

History of research activities at Baylor University Medical Center

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By the early years of the 21st century, Baylor Health Care System (BHCS) and Baylor University Medical Center (BUMC) had a well-developed research center—Baylor Research Institute (BRI)—that was able to sponsor significant basic and clinical research, with an emphasis on immunology. Even absent a large, full-time medical school faculty, Baylor had by the 1980s earned high standing in research—standing comparable to that of large, well-regarded community medical centers elsewhere in America. This article documents early research efforts, the founding of BRI and the Baylor Institute for Immunology Research (BIIR), administrative activities of BRI, and current research activities.

EARLY RESEARCH EFFORTS

Numerous physicians and scientists contributed to the development of research on the Baylor campus: Dr. Walter H. Moursund, when Baylor University College of Medicine was part of the Baylor-in-Dallas concept; medical staff members who devoted part of their time to research in the 1940s through the 1970s; Dr. LeRoy J. Kleinsasser, the first physician recruited specifically to conduct research; and medical staff members who conducted significant research while devoting virtually all of their time to patient care, even before there was an organizational entity dedicated to research. Among the medical staff members active in research prior to 1980 were Drs. Benjamin Franklin Hambleton, Joseph M. Hill, Sol Haberman, Billie L. Aronoff, Richard E. Collier, Zelig H. Lieberman, John Mallams, George J. Race, Merrick Reese, Marvin J. Stone, Ralph Tompsett, and Harold C. Urschel, Jr. As chief executive officers of the medical center, Boone Powell, Sr., and Boone Powell, Jr., encouraged and supported research and funding for research.

During the 1903-to-1920 era, research at the new institution was limited to activities of individual practitioners that were related to improvement of patient care techniques and instruments used in practice. With respect to research during Baylor University College of Medicine's earliest years, Dean Moursund noted in his history of the college:

Although the original charter of the medical college indicated that one of the objectives was the advancement of medical education through research, other matters in the life of the college during the first decade of its existence consumed the time, effort, and finances of those responsible for the school. There is no record available of any specific research projects engaged in during the time. Advances were made, however, particularly in the use of laboratory



Figure 1. Drs. Benjamin F. Hambleton and Joseph M. Hill, two early and prominent researchers at Baylor.

procedures in diagnosis and in the development and refinement of surgical techniques (1).

After 1920 when the Baylor-in-Dallas concept was promulgated, more formal research was undertaken on the Dallas campus. Medical school faculty members had access to patients in Baylor University Hospital and to limited laboratory space, equipment, and library resources in the medical school and hospital buildings. There was some basic scientific research and some clinical research.

In the field of sciences, Dr. Benjamin Franklin Hambleton (Figure 1), professor of physiology and pharmacology, became known "for having been the first to describe the movements of the intestinal villi. He also described the effects of gallbladder and appendiceal lesions on gastric secretions, and the explosive gases formed on electrical destruction of tissue" (2).

Dr. Joseph M. Hill (Figure 1), pathologist and director of laboratories, began research in hematology in 1935 that led to establishment of

one of the first and more progressive blood banks in the world. [He] initiated research into the problems of blood diseases, blood cell structure, and techniques of preparation, preservation and handling of blood. In 1938, experimental work in blood transfusion methods resulted in the development of the ADTEVAC method of drying plasma from the frozen state. Dr. Hill and engineer D. C. Pfeiffer developed the complex machine, which was one of the prototype apparati in the field. This process was used in preparing plasma for the Armed Services in World War II (2).

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The success of Dr. Hill's effort led to the establishment of the William Buchanan Blood Center with a grant from Dr. and Mrs. Stanley Seeger—as well as to the later development of the center renamed the Wadley Blood Institute and Blood Bank, which was established with a grant from Mr. Buchanan and his wife, Susie L. Wadley.

Even recognizing these two notable successes, research was limited on the Baylor-in-Dallas campus due to a lack of financial support rather than to a lack of interest on the part of faculty and medical staff members. There were no full-time, salaried faculty members and no funds for research assistants and research fellows. Space was limited, and scientific equipment was not available unless it was paid for by the individual who was interested in research. There was no foundation or other formal means of developing private financial support for research. Federal programs in support of medical research had not yet been established.

As Dean Moursund later noted, "When the college moved to Houston . . . [and] with the war at an end . . . , funds for research became increasingly available. Thus the college met its objective of advancing medical knowledge through research and investigation to a greater measure than at any time in its history" (1). Baylor College of Medicine in Houston became a leading medical research center as increasing government and private funding for medical and basic research became available.

Research at Baylor in Dallas after the move of the medical college to Houston was largely a matter of individual physicians' interests, willingness to devote their time to research, and access to private gifts to support their efforts.

The first significant institutional effort to support research at Baylor University Hospital after the medical school's move to Houston was made in 1950 when Dr. LeRoy J. Kleinsasser came to Baylor as director of surgical education and developed animal research facilities to plan and test procedures related to open heart surgery. With financial assistance from the W. W. Caruth, Jr., Fund of the Dallas Community Chest, he established a much larger Caruth Surgical Research Laboratory in 1964. The laboratory contained operating rooms, x-ray and darkroom facilities, research laboratories, and support space, as well as quarters for research animals. According to reports of the time, the operating rooms for the animals were judged equivalent to those for humans.

Other developments at BUMC helped advance interest in research. First, the A. Webb Roberts Center for Continuing Education was established in 1973, with one purpose being to bring information about research advances to practicing physicians. Initially, the continuing education programs were supported by BUMC and the University of Texas Southwestern Medical School (UT Southwestern) as a combined effort. Dr. Race was appointed dean of the Roberts Center and associate dean for continuing education at UT Southwestern. Second, the Charles A. Sammons Cancer Center was established in 1976, and under the leadership of Dr. Marvin J. Stone it developed specialties in radiation oncology, hematology, and surgical oncology, and conducted research in these fields.

Further, by the 1970s, there was continuing development statewide of regional medical programs to expand teaching and research programs for cancer, stroke, and heart disease, as

encouraged by federal legislation. Part of this activity was to stimulate cooperation, coordination, and support of organizations involved in research and teaching, such as the American Heart Association, the American Cancer Society, and, more particularly, the local Dallas Southern Clinical Society.

BUMC did not, however, have in the post–World War II years the research support of medical schools and hospitals with historic commitments to research, such as those of Johns Hopkins in Baltimore. Baylor medical staff members, administrators, and trustees envisioned a far greater research effort as part of BUMC's future.

