

The Later Years (1991–2011)

DAVID N. LOUIS AND ROBERT B. COLVIN

THE PERIOD FROM 1991 TO 2011, representing the tenures of Robert B. Colvin (1991–2006) (figure 25.1) and David N. Louis (2006–) (figure 25.2) as chiefs, has been a productive and exciting period for the department. The Anatomical and Clinical Pathology groups have continued their outstanding patient care-related services, superior teaching, and academic contributions during this time, and the reader is directed to chapters 15–22 for coverage of the clinical subspecialties through 2010.

It is more difficult to achieve a truly objective overview of the accomplishments of those still practicing as faculty in the current department, and therefore this chapter has been approached in a manner different from the previous ones. We present only major developments and have not been able to cover all the people and progress of the past 20 years. We leave it to history to tell which of these individuals and developments will have long-standing significance.

THE YEARS 1991–2006

Dr. Robert B. Colvin was appointed the fifth Chief of the Pathology Service at the Massachusetts General Hospital (MGH) on July 1, 1991. Colvin was born in Columbus, Ohio, on May 7, 1942, and raised in Henderson, Kentucky. He graduated from the Massachusetts Institute of Pathology in 1964 (B.S. in humanities) and from Harvard Medical School (HMS) in 1968 cum

laude. He trained at the MGH as a surgical intern for one year and then in anatomic pathology from 1969 to 1972. From 1971 until 1972 he was an NIH Research Fellow under the mentorship of Dr. Harold Dvorak. He subsequently served as a major in the Army Medical Corps during the Vietnam War, stationed at Walter Reed Army Institute of Research in Washington, D.C. He



Figure 25.1 Robert B. Colvin, fifth Chief of Pathology



Figure 25.2 David N. Louis, sixth Chief of Pathology

was recruited back to MGH as an Assistant Professor of Pathology in 1975 by Dr. McCluskey and promoted to Associate Professor in 1978. He became Director of the Immunopathology Unit in 1980, when Dr. Dvorak became Chief of Pathology at Beth Israel Hospital. Dr. Colvin was promoted to Professor of Pathology in 1991 and in 1993 became the Benjamin Castleman Professor of Pathology, succeeding Dr. McCluskey. Dr. Colvin has led the clinical renal pathology group since 1975 and continues in that capacity. At the time of this writing (2011) he has published over 435 papers, edited or coauthored 4 books, and trained 44 research and clinical fellows. Dr. Colvin's primary area is the immunopathology of renal disease, particularly mechanisms of graft acceptance and rejection. His research contributions are described in chapter 23.

Dr. Colvin built on the strengths of the department developed by Dr. McCluskey (chapter 13), including a strong financial position, an academically and clinically outstanding faculty,

and newly integrated Clinical and Anatomic Pathology divisions. During his first year the new Chief of Service endeavored to enhance the group's sense of being a team and reengineered an effective organization within the department. One activity that was extremely helpful in this process was a departmental retreat, the first of its kind for MGH Pathology. On October 19, 1991, 70 Pathology staff and residents gathered at the Endicott House, a chateau-style country estate outside Boston. The topics for discussion were important and complex issues for the whole department; they included subspecialty sign-out, integration and organization of research, reference laboratory, residency training program, and computer/information resources. The event was enthusiastically received and highly successful in accomplishing its goals, as many of the changes implemented over the next year were first suggested or developed at the retreat.

Organization

In April 1992 a reorganization plan, introduced at the departmental retreat, was implemented. A major goal was to clarify and strengthen relationships and responsibilities. The Pathology Service was divided into four major components, each with a Director: Anatomic Pathology (Dr. Nancy L. Harris), Clinical Laboratory (Dr. Michael Laposata), Pathology Research (Dr. James Kurnick), and the Residency Training Program (Dr. E. Tessa Hedley-Whyte). Each Director sat on the newly created Pathology Executive Committee, which also included the Director of Surgical Pathology (Dr. Robert H. Young) and the Pathology Service Administrator (Nancy Stark). This group participated in strategic planning, financial decisions, recruitment, promotions, and academic programs. In addition, each division had a steering committee to advise its Director. Task forces were formed to solve particular problems and to provide strategic planning. Dr. Jean Elrick, the MGH Senior Vice President for Pathology, worked closely with the chief and the

Pathology administrator on all matters related to the hospital. At this point the department could have been described as a near democracy; the chief solicited opinions of faculty members via committees and working groups, and then made key decisions that were based on their advice. Many of the decisions were decentralized and made by the individual directors, who sought input from the chief or others when the financial or programmatic needs were significant. In 1993 the Massachusetts General Physicians Organization (MGPO) was created, and Dr. W. Gerald Austen was named Chief Executive Officer. Its goal was to unify the physicians, giving the physician leadership equal status with the hospital leadership. The Chief of Pathology reported to the CEO of the MGPO and the President of the MGH.

