruitment of 3 new immunobiologists within Immunobiology will bring the potential for exciting new
collaborations. He is expanding these efforts and developing other sources of funding to expand this important research.

5) Strong collaborations between the Vaccine Center and the Liver Center are continuing for the development of hepatitis C vaccine. Both prophylactic hepatitis C vaccines and therapeutic hepatitis C vaccines are anticipated in the coming years. Ongoing studies with a prophylactic hepatitis C vaccine continue.

6) Dr. Sharon Frey has recently received a $1 million grant from the Gates Foundation to evaluate salmonella vaccines.

7) Additional proposals under development include clinical projects evaluating flavivirus vaccines (dengue fever, and West Nile fever) development.

We propose expanding faculty resources and bringing on young faculty to ensure growth and to replace older faculty as they retire. Taking full advantage of the DRC and proximity to research faculty in other departments will lead to enhanced funding opportunities. The Vaccine Center is a national resource and we propose to encourage other schools at SLU to conduct bridging research such as public health policy in vaccines use (SPH) or legal issues with vaccine use (Law School).

University Press Release on the VTEU Renewal

The National Institutes of Health has renewed the Saint Louis University Vaccine and Treatment Evaluation Unit (VTEU) contract for another seven years. “This is a feather in the cap for the Department of Medicine and the University” said Dr. Robert Belshe, Principal Investigator of the Vaccine and Treatment Evaluation Unit at Saint Louis University. “Funding for 7 years will allow us to conduct long-term projects and do substantial planning for contributing to improve vaccines and healthcare for the United States.”

The Vaccine Center renewal comes at an opportune time with the development of the new Doisy Research Building. The Vaccine Center currently occupies laboratories on the 8th floor and the clinic on the 1st floor for clinical trials. Recent clinical projects include evaluation of novel vaccines for influenza, including the live attenuated influenza vaccine available for children and adults age 2-49. Ongoing projects include clinical studies with avian influenza vaccine (H5, “the bird flu”). Additional ongoing studies include the Herpevac Trial for Women; Saint Louis University is coordinating 50 other academic centers to evaluate a subunit vaccine for HSV2 in women age 18-30. More than 8,300 women are participating in the efficacy field trial.

Past successes include evaluating haemophilus conjugate vaccines in infants, pneumococcal vaccines in infants and adults, evaluation of efficacy of acellular pertussis vaccines in college students, and improved vaccines for tuberculosis (BCG recombinant vaccines). Collaborations between the Vaccine Center and the Liver Center are important to the Department and to the research community. This collaboration led to the first in human studies of a prophylactic vaccine for hepatitis C. “These studies are ongoing and may lead to therapeutic vaccine trials,” said Dr. Di Bisceglie.

The Division of Infectious Diseases and VTEU have significant collaborations beyond the University, including the Midwest Research Center for Excellence for Biodefense Studies. Dr. Sharon Frey has chaired several key studies of new second and third generation smallpox vaccines for the NIH, and she has become nationally known in this area. The new Immunobiology Division chaired by Dr. Dan Hoft is another important collaboration for the study of immune responses to vaccines.
## DEPARTMENTAL RESEARCH ACTIVITIES

**SAINT LOUIS UNIVERSITY**  
DEPARTMENT OF  
RESEARCH  
FISCAL YEARS

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