In BUMC's long-range planning effort begun in 1963 under the leadership of Boone Powell, Sr., a comprehensive approach was taken to planning for the institution's and medical staff's future. A 10-member committee on research programs that included medical staff members, trustees, and administrators participated in development of the institution's long-range plan. It was agreed that one of the 3 major objectives of BUMC was to serve as a research center. The committee recommended specific actions to stimulate research. While research was encouraged on the part of medical staff members, patient care and graduate medical education continued to be accorded higher priority.

In the late 1960s and 1970s, numerous developments were related tangentially to research, even if they did not create a specific BUMC research enterprise. In 1979 there was a movement to establish a Baylor University College of Health Sciences in Dallas which would incorporate the ongoing Baylor dental school program and the Baylor Waco graduate degree programs in the basic sciences, which at that time could offer a doctorate in microbiology, anatomy, and chemistry. A task force looked at combining these activities with the Baylor School of Nursing into a medical school, using the basic sciences at the dental school in cooperation with the clinical programs in BUMC. Each department of the hospital had a large residency program, headed by individuals such as Dr. Robert Sparkman in surgery, Dr. John Fordtran in medicine, Dr. Reuben Adams in obstetrics and gynecology, Dr. George J. Race in pathology, Dr. Fritz Barton in plastic surgery, Dr. Ben Mitchel in thoracic surgery, Dr. A. D. Sears in radiology, and Dr. E. M. Krusen in physical medicine. A division of research was contemplated along with an academic graduate program. This program was never approved by the BUMC trustees or the Baylor Waco trustees and hence never developed. However, it laid groundwork for more research development.

In 1980, during the next cycle of long-range planning, a task force on education and research was activated. It recommended, among other things,

- The encouragement of all physicians, through chiefs of service, education directors, and administrative staff, to take part in clinical research and to report their findings in appropriate medical journals
- The inclusion in all future agreements with hospital-based physicians a statement that defines their role, if any, related to conducting and reporting clinical research in their areas of expertise
- The establishment of research positions and the seeking of funding sufficient to provide at least one half the researchers' salary requirement
- The establishment of research fellowships



Figure 2. Dr. George Race, early president of Baylor Research Foundation, with Dr. Lester Matthews, executive director.

- The establishment of a grants management office to assist researchers at Baylor in obtaining and managing grants from private, state, and federal sources
- The establishment of a professionally staffed publications office to assist in the development of manuscripts for publication (3)

The task force's recommendations were approved in principle and implemented as financing could be arranged.

Mr. Powell requested that BUMC's planning consultant, Dr. H. Lawrence Wilsey, prepare a more detailed plan for the development of research. With the collaboration of Dr. Race and others, *A General Plan for the Development of Research at BUMC* was completed in 1982. The plan, implemented by Mr. Powell with the assistance of Dr. Wilsey and Dr. Race, recommended an institutional structure for research and specified how research should be developed and financed (4).

INCORPORATION OF BAYLOR RESEARCH FOUNDATION

The plan for development of research, after approval by BUMC's trustees, led to prompt incorporation of the legal entity to be responsible for research—the Baylor Research Foundation—the election of directors, and the selection of an executive to give scientific direction to the work of the new research enterprise.

The Baylor Research Foundation was incorporated in 1982 as a nonprofit organization exclusively for charitable, educational, and scientific purposes; its chief purpose was to promote and support medical research, medical care, training and teaching, and public health. Boone Powell, Sr., Boone Powell, Jr., and H. Lawrence Wilsey signed the articles of incorporation on November 3,



Figure 3. Home of the Baylor Research Foundation on Elm Street, 1988.

1982. The board of trustees was led by Mr. Powell, Sr., as the first chairman. Later Dr. Race was named chairman (*Figure 2*).

Initial directors of the Baylor Research Foundation, in addition to the incorporators, included 7 BUMC chiefs of service and senior medical staff members: Drs. Dolores M. Carruth, pediatrics; Adrian E. Flatt, orthopaedics; John S. Fordtran, internal medicine; George J. Race, pathology; Marvin J. Stone, Sammons Cancer Center; Ralph R. Tompsett, infectious diseases; and Jesse E. Thompson, surgery. Seven directors were from the Dallas business community: Carl B. Casey, Michael L. George, Devon Giacalone, William L. Hutchison, Hylan B. Lyon, Jr., C. Vincent Prothro, and Gary B. Wood. Baylor University in Waco was represented by 2 directors: Dr. William D. Hillis, executive vice president for administrative affairs, and Dr. W. Keith Hartberg of the department of biology. Other directors included Dr. Hector R. Acuña of Mexico City, former executive head of the Pan American Health Organization; Dr. Anne R. Race, a practicing psychiatrist and member of BUMC's medical staff; and Dr. J. Lester Matthews, a scientist who became the day-to-day executive of the Baylor Research Foundation.

Shortly after the Baylor Research Foundation was established, administrative and financial accounting procedures were established to conform with BUMC's and the US government's requirements for the administration of research grants. BUMC, Baylor Research Foundation, and the BUMC Foundation coordinated their fund development, accounting, and financial management activities.

In 1982, when the foundation first began operations, 4 basic science laboratories were set up. In 1988, a building at 3812 Elm Street was remodeled and became home to the laboratories and to the foundation's administration (*Figure 3*). A liaison was also formed with the Mayor's Task Force on Biotechnology, which was headed by Gary Wood, one of the foundation's directors, and with the Mayor's Commission on Development of a Medical Task Force.

The research foundation developed its own identity. Baylor Research Foundation received defense initiative awards of \$2.1 million. During a visit, Senator Phil Gramm showed great interest in research activities. Other early visitors were Major Eugene Fox and various individuals who were interested in developing laser dye technology to sterilize blood for blood banks.

Louis Beecherl was an active trustee who encouraged and supported the development of research at BUMC. He noted as early as 1989:

With Baylor's large and diverse patient population, there is a great opportunity and obligation to conduct clinical research, and this is being done at an accelerated pace. However, to be effective, the clinical researcher, in some cases, needs access to a basic research lab and the interchange of ideas that goes with it. One point that is hard to define is what is basic research, and this is a point made by the peer reviewers in some of their comments. There is an interim area between clinical and basic research known as applied research, and according to Dr. Matthews, the support mission of Baylor Research Foundation is probably more applied research. In my opinion, for the next 5 to 10 years, the number one mission of Baylor Research Foundation should be to furnish the core lab support for the clinical researchers, and secondarily, to do true basic research (5).