A major organizational shift with respect to the overall department occurred in 1993, when the MGH and Brigham and Women's Hospital (BWH) agreed to merge as Partners HealthCare in a joint effort to create a health care system. This remarkable liaison of long-term rivals was motivated by predictions of severe downsizing of hospitals and increasing competition in health care delivery. The Laboratory Strategy Task Force, composed of Drs. Ramzi Cotran (chair), Robert Colvin, Jean Elrick, Robert Handlin, Michael Laposata, and Gerald Winkleman, met every other Friday from 8:00 to 10:00 A.M. at the Prudential Center offices of Partners (located halfway between MGH and BWH) to discuss ways to integrate the laboratories and consider commercial laboratory options. The group heard from many consultants, without reaching a definitive conclusion. Cross-transfer of specialized tests (more than 200,000 a year) and joint purchasing and contracting achieved savings of over \$2 million a year, but consolidation of the laboratories remained an unattractive option to the participants. Finally, in 1997, Partners' leadership asked for a high-level estimate of the savings if the clinical laboratories were combined.

William Hynes, the MGH Pathology administrator, came up with an estimate of \$3 million annually, but about 10,000 specimens a day would have to travel through downtown Boston traffic to the other institution—an unacceptable risk. One significant change of the Partners merger was that Cytogenetics was centralized at BWH in 1996 under the direction of Dr. Cynthia Morton. Dr. Leonard Atkins had established the first cytogenetics laboratory in Boston in 1957 at the MGH (chapter 7), which he had run until he became a much-appreciated member of the new common laboratory.

In 2003 the department reorganized internally again as part of a comprehensive strategic planning process stimulated by a five-year external review by HMS. The goal of this reorganization was to foster integration of expertise across Anatomic and Clinical Pathology, improve efficiency, and promote research. Three divisions continued, now headed by associate chiefs, who were Drs. Robert H. Young for Anatomic Pathology, Michael Laposata for Laboratory Medicine, and David N. Louis for the renamed Molecular Pathology and Research. An Associate Chief for Operations (Dr. Kent B. Lewandrowski) and one for Education (Dr. W. Stephen Black-Schaffer) were added. These individuals, with William Hynes, Director of Finance and Administration, formed the Pathology Executive Committee, which met biweekly to advise the chief and manage the department. Infrastructure functions, such as operations, human resources, informatics, and finance, were centralized and made common among the divisions.

Subspecialization

Dr. Colvin recognized that the discipline of pathology was challenged by the increasing complexity and volume of cases expected of surgical pathologists, which interfered with academic productivity, quality of diagnosis, and teaching. In looking for other models, he was struck by the success of neuropathology and his own specialty,

nephropathology. In both fields the pathologists were subspecialized and were academically active, often engaged in funded research complementary to their clinical duties. At the retreat in 1991, the subject of subspecialization for surgical pathology was discussed but, though the idea held some attraction, the department realized that subspecialization would require at least two pathologists in each subspecialty and that the group was understaffed in some areas. Moreover, some of the younger staff members did not wish to focus on a single subspecialty. Subsequent years brought recruitment of expertise in under-represented fields and the realization that the system could be flexible enough to allow more than one subspecialty per person. In the meantime, the inefficiencies of general surgical pathology in an academic setting became apparent: more and more cases had to be shown to experts, delaying sign-out and inhibiting resident teaching. On July 1, 1995, under the leadership of Stephen Black-Schaffer, Robert Young, and Nancy Harris (see Black-Schaffer, Young, and Harris, "Subspecialization of Surgical Pathology at the Massachusetts General Hospital," *American Journal of Clinical Pathology* 106:S33–S42, 1996), the department instituted complete subspecialty sign-out rotations for the staff pathologists and residents. The department was the first in the world to take this approach, which has proved successful and has served as a model for large hospitals and cancer centers in the United States that have subsequently made this transition.

The system required operational changes. Fourteen anatomic subspecialty services were established, each with at least two staff members and headed by a senior staff member. These included Autopsy, Bone/Soft Tissue, Breast, Cardiac/Pulmonary, Cytology, Dermatopathology, Ear Nose and Throat, Gastrointestinal, Genitourinary, Gynecological, Hematopathology, Neuropathology, Obstetrics/Fetal Pathology, and Renal Pathology. Specimens were assigned to a subspecialty at the point of accession. Residents

rotated on one service at a time for a week and signed out with a subspecialty staff member. Frozen section coverage was not subspecialized (with the exception of the ongoing subspecialty coverage for neuropathology, head and neck pathology, and bone and soft tissue pathology) for practical reasons; it continued to be provided by experienced staff who had ready access to subspecialty consultation if that was indicated.

Scheduling of subspecialized coverage was a challenge, since 14 rotations had to be staffed from a small subset of subspecialists, and the number in each field had to be matched to the workload, both subject to variation. Since each rotation was different, the amount of work fluctuated, depending on the number of specimens and their complexity. Dr. Black-Schaffer developed an innovative and systematic approach to the problem, based on the Medicare physician work relative value units (RVUs) for each service, sometimes corrected on the basis of an assessment that the actual work was either less or more than the Medicare estimate. Because of Dr. Black-Schaffer's good judgment and sophisticated spreadsheets, management of this aspect has been labor-intensive but generally satisfactory.