To encourage the new research endeavor, Mr. Beecherl also sponsored the appointment of an advisory committee for cell biology and related programs, which comprised 13 distinguished scientists from academic medical centers across the nation. The committee, in meetings with board members and BUMC research scientists and physicians, provided helpful insights and guidance for the early development and focus of Baylor Research Foundation's research activities.

A strategic plan was later adopted that charted the role of BUMC's research activities. An organ transplantation program had been developed under Dr. Göran Klintmalm and others for liver and heart transplantation activities. These activities were in need of support from clinical research programs. The Sammons Cancer Center was developing individual programs that involved cancer research, immunology in particular.

CHANGE OF NAME TO BAYLOR RESEARCH INSTITUTE

Changes in BHCS's corporate structure as the system developed in the 1990s made it desirable to change the research entity's corporate status and name. Hence, articles of amendment were filed on March 11, 1991, which changed the corporate name to Baylor Research Institute. Revised corporate documents were subsequently adopted by the board of trustees of BHCS on November 27, 2001, which established the entity as a membership corporation with BHCS as the sole member. The revised bylaws brought up to date the purpose of the corporation, defined more specifically the membership of the board of trustees, defined the responsibilities of the very important institutional review board (IRB), and provided for the appointment of a community advisory committee. Explicit provisions were made to ensure compliance with applicable laws and regulations, to avoid conflicts of interest, and to indemnify trustees and officers of the corporation (6).

THE PRESIDENCY OF DR. JOHN FORDTRAN AND A FOCUS ON IMMUNOLOGY

Dr. Race continued as chairman and Dr. Matthews as executive director of the research foundation until they retired. In 1991, Dr. John S. Fordtran, BUMC's chief of internal medicine, became president of the research foundation (*Figure 4*). He continued in that position until 1999, several years after his retirement as chief of medicine at the close of 1995.

Dr. Fordtran had excellent qualifications to direct and control the quality of research at BUMC, having been heavily engaged in research while on the faculty of UT Southwestern and having continued that research at BUMC. Findings from his research—which received 40 years of continuous funding from

the National Institutes of Health (NIH)—have been published in many scientific and professional journals and books. In addition, Dr. Fordtran published a textbook on gastroenterology in collaboration with Dr. Marvin Sleisenger that has been recognized as the definitive text throughout the world.

During the years of Dr. Fordtran's leadership, the volume and variety of research conducted under the auspices of the research foundation increased. Major attention was given by Dr. Fordtran to quality of research and to ethics in research (7).

From 1982 until the early 1990s, members of BUMC's medical staff and scientists were encouraged to seek their own financing for worthwhile research. Hence, the research undertaken was diverse but tended to be underfinanced and unsure of continued financing.

Under Dr. Fordtran's leadership in 1991, there was a comprehensive review of scientific programs. A strategic plan was developed and approved by BUMC's board of trustees and the BUMC medical board. In 1993, a further major decision was made: BRI would focus its basic science efforts on immunology in recognition and support of BUMC's organ and bone marrow transplantation programs. Dr. Fordtran led this refocusing of efforts from 1993 until 1999.

The directors of BRI, on the recommendation of Dr. Fordtran, adopted a new statement of purpose:

The purpose of BRI is to foster and support medical research, medical care, medical training and teaching, and public health. Medical research leads to improvements in medical care, which, in turn, improves public health. Improvements in medical care derived from medical research must be disseminated and taught to physicians and other health care professionals in order to benefit patients. These are the activities the Institute will foster and support. Activities will be sponsored at Baylor University Medical Center and elsewhere by the Institute and through international cooperation projects in which the Institute participates.

In keeping with the strategic plan, only research that supported BUMC's highly specialized and rapidly developing patient care programs in organ transplantation and cancer would be supported. The Sammons Cancer Center under Dr. Stone's leadership was developing research in cancer, immunology, and bone marrow transplantation. Dr. Klintmalm and colleagues were developing liver transplantation, as well as transplantation of other organs, and multiple-organ transplantation. Anesthesia research was developing rapidly under Dr. Ramsay's leadership. In other fields, similar efforts to participate in research were being developed. At this point, there was a decision to focus research efforts on activities closely related to clinical programs, because the translation of basic research to the bedside was important. Improvements in diagnosis and treatment and in the understanding of disease mechanisms involved the basic sciences, but they were organized to support clinical programs. BRI did not have the resources or the academic research affiliations to maintain a



Figure 4. Dr. John S. Fordtran, president of Baylor Research Institute from 1991 to 1999.



Figure 5. The Zelig H. Lieberman Research Building, current home of the Baylor Research Institute and the Baylor Institute for Immunology Research.

first-class basic science department. Therefore, freestanding basic science units were not considered best for BUMC and were phased out in favor of clinically relevant programs. The number of clinical programs that developed in large measure depended on their source of funding. The transplantation program headed by Dr. Klintmalm was instrumental in developing its own sphere of influence. The same was true of the research programs in the Sammons Cancer Center, in the departments of radiology and pathology, and in other parts of the institution. BRI then became less of a research center and more of a supervisory body.

DEVELOPMENT OF THE BAYLOR INSTITUTE FOR IMMUNOLOGY RESEARCH

To pursue the focus on immunology, 4 initial steps were taken. First, BIIR was created within BRI. This step was in keeping with the 1982 *General Plan for the Development of Research*, which provided for unincorporated institutes with specific focuses to be established from time to time. Second, a highly qualified scientist with eminent qualifications and reputation within the field was selected to plan, direct, and lead the major research effort. Third, financial support was developed to continue a major immunology research effort. Fourth, appropriate research facilities and equipment were provided to support the research effort.

Dr. Jacques Banchereau, a scientist recognized for his research in immunology, was recruited. He came to BUMC in 1996 to develop the institute and holds the Max and Gayle Clampitt Chair for Immunology Research. Before coming to Baylor, Dr. Banchereau was director of the Schering-Plough Laboratory for Immunological Research near Lyon, France, for more than a decade. He was among the early researchers to discover how to grow human dendritic cells. Dr. Banchereau has investigated various areas of immunology and cancer. In addition to studying dendritic cells, he has devoted a significant part of his career to the study of novel cytokines, proteins secreted mostly by cells of the immune system that affect the behavior of other cells. He also has studied antibody-producing B lymphocytes, research he continues to pursue vigorously at BIIR.

A major effort was begun in 1994 to develop financing for the immunology program and for a purpose-built research facility. Mr. and Mrs. Louis A. Beecherl, Jr., provided the lead gift, and

Mimi Lay Hodges and Max and Gayle Clampitt endowed the chair of Dr. Banchereau. The initial fundraising drive yielded an \$18 million endowment.