The original goals were to (1) provide the most accurate diagnoses, (2) maximize clinical efficiency, (3) enhance communications with clinicians, (4) promote faculty research efforts, and (5) optimize teaching of residents and fellows. In 2003 Dr. Colvin evaluated whether these goals had been achieved. Improved accuracy was evident in the number of revised and corrected reports, which significantly diminished from 1995 to 2002 by 24 percent and 66 percent, respectively. The efficiency improvement showed as a 38 percent increase in RVUs per full-time equivalent (FTE) pathologist and a 10 percent decrease in turnaround time. Communication with clinicians could not be quantitated, but over that period new conferences, joint fellowships, and collaborative research projects were established. Indeed, one radiologist was



Figure 25.3 MGH Pathology, 1995. Front row, left to right: Atul Bhan, Nancy Harris, Robert McCluskey, Stephen Black-Schaffer, Austin Vickery, Robert Scully, Robert Colvin, Tessa Hedley-Whyte, Michael Laposata, Eveline Schneeberger, E. P. Richardson. Second row: David Louis, Martha Pitman, Andrew Rosenberg, Benjamin Pilch, Fiona Graeme-Cook, Thomas Flotte, Wanda Szyfelbein, Richard Dickersin, Robert Young, Max Goodman. Third row: Daniel Koelliker, Carolyn Compton, Volker Nিকেleit, Barbara Centeno, Teri Cooper, Suzanne Keel, Debra Bell, Esther Oliva, John Eichhorn, Jane Yang, Jun Teruya, Fred Preffer. Fourth row: Simon Bergman, Metin Ozdemirli, Lisa Lerner, Elizabeth Bailey, Darryl Palmer-Toy, Judith Ferry, Horace Wu, Mark Edgar. Fifth row: Will Hanson, Atsushi Mizoguchi, Emiko Mizoguchi, Matthew Meyerson, Edwin Monuki, Andrea Flieder, Petur Nielsen, Robert Cheek. Sixth row: Giuseppe Andres, Lawrence Zukerberg, Edward Ruffolo, Shane Meehan, William Yong, Michael Pins, Ross Wheeler, Douglas Flieder, Scott Urban.

overheard recommending MGH to a patient getting a mammogram because “MGH has five breast pathologists.” As to academic activity, there was no measurable change in publication output (remaining at 3.6 publications in PubMed per year per faculty member in 1995 and 2001). There was, however, a correlation with research grants. In 1995, 13 percent of the general surgical pathologists had at least 10 percent salary support from grants, in contrast to 67 percent of those focused on one subspecialty. In 2003 there was

a 39 percent increase in the number of faculty with grant support, and the percentage correlated inversely with the number of subspecialty rotations by the faculty member (52 percent of the 23 with one subspecialty grant support, versus 30 percent of the 20 with two subspecialties, and 0 percent of the 3 with three subspecialties). The change was especially notable in the junior faculty, who increased from 26 to 53 percent having grant support. The residents and fellows commented that it was easier to learn when they were



Figure 25.4 MGH Pathology, 2001. First row, left to right: Nancy Harris, Michael Laposata, Robert McCluskey, Robert Scully, Robert Colvin, Tessa Hedley-Whyte, Eugene Mark, Eveline Schneeberger, Atul Bhan, Martin Mihm. Second row: Benjamin Pilch, Richard Kradin, Robert Young, Stephen Black-Schaffer, Debra Bell, David Li, David Louis, Fiona Graeme-Cook. Third row: Fred Preffer, Grace McKee, Wanda Szyfelbein, Christopher Stowell, Judith Ferry, William Faquin, Bizan Bandarchi, Andrew Rosenberg, Ulysses Balis. Fourth row: Kristina Braaten, Paula Arnell, Mari Mino-Kenudsen, Rosemary Tambouret, unidentified, Neal Smith, Petur Nielsen, Martha Pitman, Qun Dong, John Eichhorn, Javad Beheshti, Alexander Kratz (partially obscured), James Flood, Esther Oliva, Timothy Skelton, Yukihiko Imai. Fifth row: Melinda Lerwill, Maryam Mohammadkhani, Mohammad Mahmood, Sam Dadras, Elena Brachtel, Danielle Elliot, Lisa Gallagher, Jan Schmidtko, Artur Zembowicz, Thomas Flotte, Souhad Younes. Sixth row: Zoe Tang, Wen Jing, Aqing Chen, Vikram Deshpande, Dion Buckner, Shamila Mauyyedi, David Coon. Last row: Soner Altiok, Gary Letts, unidentified, David Andrews, Susan Saidman (partially obscured), Anat Stemmer-Rachamimov, Leo Cheng, Gregory Lauwers, Henri Sevestre, Kenneth Harris, Asif Rashid, Heike Varnholt, Stuart Houser, Zbigniew Szczepiorkowski, Emiko Mizoguchi, Drucilla Roberts, Adriana Corben, Lyn Duncan.

focused on one organ system at a time, there was a more manageable workload for daily sign-out, and sign-out was more efficient. When a vote was taken in 2003, 97 percent of the staff and 100 percent of the residents preferred the subspecialized sign-out system. The subspecialty program became a strong attraction for recruiting residents and faculty, and it has been noted that subspecialization enhances the ability of pathologists

to interpret and integrate molecular, imaging, and other sophisticated tests in their diagnostic reports.