The fourth major prerequisite to the development of the immunology research program—the provision of appropriate research facilities and equipment—was met through the development of the Zelig H. Lieberman Research Building on Live Oak Street, near both the BHCS Dallas campus and downtown Dallas (*Figure 5*). The 2-story, 44,500-square-foot building has a classic granite and glass exterior and a modular interior layout that will accommodate 120 scientists, researchers, and support staff. The building is named for Dr. Zelig “Zeck” H. Lieberman, one of Baylor’s distinguished and respected surgeons. The Lieberman building has 5 laboratories, with space for 4 more. The building also includes the Marvin J. Stone Library and the John S. Fordtran Conference Room, which honor two physician-scientists who have contributed greatly to the development of research at BUMC.

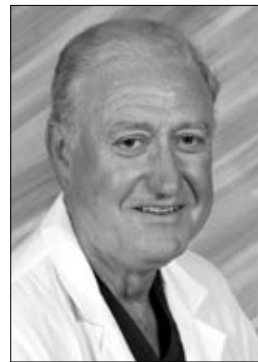


Figure 6. Dr. Michael A. E. Ramsay, president of Baylor Research Institute since 2000.

THE PRESIDENCY OF DR. MICHAEL RAMSAY AND ADMINISTRATIVE DEVELOPMENTS

Dr. Michael A. E. Ramsay was selected as president of BRI in 2000 upon Dr. Fordtran’s retirement (*Figure 6*). Since 1989, he has also been chief of the Department of Anesthesiology and Pain Management at BUMC, where he has conducted research particularly in transplantation anesthesia. He is renowned for the Ramsay Sedation Scale, which he developed with Dr. Roy Simpson in 1974 and which is now used internationally. Dr. Ramsay was also one of the first 3 members of the medical staff to be appointed to the BUMC board of trustees in 1999.

Under Dr. Ramsay’s leadership, there has been a tremendous growth in research activity during a time of increased federal regulatory and compliance requirements. In response, changes were made in the administrative infrastructure of BRI. In 2000, BRI’s operating bylaws were reconstituted to create a board of trustees with increased involvement in the governance of the institute. The number of active human research projects grew to over 500 protocols in 2003. Additional administrative functions, programs, and trained staff were added to accommodate the increasing volume and responsibilities. Oversight increased with the initiation of a random audit system.

In 2000, the Office of Sponsored Research’s responsibilities were divided to form 2 separate and distinct departments, the Office of Sponsored Research and the Office of Research Compliance. The Office of Sponsored Research continued to serve as a liaison with research sponsors in budget development, grant submissions, and contract negotiations. The number of grant submissions grew from over \$28 million in the 2000–2001 fiscal year to over \$50 million in the 2002–2003 fiscal year. In the same time period, the number of contracts negotiated increased from 44 new contracts worth \$3.4 million to 83 new contracts totaling \$16.4 million.

The Office of Research Compliance was created to assume the administrative responsibilities of the IRB and the institutional animal care and use committee. The increasing volume of research projects as well as the increased focus on the role of the IRB in human subject protection necessitated enhancements in both the expertise of staff and operations. As a result, in 2002 the Office of Research Compliance became the Office of Research Subject Protection, and a certified IRB professional was recruited to serve as director of the office. This addition enabled BRI not only to greatly improve the human subject protection program's substance and administration but also to enhance the expertise of the support provided to investigators and the members of the IRB. Additionally in 2002, the reporting lines changed for the IRB; the IRB became a committee of the BRI board of trustees to better serve all entities of BHCS.

One objective of the Office of Research Subject Protection is to ensure that all research conducted at Baylor complies with government regulations and standards and to keep abreast of changes in federal and state regulations. The effectiveness of this office was enhanced with the implementation of an automated tracking system to improve control and management of the processes required for compliance with research regulations.

The Office of Research Subject Protection accomplished a major goal with the development and implementation of a credentialing program for research personnel and the IRB. In January 2003, all investigators, research nurses, coordinators, assistants, IRB members, and staff completed the newly created credentialing program through BRI. The credentialing program for investigators and staff includes 3 separate requirements that must be met before any research study is submitted to the IRB. The credentialing for IRB members is a multitiered program involving review of the educational information included in each IRB packet as well as completion of BHCS training in human research protection. More than 250 investigators, 50 research nurses, coordinators, and assistants, and 40 board members have completed the program and are credentialed through BRI.

The credentialing process laid the groundwork for BRI's human research protection program to seek accreditation from the Association for the Accreditation of Human Research Protection Programs. This association is a not-for-profit organization that maintains rigorous standards for the protection of human participants in research as a means of fostering continued growth and confidence in scientific investigation. Preparing for the accreditation visit had a significant positive influence on BRI's human subject protection program. Accreditation raised the level of protection for human research subjects and provided additional guidance to research personnel by broadening their perspectives of the issues.

The accreditation process involved all aspects of the human research subject protection program and required extensive policy development and revision. Upon completion of the background work, a team of reviewers spent 3 days at BRI and BUMC reviewing policies and records and interviewing individuals involved in the human subject protection program. As a result, BRI was granted full accreditation in December 2003 and became the first private research institute to obtain such status.

Because over 1000 new drugs, biologics, and vaccines are in the development process, either in clinical trials or awaiting

approval at the Food and Drug Administration (FDA), physicians often needed trained nurses and research coordinators to assist with clinical research. To address this increasing need, BRI moved forward with the development of the Clinical Trials Office, which opened in 2002. The Clinical Trials Office greatly enhanced the capabilities of BRI to serve physicians in conducting industry-sponsored research projects. This office has made available a number of resources for investigators. The success of the Clinical Trials Office has been remarkable, and it continues to expand services. One of the resources introduced was the Study Manager™ electronic management system that includes a contact database and screens for study management. This innovative software not only assists in the management of research studies but is also used in fund accounting and regulatory administration. Plans are currently in progress to upgrade Study Manager to the more user-friendly web version. In 2003 the Clinical Trials Office provided support for 7 additional investigators and 12 new NIH-sponsored trials and coordinated 21 new IRB-approved studies. The Clinical Trials Office's objective is to help investigators comply with government standards so they can focus their energies on research. Through the Clinical Trials Office, BRI can support researchers in designing successful trials, creating realistic budgets, and managing trials, thus optimizing the chances of successful completion. The Clinical Trials Office also provides an entry point for pharmaceutical companies to access BHCS and be linked to appropriate researchers in a basic "turnkey" operation.

In 2002 the construction of the new Baylor Jack and Jane Hamilton Heart and Vascular Hospital necessitated the relocation of the Caruth Surgical Laboratories. Space for these activities was established in the Zelig H. Lieberman Building. With this move, the laboratory was renamed the BioScience Center to reflect the technology and diverse range of services provided by that group. BRI employs an attending veterinarian to provide oversight and care to the laboratory animals as well as to advise investigators in the development of research protocols utilizing animals. The BioScience Center staff is responsible for the procurement, care, and maintenance of the animals used in research.

Increased national attention on research compliance provided the impetus for BRI to expand compliance efforts. In 2002, BRI established a Quality Assurance Office. This office focuses on process improvement, document and process control, and compliance. It audited clinical trials and surveyed research subjects to ensure research subject protection. It also ensured laboratory quality by reviewing quality control efforts, reviewing standard operating procedures, and providing training in good manufacturing practices.

The Office of Financial Management was reorganized in 2003. The controller position was elevated to include more strategic financial planning functions, and basic accounting functions were moved to the BHCS corporate accounting division. This realignment maximized accounting resources and focused the controller position on management of the financial aspects of research growth.

A formal BRI advisory board was established in 2003. This board advises the presidents of BRI, BUMC, and BHCS on research matters, specifically scientific merit and applicability to Baylor's mission and objectives.



Figure 7. Dr. Priscilla Hollander speaking about her research at a Focus on Research forum.

To educate and inform physicians and researchers about ongoing research throughout BHCS, BRI sponsors a monthly research meeting, Focus on Research (*Figure 7*). This meeting is held at BUMC, and physicians and scientists share their latest research activities. Other avenues of information sharing available to researchers and staff include workshops on regulatory issues and in-service training provided by outside professionals. Monthly research coordinator meetings continue to provide a forum for information and exchange for all clinical staff.

With the goal of building synergy between our teaching programs and those of other educational organizations, collaboration in a number of fields is under way with UT Southwestern, the University of Texas at Dallas, the University of North Texas, Baylor University, Southern Methodist University, and Texas A&M University System Health Science Center/Baylor College of Dentistry.

BRI is also working with the Greater Dallas Chamber of Commerce Technology Business Council to promote the development of biotechnological industries in the Dallas–Fort Worth area and with several other organizations to promote biotechnology throughout Texas.

ENDOWED CHAIRS

A key goal for BHCS is the support of major clinical programs through funding of endowed chairs. The following chairs have been named within the past 8 years (*Figure 8*):

- Jacques Banchereau, PhD, the Gayle Clappitt Chair for Immunology Research
- David J. Ballard, MD, PhD, BHCS endowed chair for health care research
- Paul A. Grayburn, MD, Dr. Paul Thomas Congestive Heart Failure Endowment Chair
- C. Richard Boland, MD, endowed chair in gastrointestinal disease research
- Harold C. Urschel, Jr., MD, Cardiovascular and Thoracic Surgical Research, Education, and Clinical Excellence Chair

In 2002, A \$5 million grant was obtained from the Caruth Foundation via the Communities Foundation for a chair in transplant immunology. This donation was matched by another \$5 million from the BHCS Foundation. An international search was undertaken to seek an appropriate world scientific leader to



Figure 8. Holders of endowed research chairs: Drs. Jacques Banchereau, David J. Ballard, Paul A. Grayburn, C. Richard Boland, and Harold C. Urschel, Jr.

fill this position. A short list of candidates has been made and an announcement of the successful candidate is expected shortly.

At the start of 2004, a very generous donation from Mr. Louis Beecherl created the Ramsay Chair for Cancer Immunotherapy at the BHCS Foundation to recognize the contributions and in honor of Dr. Michael Ramsay, president of BRI. The holder of this chair has not yet been named.

RESEARCH IN 2004

Approximately 500 research protocols were active in 2004. Some of the major research efforts under way by Baylor's medical and scientific staff are summarized below.

Cardiology

Under the leadership of Dr. Paul A. Grayburn, BUMC is involved in 3 cardiology studies. The first is the Surgical Treatment of Ischemic Heart Failure trial, an NIH-funded randomized trial to determine whether coronary artery bypass grafting surgery improves long-term survival compared with medical therapy. Over the next 3 years, 100 centers in the USA, Canada, and Europe will recruit 2800 patients for this effort. The second is a Baylor-led, NIH-funded clinical study that will define the mechanism of functional mitral regurgitation in ischemic cardiomyopathy, define the effect of therapy on the disease's mechanism and severity, evaluate the effect of severity on prognosis, and evaluate the effect of myocardial viability on the mechanism of functional mitral regurgitation. The third study makes use of a technique developed in Dr. Grayburn's laboratory, wherein genes or drugs are attached to gas-filled microbubbles, which are then circulated through the intravascular space and mechanically destroyed by ultrasound within the target organ. This technique should allow precise delivery of agents to any anatomical site. Past research has shown that genes can be delivered to rat myocardium to stimulate angiogenesis. Current work is investigating whether several genes can rescue islet function in rats.

Cardiovascular and thoracic surgery

A group of investigators—including Drs. Edson Cheung, Baron Hamman, Robert Hebler, Jr., Carl Henry, Dan Meyer, Steves Ring, and Harold Urschel, Jr.—are evaluating new techniques and devices to benefit their patients. Examples of specific efforts include the following:

- Use of the carbon dioxide laser to make myocardial revascularization holes from the epicardial surface of the heart in areas not serviced by coronary artery bypass grafts
- Study of coronary artery bypass surgery in obese patients
- Clinical study of Syncrus, a postoperative defibrillating system
- Use of a microwave and cryoprobe to ablate the area producing atrial fibrillation
- Testing of a miniature cardiopulmonary bypass apparatus
- Study of beating heart surgery
- Evaluation of the impact of cardiac surgery on neurocognitive function
- Review of an antibleeding substance or “glue” that decreases postoperative bleeding
- Evaluation of the DeBakey VAD, a smaller and more efficient artificial left heart support device
- Performance of left ventricular modeling
- Use of a robotics system to implant a prosthetic mitral valve
- Evaluation of a stentless aortic valve prosthesis and a new stented pericardial valve
- Comparison of the use of nitinol self-closing clips versus suture in surgery
- Introduction of a new technique, endoscopic radial artery harvesting for coronary artery bypass grafting

Dermatology

Dr. Alan Menter and his team have been involved in more than 50 clinical trials since 2000. They have done basic research—collaborating with Dr. Anne Bowcock at Washington University in St. Louis to demonstrate a unique gene expression profile in patients with psoriasis—and have focused on evaluating new therapies for psoriasis. Several of the studies involved biologic response modifiers, which target specific components of the immune system. Baylor is leading the national phase III study for one such biologic, infliximab, and recently published results with 2 other notable drugs, alefacept (which targets the CD2 molecule of activated T cells and was approved by the FDA in 2003) and etanercept (which decreases the concentration of tumor necrosis factor and is expected to be approved by the FDA in 2004).