Faculty

In 1991 there were 57 faculty members in MGH Pathology. By 2006 the number had increased 33 percent to 76, 53 of whom were recruited by Dr. Colvin (figures 25.3 and 25.4). Among the notable

additions were Kent B. Lewandrowski (1991), now Associate Chief of Pathology for Clinical Services; David N. Louis (1992), now Chief of Pathology; Lyn Duncan (1994), head of Dermatopathology; Walter (“Sunny”) Dzik (1998), Codirector of the Blood Transfusion Service; J. Keith Joung (2000), now Associate Chief for Research; Gregory Y. Lauwers (2000), now Vice Chair of Pathology; David C. Wilbur (2001), Director of Cytopathology; Matthew P. Frosch (2001), now head of Neuropathology; Guillermo (Gary) Tearney (2001), a senior investigator in the Wellman Center for Photomedicine; James Stone (2003), head of Cardiovascular Pathology and now Director of the Autopsy Service; A. John Iafrate (2004), head of Diagnostic Molecular Pathology; and Bradley Bernstein (2005), now a Howard Hughes investigator.

In 1991 there were six Professors of Pathology (McCluskey, Scully, Vickery, Mihm, Schneeberger, and Colvin), a number that doubled during Dr. Colvin’s 15 years as chief. Nine faculty, including four women, were promoted to Professor (E. Tessa Hedley-Whyte, Nancy L. Harris, Robert H. Young, Carolyn C. Compton, Atul K. Bhan, Michael Laposata, David N. Louis, Mary Jane Ferraro, and Eugene J. Mark). Dr. Colvin established the Professors Committee to oversee the promotions process and to monitor academic progress of junior faculty. The faculty was productive during this era, publishing an average of about one paper per working day, not including the Case Records of the MGH. A remarkable number of books were published, prompting Dr. Colvin in 2002 to have a display case built for these contributions just outside the chief’s office suite.

Anatomic Pathology

From 1991 to 2006 the surgical pathology specimen volume increased from 39,633 to 71,595 and cytopathology from about 36,000 to 60,000. These increases caused strains at all levels in the department and required additions of faculty,

residents, technical support, and space. By 2006 there were 48 full- or part-time faculty with anatomic pathology clinical duties, an increase of 33 percent of the faculty and a 79 percent increase in the work.

Several new clinical services were established. In 1991 a formal Fine Needle Aspiration (FNA) Service was started by Dr. Ann Thor; Dr. Martha Pitman later became the director (chapter 19). FNA proved popular (procedure volume increasing from 180 to 800) and in 2002 dedicated patient rooms for outpatient FNA procedures were added to the MGH Avon Center, where outpatients made appointments with pathologists for FNA. In 1994 Eye Pathology was partially incorporated into the MGH practice from the Massachusetts Eye and Ear Infirmary, directed by Dr. Thaddeus (Ted) Dryja, who joined the MGH staff. In 1995 MGH restarted its obstetrical services, and Dr. Drucilla Roberts, a perinatal and developmental pathologist, was recruited from BWH to the MGH staff to start an obstetrical-perinatal pathology service. A fluorescence in situ hybridization (FISH) laboratory for Her2/neu was established in Cytopathology in 2001, and in 2005 the Molecular Diagnostics Laboratory for surgical pathology was inaugurated; John Iafrate was its founding director (see below).

Among the first renovations in the department was the 1992 remodeling of the residents’ room and sign-out space on Warren 2, tripling the number of sign-out rooms to six and equipping them with multiheaded microscopes and computers. In 1998 the Frozen Section Laboratory, accessioning space, and grossing areas were expanded and moved to Blake 3, adjacent to the operating rooms. The Histology Laboratories were moved and enlarged across the hall from the Frozen Section Laboratory and grossing areas, making for efficient processing of samples, and the Cytology Laboratory was expanded into the previous Histology space on Warren 1. The Immunopathology Unit on Cox 5 was moved to new space on Warren 5 in 2000, in order for the

Cox Building to accommodate growing clinical facilities from other departments.