Endocrinology

The Baylor Endocrine Center, under the leadership of Dr. Priscilla Hollander, is involved in 20 studies to improve treatment of patients with diabetes. Most notably, it is assessing the use of inhaled insulin, which is more convenient for patients; testing the safety and efficacy of a new form of long-acting insulin called glargine; and studying 3 antiobesity compounds—a genetically engineered second-generation ciliary neurotrophic factor, an antagonist for the cannabinoid CB1 receptor, and a CCK-A receptor agonist/CCK-B receptor antagonist.



Figure 9. Researchers in Dr. Boland's laboratory investigating the genetics of colon cancer.

Gastroenterology

BUMC's gastroenterology division, led by Dr. C. Richard Boland, is currently involved in 3 research endeavors (Figure 9):

- The study of 2 forms of hereditary colon cancer, familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer. The research team is detecting germline mutations and attempting to reverse the process that predisposes some inflamed tissue to relax its mismatch repair system and thus develop cancer.
- A study to determine if the JC virus plays a causative role in colon cancer development. The researchers have hypothesized that the JC virus infects the colon in childhood and that the rearrangement of the virus' transcriptional control region occurs later in life, which induces chromosomal instability, the initiating event in colorectal carcinogenesis. If experiments are able to confirm the hypothesis, the team will propose clinical trials to see whether primary immunization or adoptive immunity might delay or prevent the cancer.
- An NIH-funded clinical trial to determine if certain drugs can prevent new adenomatous polyps from forming and thus theoretically prevent cancer from developing.

In addition, Dr. John Fordtran has been an active investigator in the gastroenterology division for many years. Examples of recently published projects include the effect of octreotide on fluid absorption, intestinal chloride secretion in cystic fibrosis, measurement of fecal bile acids in malabsorption, and abnormal passive chloride absorption in cystic fibrosis. These studies have been published in *Alimentary Pharmacology and Therapeutics*, *American Journal of Human Genetics*, *Journal of Laboratory and Clinical Medicine*, and *Journal of Clinical Investigation*.

Health care research and improvement

BHCS's Institute for Health Care Research and Improvement, under the direction of Dr. David Ballard, conducts and facilitates research related to clinical effectiveness and quality necessary to achieve the BHCS strategic goal of "aligning and expanding research to advance best care." The center designs and implements a wide variety of innovative health care research projects across BHCS. One recent effort was a randomized controlled trial of strategies to improve diabetes care. The trial examined the effectiveness and costs of physician profiling and care coordination by a diabetes resource nurse in the HealthTexas Provider Network. This million-dollar project was funded primarily with \$850,000 from the American Diabetes Association and \$185,000 from Pfizer.

Immunology

An international team of scientists and physicians collaborates at BIIR to study key diseases that involve the immune system (Figure 10).

Dendritic cell biology and dendritic cell-based cancer vaccines. BIIR is conducting research into the biology of dendritic cells and applying the knowledge about dendritic cells to develop vaccines to treat cancer. Dr. A. Karolina Palucka leads efforts to perform molecular and biological analyses of dendritic cells. Two major differentiation pathways have been identified: myeloid dendritic cells and plasmacytoid dendritic cells. BIIR scientists are pursuing the hypothesis that distinct subsets of myeloid dendritic cells exist, each driving a distinct type of immune response. These subsets of myeloid dendritic cells are generated in response to different cytokines, the secretion of which may be triggered by different microbes. Plasmacytoid dendritic cells are remarkable because of their ability to secrete large amounts of type I interferon. BIIR scientists have revealed their fundamental role in the reactivation of memory immune responses. In particular, plasmacytoid dendritic cells contribute to the eradication of viral infection through the stimulation of specific humoral and cytotoxic immune responses.

In addition, supported by a large contract from the Defense Advanced Research Project Agency, BIIR researchers are developing Humouse, a new *in vivo* model of the human immune system. This model involves "humanizing" mice through transplants of human CD34+ hematopoietic progenitor cells and co-engraftment of human mesenchymal stem cells. A model has also been created that includes a human cancer. These mice will be used to test many aspects of the cancer vaccines with the goal of increasing the vaccines' efficacy.

The search for dendritic cell therapies to treat cancer is led by Dr. Jacques Banchereau and Dr. Karolina Palucka. Dendritic cells are made in the laboratory by culturing, in the presence of cytokines, patients' stem cells that have been isolated from their blood or bone marrow. The dendritic cells are then loaded with tumor antigens and finally reinjected into the patient. The loaded dendritic cells may serve, then, as a cancer vaccine. Melanoma, prostate cancer, and breast cancer have been targeted for clinical trials. These studies are performed in collaboration with numerous oncologists at BUMC and Texas Oncology and rely on efforts of BIIR's division of cellular immunotherapy, which is led by Dr. Joseph W. Fay.



Figure 10. Researchers share ideas in the Baylor Institute for Immunology Research: (left to right) Drs. Virginia Pascual, Jacques Banchereau, and Karolina Palucka.

Over the past 5 years, the division has conducted clinical trials with 7 different investigational new drugs, and trials with 2 more drugs are planned. The FDA audited the dendritic cell vaccination program in October 2002 and showed that the vaccines are of potential therapeutic value. Results from the clinical trials in melanoma to date have shown the following: 1) vaccination with dendritic cells is remarkably safe; 2) some patients with metastatic melanoma have developed partial and complete clinical responses following vaccination; 3) some patients developed tumor-specific T cell immunity in response to dendritic cell vaccinations; 4) patients who did not develop tumor-specific immunity did not show clinical regression; 5) melanoma in patients who developed short-term tumor-specific immunity eventually progressed or relapsed when immunity disappeared; and 6) patients who developed long-term tumor-specific immunity are the clinical responders.