In 2002 Dr. A. Bernard Ackerman (chapter 18) contacted Dr. Colvin, expressing interest in donating funds for a room for a multiheaded microscope for teaching and study. Dr. Ackerman was motivated by his affection for Benjamin Castleman, who had supported his early career at MGH. His generosity culminated in the creation in 2007 of the elegant Ackerman Room in the basement of the Warren Building, which houses a 10-headed microscope, Dr. Ackerman's antique microscopes (about 50), and memorabilia of his career. It has become a popular place to hold teaching conferences with residents, fellows, and clinicians.

In 2003, Kent Lewandrowski assumed oversight of all Pathology clinical operations, lending his valuable experience and expertise to the Anatomic Pathology division. One of the goals achieved was to shorten surgical pathology turnaround time, which was reduced from 3.5 to 2.5 days, and cytopathology from 10 to 6.9 days. This change was the consequence of improved operations, additional equipment and staffing, and quarterly monitoring by service and individual pathologists, which was distributed throughout the department and factored into the quality assurance and credentialing process.

Dr. Frederick ("Fritz") C. Koerner handed over the leadership of the Autopsy Service to Dr. Eugene Mark in 1996 (chapter 15). The Autopsy volume went from 355 in 1991 to 406 in 2006. The autopsy suite was renovated for the first time since it was built in the 1950s with a \$1 million facelift in 2005. The new space permitted a viewing room for teaching and greatly improved lighting and ventilation. Dr. Mark built a strong program, expanding the forensic activities and improving turnaround time to 24 days.

Clinical Pathology

Two of Dr. McCluskey's most significant achievements (chapter 13) were his recognition that the

clinical laboratories should be unified under the administration of Pathology and his 1989 recruitment of Dr. Michael Laposata as the first Director of the clinical laboratories. Administrative efforts continued under Dr. Colvin to effect these changes, and by 1995 the directors of the major laboratories were members of the Pathology Service. By 2006 the structure was widely accepted throughout the hospital, and the contribution of pathologists to patient care was augmented and further appreciated. The Division of Laboratory Medicine was created in 1998 to recognize that the scope extended beyond the Clinical Laboratories to include teaching and research.

Among the innovations in clinical pathology were the creation in 1993 of the Molecular Diagnostics Laboratory in Microbiology, implemented and directed by Dr. Angela Caliendo (now directed by Dr. Eric Rosenberg; chapter 21), and DNA testing for bone marrow transplants, started by Dr. Susan Saidman (chapter 22). Dr. Laposata created a formal series of lectures for Pathology residents that covered the entire span of clinical pathology; the series has been regarded as a major strength of the MGH Clinical Pathology Training Program ever since. Weekly case discussions were held with the Medicine resident team to discuss the interpretation and contribution of laboratory tests to the management of the patients. A "value added" interpretive report was instituted for coagulation testing that was widely praised and led to the laboratory's providing reference services. In 2003, Dr. Lewandrowski designed and implemented a point-of-care laboratory ("kiosk") in the Emergency Room (ER) area to provide rapid turnaround for cardiac and other tests. The result was an overall shortening of average ER stays by 45 minutes, and this was the basis for a Bowditch Award for Dr. Lewandrowski in 2005. The Core Laboratory, directed by Dr. Anand Dighe, was fully implemented by 2007.

The volume of tests generally increased over this period, and efficiency improved because of

automation and new laboratory information systems. For example, for the five years 1996–2001, the volume increased 27 percent to 6,907,312 billable tests, and the test per FTE pathologist decreased by 22 percent. This was accomplished without any increase in space.

Education

Dr. E. Tessa Hedley-Whyte directed the residency program for 11 years, passing the torch to Nancy L. Harris in 1996, who served until 2001 and was succeeded by Dr. Stephen Black-Schaffer. From 1991 to 2006, the number of MGH-funded residency positions increased by 25 percent (from 28 to 35). In 1993 a Clinical Pathology Residency position was added, which was filled by a series of outstanding research-oriented residents, including Drs. Jeannie Lee, Matthew Meyerson, J. Keith Joung, and James Versalovic, all of whom have gone on to successful research careers.

In the early 1990s studies were published suggesting that managed care would create a great reduction in the need for pathologists. Although the prediction proved false, damage to Pathology residency recruitment had already been done, as the number of U.S. medical school seniors matching in Pathology decreased between 1995 and 1998 by 45 percent, to 128. For many years the MGH training program in Anatomic Pathology had been known for its high volume of challenging case material, which provided trainees with an unparalleled opportunity to develop expertise in surgical pathology. It had also been rumored to be a program in which residents worked harder than in other programs. In combination, the managed care prediction and the rumors about the difficulty of the work had a significant negative effect on MGH Pathology recruiting efforts.

In the spring of 1998, under the leadership of Drs. Harris and Black-Schaffer, and with the help of three outside experts, staff and residents worked together through a series of task forces to redesign the Anatomic Pathology curriculum. The new curriculum was based on training

goals, rather than work to be done. The guiding principle continued to be that young physicians learn best by having responsibility for patient care in a supervised, supportive setting. A new principle was added, however, that work does not equal education, so not all cases would necessarily have residents. The department added personnel to substitute for residents in surgical pathology grossing (e.g., doubling the number of pathologist assistants) and established a pathologist assistant student work-study program. The result was decreased work per rotation, more specialty rotations, more time for molecular and other special pathology techniques, and an opportunity for residents to “customize” some rotations with electives, according to their needs or interests. Most of these changes were clear improvements; however, the lack of a resident for every case had mixed reviews. The residents were happy to give up some unedifying tasks, such as dissection of mesenteric lymph nodes, but wanted to see all the interesting cases. Staff found it was sometimes faster and more flexible to sign out without residents, but they were not happy to lose the opportunity to teach—one of the reasons they were attracted to MGH. Fortunately, the department was able to increase the number of residency positions by five, starting in 2003, to a total of 35, which fit the teaching program much better to the clinical service. The changes made in the program anticipated the later national work hours requirements and made the MGH program much more attractive overall. Dr. Black-Schaffer has since become President of the national organization of pathology residency directors (PRODS) and played a leading role in the design of residency training nationwide.

With the increase in subspecialization in the field of pathology came the need for additional fellowship programs. Several fellowships were established or named during this era, including those named for James Homer Wright (Hematopathology), Tracy Mallory (Surgical Pathology), Benjamin Castleman (Surgical Pathology),

Robert McCluskey (Immunopathology/Renal Pathology), Robert Scully (Gynecologic Pathology), E. P. Richardson Jr. (Neuropathology), Priscilla and Edgar Taft (Cytopathology), Austin Vickery Jr. (Surgical Pathology), Morten Grove-Rasmussen (Blood Transfusion), and the Gillette fellowship in Women's Cancers (the last funded by the Gillette Center for Breast Cancer at MGH). Joint fellowships approved by the Accreditation Council for Graduate Medical Education were created with the Harvard hospitals in Molecular Genetic Pathology and in Dermatopathology (chapter 18). Overall, there were about 21 fellowship positions, including those on NIH Training Grants.

The number of postgraduate courses was expanded during the 1991–2006 period under the leadership of Dr. Robert Young, who served on the HMS Department of Continuing Education Committee. A new aspect was holding the courses outside the Boston area (e.g., Arizona, Florida, Italy). Among the regular offerings during this time (with their directors) were “Current Concepts in Surgical Pathology” (Mark, Young, Harris), “Practical Placental Pathology” (Roberts), “Gynecologic and Obstetric Pathology” (Scully, Young, Crum), “Gastrointestinal, Liver and Pancreatic Pathology” (Odze, Lauwers), and “Urologic Surgical Pathology for the Practicing Pathologist” (Young). In addition to providing funds to fulfill the academic mission of the department, all these courses had the benefit of showing the diagnostic, research, and teaching activities of the department in a highly positive light, and they have demonstrated the leadership of the department in diagnostic pathology in many venues. These courses received very positive evaluations, and the course directors frequently receive letters from the Dean of Continuing Medical Education or the Dean of HMS, noting that their presentations ranked in the highest tier of HMS postgraduate courses.

In 2001, Dr. Robert Scully retired after 27 years as the Editor of the Case Records of the MGH. As a result of a search committee review

that involved the Editor of the *New England Journal of Medicine*, Dr. Jeffrey Drazen, Dr. Nancy L. Harris was selected as the next Editor of the Case Records and appointed a part-time Deputy Editor of the *NEJM*, an indication of the importance *NEJM* placed on this activity. Dr. Harris implemented a number of changes, focusing particularly on treatment issues and pathogenesis to bring the discussion into the arena of current clinical interest (chapter 24).

Members of the department played many roles in various HMS courses and in the medical school teaching structure, spending close to 1,000 contact hours per year and as many hours in preparation and administrative work. Dr. Colvin played a leadership role in the “New Pathway” at HMS, initiated in 1984 by Dean Daniel Tosteson, the goals of which were to promote problem solving via case-based tutorials and integrating across disciplines. Dr. Colvin designed and led “Identity, Microbes and Defense,” a 12-week course that combined general pathology, immunology, and microbiology for the first-year students. He also served as the Master of the Oliver Wendell Holmes Society from 1990 to 1992. For many years Drs. E. P. Richardson Jr. and Tessa Hedley-Whyte taught in the preclinical neuroscience courses. The development of the combined Harvard-MIT Health Sciences and Technology (HST) Program provided an additional opportunity for MGH faculty to teach. Dr. David Louis was the director and principal instructor for the neuroanatomy portion of the HST course on the human nervous system from 1994 through 2000, followed by Dr. Matthew Frosch. Dr. Kamran Badizadegan was the founding course director for “Principles and Practice of Human Pathology,” a full-semester, graduate-level course designed primarily for doctoral students in the Leder Human Translational Biology program at HMS and Graduate Education in Medical Sciences at HST.