Autoimmune diseases. The institute also focuses on common autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus (SLE), psoriasis, thyroiditis, scleroderma, multiple sclerosis, ulcerative colitis, Crohn's disease, and diabetes. Leading the effort is Dr. Virginia Pascual, assistant professor of pediatrics at UT Southwestern. The goal of Dr. Pascual's laboratory is to understand the alterations of the immune system that lead to the development of SLE and arthritis in children. The long-term goal is to apply these discoveries to the design of novel therapies, such as bone marrow transplantation.

The recognition of the fundamental role of dendritic cells in the control of tolerance and immunity led to the hypothesis that SLE may be driven through unabated dendritic cell activation. BIIR scientists have made fundamental progress in understanding the pathogenesis of SLE. First, they showed that monocytes from SLE blood include cells that act as dendritic cells. These cells are being generated in response to circulating interferon- α . Second, they found that interferon- α is a powerful inducer of plasma cell differentiation and survival, possibly explaining the hypergammaglobulinemia observed in patients with SLE. Third, they confirmed the role of interferon using oligonucleotide microarrays and showed that SLE blood cells overexpress granulopoiesis-related and interferon-induced genes. Repeated intravenous infusion of glucocorticoids, the standard treatment of disease flares, shuts down the interferon signature. Thus, SLE may be controlled by targeting interferon- α , and this treatment may benefit all patients with SLE. Accordingly, a program has been launched to generate anti-interferon antibodies for therapy. This unique therapeutic approach might offer relief to these patients in the same way that antitumor necrosis factor therapy offers relief to arthritis patients.

Infectious diseases. BIIR scientists have developed a program aimed at improving protection against infectious agents through the manipulation of dendritic cells. Data collected to date suggest that granulocyte colony-stimulating factor, a cytokine that increases granulocyte counts, as well as plasmacytoid dendritic cells, partially protect mice from anthrax. Perhaps more important, the survivors become resistant to another exposure to anthrax, suggesting specific immunity. Researchers are also studying the pathophysiology of respiratory syncytial virus, a disease that does not induce protective immunity and for which no vaccines are available.

Related to infectious diseases are analyses of gene expression patterns in patient blood samples, in vitro-activated blood cells, and in vitro-generated dendritic cells subsets and T cells cultured with unique dendritic cell subsets. Researchers have now generated an extensive database of human samples in health and disease; they expect that microarray-based biosignature analysis of blood will help establish disease diagnosis, disease prognosis, and assessment of therapeutic responses.

Several fields of inquiry in immunology are related to BIIR's role as the lead center in the Cooperative Center for Translational Research in Human Immunology and Biodefense, which is supported by a grant from the National Institute for Allergy and Infectious Diseases. The project also involves investigators at Yale University, Rockefeller University, the University of New Mexico, and UT Southwestern Medical Center. The goal of the project is to develop potent human vaccines as biothreat countermeasures.

Metabolic disease

The Kimberly H. Courtwright and Joseph W. Summers Institute of Metabolic Disease, led by Dr. Charles Roe, studies clinical and pathophysiological aspects of inherited metabolic diseases. The researchers hope that their findings will also lead to therapeutic applications for "acquired metabolic disorders," such as heart disease and diabetes. General areas of research include neurotransmitter disorders, methylation disorders, fat oxidation

disorders, and branched-chain amino acid disorders. Dr. Roe studies nutritional approaches to inherited diseases, development of new diagnostic technology, and development of new treatment strategies. His recent clinical trial, conducted with Dr. Jonathan Whitfield, chief of neonatology at BUMC, studied the prevention of apnea and bradycardia in premature infants. Another area of interest is the development of a treatment strategy designed to bypass the missing steps in the metabolic pathway for fat oxidation. Dr. Roe is developing a program of collaborative investigations and training at the institute with colleagues in Asia and Europe.

Dr. Keith Hyland heads the neurochemistry laboratory, which has recently expanded from focusing on neurotransmitter metabolism disorders (catecholamines and serotonin) to other diseases that affect central nervous system function. A 2000 grant from the NIH allowed the laboratory to develop the methodology to investigate polyamine metabolism. Dr. Hyland's laboratory provides the only clinical diagnostic service for pediatric neurotransmitter diseases in the nation. The laboratory also is used frequently as an analytical resource for studies initiated in other Baylor departments and facilities nationwide.

The molecular research laboratory, led by Dr. Jiahuan Ding, is working to identify the molecular defects of fatty acid beta oxidation disorders and other diseases, as well as to develop novel treatment strategies, including stem cells for tissue repair and cell therapy. Research of bone marrow stem cells' differentiation into neural and cardiac cells for the study of inherited disorders is also in progress. Dr. Ding also collaborates with Dr. Grayburn in ultrasound targeted microbubble destruction studies.

Dr. Teodoro Bottiglieri has focused on neuropharmacology research. Although primarily concerned with the pediatric population, research studies now include potential therapeutic interventions for acute lymphoblastic leukemia, HIV infection, depression, Parkinson's disease, Alzheimer's disease, vascular dementia, and stroke. The use of transgenic animal models is a key tool of the program. Dr. Bottiglieri has collaborated in projects with Dr. Cara East, a BUMC cardiologist, and has participated in numerous collaborative NIH-funded studies.

The mass spectrometry laboratory, led by Dr. Lawrence Sweetman, provides metabolite analyses to support Dr. Roe's triheptanoin dietary therapy clinical research. The laboratory has an ongoing project with BUMC's nephrology department concerning 5-oxoprolinuria caused by chronic toxicity of acetaminophen in patients with kidney failure and conducted research on the effects of maternal smoking on amino acids and acylcarnitines.

Oncology

Baylor's research efforts in oncology focus on drug studies, risk assessment and cancer prevention, and development and use of new biologic agents.

Many BUMC oncologists participate in multicenter phase II and III trials of chemotherapeutic agents and protocols. Investigators include Drs. Joyce O'Shaughnessy, Stephen Jones, Robert Mennel, Barry Cooper, and John Pippin.

Dr. Joanne Blum leads the Hereditary Cancer Risk Program, which provides risk analysis and genetic testing for breast and ovarian cancer. The registry of the program provides a patient population for a wide variety of research endeavors. Some such studies have focused on the psychological impact of a *BRCA1*

or *BRCA2* test result of variant or uncertain significance, the effect of other genes that may modulate the risk of breast or other cancers in women who carry a *BRCA1* or *BRCA2* mutation, and the reduction of cancer risk in carriers of the mutations who undergo prophylactic surgeries.