Beyond their direct involvement in teaching, members of the department participate in other activities related to the teaching mission of HMS. Members served on or chaired the Pathology

Education Committee; the Executive Committee of the Academy; the Committee for Tutoring Excellence; the Committee for Professional Development; the Curriculum Committee; the Planning Committee; and the Harvard-Macy Program. Dr. Thomas Aretz was the Director for International Education, Harvard Medical International, and has been a leader in these efforts to support and promote teaching at HMS. Members of the department were recognized for these efforts through several highly competitive HMS teaching prizes during this time—for example, the Irving M. London Teaching Award (Dr. Louis), the Preclinical Teaching Prize given by the Graduating Class (Drs. Laposata and Aretz), the Teaching Prize for Second Year Teaching (Dr. Laposata, Compton, and Aretz).

Research

In 2001 a new Division of Molecular Pathology and Research was created under the direction of David Louis to encourage the further development of the departmental translational and basic research programs. A letter to the staff from Dr. Louis stated that the goals were to (1) promote the research activities of the staff, residents, and fellows; (2) provide a focal point for efforts to advance molecular diagnostics; (3) oversee research training of the residents and fellows; and (4) provide cohesion and visibility at MGH for the rapidly developing field of molecular pathology. The division would be “at the same level in our departmental organization as CP and AP. Any member of those divisions can also be a member of the Division of MPR, whether involved in clinical or basic research, and whether or not the research is funded through grants.”

By 2005 the department had 18 principal investigators with extramural support, and the annual extramural funding had tripled from 1991 to \$8.0 million direct costs (\$12.2 million total), the majority (\$5.2 million) from NIH. A long-standing departmental NIH Training Grant begun in 1978 continued to support five fellows each year, and it was expanded to support seven

fellows per year in 2006. The research space committed to pathology investigators was about 20,000 square feet, divided principally among Charlestown Navy Yard 6 and 7 (13,000 square feet), Simches (3,000), Gray 2 (1,500), and Thier (2,000). Pathology research faculty also worked in laboratories in other departments occupying an additional 6,000 square feet. The MGH Tissue Repository was put under the direction of the Pathology Service through the efforts of Dr. Louis and Dr. Daniel A. Haber, Director of the MGH Cancer Center. Under Dr. Louis's leadership, the department identified a major research theme: the molecular pathology of cancer. In collaboration with the MGH Cancer Center, he developed a five-year recruitment and space plan that improved the quality and direction of Pathology research, facilitated collaboration with other MGH researchers, and increased levels of external funding.

Among the notable research faculty recruits during Dr. Colvin's tenure were Drs. David Louis (1992), Dennis Sgroi (1994), Atushi Mizoguchi (1999), R. Neal Smith (1999), J. Keith Joung (2000), Matthew P. Frosch (2001), Anat O. Stemmer-Rachamimov (2001), Guillermo Tearney (2001), Sandra Orsulic (2002), James Stone (2003), A. John Iafrate (2004), and Bradley Bernstein (2005). Strong programs were established in neuropathology, molecular basis of neoplasia, and immunopathology. Space limitations permit only a brief mention of some of the scientific highlights of 1991–2006.

Ivan Stamenkovic identified, cloned, and determined the function of CD44, a leukocyte surface molecule that serves as a receptor for hyaluronic acid (1990–1991) and promotes metastasis by anchoring MMP-9. Nancy Harris led the development of a new standard classification of lymphoma (1994), known as the Revised European-American Lymphoma (REAL) classification: her first authored report in 1994 has received over 4,500 citations as of this writing. David Louis published the first demonstration of the use of genetic markers for guiding brain

tumor therapy (1998). The detection of the prognostically favorable loss of chromosomes 1p and 19q has become a standard clinical test in gliomas. Novel forms of antibody-mediated rejection were recognized by Robert Colvin and his colleagues and incorporated into the international diagnostic classification (1998–2002). Guillermo Tearney's group in the Wellman Laboratories developed novel ways of imaging pathological processes in vivo by optical coherence tomography (1997–2003). Robert McCluskey showed that megalin, a member of the LDL-receptor family, is a high-affinity thyroglobulin receptor expressed on thyroid cells and mediates transcytosis of thyroglobulin, rather than transport to lysosomes, and thereby can suppress hormone release (1999). Lawrence Zukerberg identified a new member of the cell cycle apparatus, Cables, which regulates cdk2, and with Chin Lee Wu he showed that it was lost in the majority of colon cancers (2001). Lyn Duncan played a major role in establishing the clinical significance of melastatin expression in melanomas (2001), work that has led to a multicenter trial. Dennis Sgroi used laser capture microdissection and microarrays to demonstrate the genes active in early-stage breast cancer and predict response to therapy (2004). Telepathology reached a threshold of support through a \$1.7 million Department of Defense grant to David Wilbur. Synthetic zinc finger proteins were developed as a powerful research tool by Keith Joung and his colleagues (2001–2006), which led to the development of an open-source method. The last recruit of the era was Brad Bernstein, who discovered chromatin patterns that regulate cell fate (2006) and went on to become a Howard Hughes Investigator.