Baylor physicians have long played a role in groundbreaking research on the prevention of breast cancer. Baylor began participating in the Breast Cancer Prevention Trial in 1992; that study led to FDA approval of tamoxifen in 1998. Baylor researchers are now participating in 2 breast cancer prevention research trials, STAR (the Study of Tamoxifen and Raloxifene) and BCPT (the Breast Cancer Prevention Trial). Baylor Sammons Cancer Center and its 3 satellite centers rank number 7 among 197 clinical centers in meeting the enrollment objective of STAR.

Baylor has been very active in using new biologic agents to treat cancer. Dr. Joseph Fay leads a clinical team that collaborates with Dr. Jacques Banchereau of BIIR in studies of dendritic cell-based anticancer vaccines.

Dr. John Nemunaitis and Dr. Casey Cunningham of the Mary Crowley Medical Research Center have studied and characterized 89 new agents, treated 1932 cancer patients, and performed 123 FDA-approved clinical trials in oncology since 1992. Their studies involve biological approaches, small molecules, cytotoxic agents, and gene therapy. Among notable discoveries are the use of immune-activating genes to stimulate immune responses against cancer and use of the “conditional replicating” viral vectors, which are genetically altered to grow and expand within individual cancer cells. Dr. Nemunaitis received worldwide attention in spring 2004 for developing a vaccine that suppresses lung cancer in some patients.

A collaborative initiative is under way between the Mary Crowley cancer research program, BIIR, Texas Oncology, and US Oncology to expedite clinical trials of cancer vaccines.

Orthopaedics

The Department of Orthopaedic Surgery, led by Dr. Robert W. Jackson, researches the treatment of normally unreparable meniscal damage (*Figure 11*). Clinical researchers are exploring options for healing injuries to the avascular zones and have had encouraging results with several photoactive dyes that work as collagen-bonding agents for the repair of avascular meniscal tears. The concept of forming a tissue bond by simply catalyzing the formation of covalent bonds between the tissue surfaces is novel and potentially solves the “barrier” problem occurring when foreign material is retained within the repair, as seen with “glues.”

Dr. James W. Brodsky has continued research on the design of the ankle prosthesis. One such ankle prosthesis that has promising results is the Scandinavian Total Ankle Replacement, which consists of a tibial plate, a talar component cap, and a sliding polyethylene meniscus. BUMC is one of only 10 institutions in the USA chosen to participate in an FDA-approved clinical trial of this prosthesis.

Surgery

The BUMC Department of Surgery has participated in numerous prospective national multicenter trials, including studies for malignancies of the esophagus, breast, head and neck, and melanoma, as well as new types of implantable ports. Several



Figure 11. Orthopaedic research led by Dr. Robert Jackson.

publications resulted from research efforts in the areas of parathyroid surgery, esophageal cancer, breast cancer, laparoscopic gastric bypass, cardiothoracic surgery, and vascular surgery. Recent projects include the following:

- Testing of a novel strategy of complete tumor debulking with intraperitoneal hyperthermic chemotherapy
- Study of patients with micrometastases found upon sentinel lymph node biopsy to determine when complete axillary dissection is needed
- Use of the quick intraoperative parathyroid assay in parathyroid surgery
- Review of results with carotid artery stent placement, bariatric surgery, and the Nuss minimally invasive corrective procedure

Transplantation

From its inception, Baylor's transplantation services was organized as a clinical research unit. Although good clinical care does not necessarily yield good data for research publications, good research data always contribute to exceptional care (*Figure 12*). Consequently, transplantation services has a research staff of 19, including managers, statisticians, information systems managers, research nurses, and quality assurance personnel. Thanks to this dedicated research capability, investigators have published more than 400 scientific papers and abstracts. Two recent studies examined the risk of recurrence of autoimmune hepatitis in the transplanted liver and, in the largest study of its kind, the incidence of graft-versus-host disease among liver transplant recipients. Currently, Baylor is the primary and principal inves-



Figure 12. Dr. Göran Klintmalm with a transplant recipient.

tigator of an 18-center randomized trial for immunosuppression of patients with hepatitis C. Patients will be randomized into one of 3 groups: 1) conventional therapy without mycophenolate mofetil but with steroids; 2) conventional therapy including mycophenolate mofetil and steroids; and 3) conventional therapy with mycophenolate mofetil and daclizumab but no steroids. This is the largest study ever done in hepatitis C patients, and the results will have worldwide implications. These are but a few examples of the translational research being done in transplant services at BUMC and Baylor All Saints Medical Center at Fort Worth.

World-renowned expert Dr. Gary L. Davis joined BUMC as director of the division of hepatology at BUMC and added even more substance to Baylor's already exceptional liver transplant program. His clinical research focuses on new ways to help patients who do not respond to currently available antiviral drugs. He is studying novel drugs that inhibit the ability of hepatitis viruses to replicate and is investigating immune modulatory drugs that may facilitate the hosts' ability to clear viral infections. With regard to transplantation, he is engaged in studies to develop treatment strategies that will clear hepatitis C before liver transplantation

to prevent virus recurrence in the new graft. He and his group have recently completed their first studies with hyperimmune globulin to the hepatitis C virus. One problem after transplant is that the potent drugs used to suppress rejection also may block the patient's ability to fight hepatitis recurrence. BUMC is leading a nationwide study to identify the optimal posttransplant immunosuppressive regimen that balances these risks.

BRI recently completed an international search resulting in the selection of a first-class scientist, Dr. Bashoo Naziruddin, to direct the pancreatic islet cell transplantation laboratory. This new research program, under the medical direction of Dr. Marlon F. Levy, may eliminate the need for insulin for many patients with diabetes. The construction of a pancreatic islet cell transplant laboratory is under way in the Zelig H. Lieberman Building. This sophisticated and well-controlled laboratory space will provide the good manufacturing environment required by the FDA for the preparation and processing of the islet cells for transplantation.

LOOKING TO THE FUTURE

BRI looks forward to new opportunities in 2004, including the exciting possibility of starting a biotech company to manage BRI's business ventures and intellectual property. In addition, fundraising for research, including the endowments that are the keystones for development of clinical research programs, will be a priority. These investments promise significant returns for the people and communities we serve.

BRI will remain focused on the type of research that serves the mission of BHCS and moves from the bench to the bedside. The Baylor research mission has been clearly defined and sets BRI apart from many other research centers:

To improve the medical care and well-being of our community—nationally and internationally—through innovative, clinically relevant research, that is consistent with the mission and values of the Baylor Health Care System.

The continued investment in research and education will be the cornerstone for the future of the health care system.

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