Pathology Informatics

For many years the department had used the CoPath program for anatomic pathology, a system that had incorporated many suggestions made by Dr. Black-Schaffer. In 2000 the Pathology Informatics Unit was created, and

Dr. Ulysses Balis, who joined the department in 1999, was named Director. He led the conversion from CoPath to PowerPath and wrote much of the software for the new features. Among the changes were a barcode tracking system for slides, automatic printing of slide labels by subspecialty, detailed coding libraries and feedback on billing, and easier editing of reports. The department also entered the digital era during this time, as all conferences were transmitted via digital cameras and the first departmental Web site (1995) went online. Sunquest was implemented in the Clinical Laboratories in 1999.

Financial Aspects

The years 1991 to 2006 were a difficult time for pathology reimbursement nationwide. The only way to maintain clinical income was to increase productivity of faculty members (cases signed out per year or RVUs per year), which placed a premium on the efficiency of the sign-out process and the billing recovery. In 1998 the department made a concerted effort to improve billing efficiency through combined efforts in the MGPO Billing Office and review of submitted bills by William Hynes. A computer system that screens the bills for incomplete or inconsistent information greatly decreased the rejection rate. The net result was an increase in receipts of about 24 percent over the subsequent three years and a 33 percent decrease in mean time of the accounts receivable.

The increase in revenues offered the opportunity to establish an objective salary structure that was based on clinical service, academic rank, research support, leadership or administrative activities, and experience. Bonuses were based on productivity and contributions in the previous year. The department was committed to sustaining the academic activities of the full-time faculty, providing support from practice funds for at least one day a week of academic activities. Overall, the salaries progressively increased to the 75th percentile by 2007.

*Other Events of Note: The Centennial and
New HMS Professorships*

In 1996 the department celebrated its 100th anniversary. Robert Colvin commissioned a Centennial Celebration, organized by Austin Vickery and Robert Scully, that was held over a day and half in October 1996. More than 250 current and former members of the department from around the world (from Iceland and England to the Philippines and Japan) convened to hear a series of talks, which included historical facets of the early development of pathology at the MGH, activities of alumni and staff, and perspectives on pathology in the future. Anna Castleman, Benjamin Castleton's widow, was the guest of honor, and Dr. Samuel O. Thier, the MGH President, attended. A wonderful group photo of the attendees in front of the Bulfinch steps hangs

in the chief's office. By all accounts, the celebration was a success, and attendees vowed not to wait another 100 years for the next large alumni reunion.

A singular event occurred on February 9, 2000, after Austin Vickery ("Vic") had retired in 1998. Vic asked for an appointment to see Dr. Colvin. He came into the chief's office at 10:01 in the morning and in his deep, booming voice said, "Sit down, Bob. I think you are going to like what I have to say." Vic and his wife, Amelia Frances Vickery, were endowing an HMS professorship in surgical pathology to be based at MGH. Endowed professorships are rare and most precious, and this was only the second in the MGH Pathology department. HMS at the time required a donation of \$2.75 million. The terms of the gift state: "It is the intent of the Donors to support the Department of Pathology at the



Figure 25.5 Reception at Harvard Medical School for the Robert E. Scully Professorship of Pathology, 2006. Left to right: Peter Slavin (President of MGH), Robert Scully, Joseph Martin (Dean of HMS), Robert Colvin, Robert Young (who would become the first Robert E. Scully Professor of Pathology).

Massachusetts General Hospital. The initial and subsequent incumbents of the Amelia Frances and Austin L. Vickery, Jr. Professorship in Pathology shall be a Professor appointed in the Department of Pathology at the Massachusetts General Hospital, with a specialty in surgical pathology.” The first incumbent in 2000 was Dr. Nancy Harris. Sadly, Amelia Vickery died in 2002, not long after this generous gift was made. But Austin Vickery was not finished with his overwhelming generosity to the MGH. After his death in 2005, he left a further donation of \$4 million to support the Pathology department. With some of the income from this endowment the Vickery Grants were subsequently established, to provide support for clinically oriented Pathology faculty, in collaboration with residents and fellows, to initiate research projects. This has permitted the faculty to take advantage of new opportunities in pathology, such as the molecular analysis of tumors, which cannot be readily done without financial support.

Drs. Colvin and Young initiated a fund-raising effort in 1994 to establish an HMS professorship to be named for Robert E. Scully. Many alumni, friends, and staff were generous contributors, but the “big” gift remained elusive, until Dr. Vickery’s donation, a portion of which was used to complete the Scully Professorship. In August 2001, at his eightieth birthday party, Dr. Scully had told Dr. Colvin that he would not retire until his beloved Red Sox won the World Series (which had not happened since 1918). Dr. Colvin surmised that this may have been the reason that the Red Sox prevailed for the first time in 86 years in 2004; Dr. Scully was able to attend one of the critical games. On January 1, 2005, Dr. Scully retired, quite satisfied with his career and his Red Sox. A dinner was held on July 28, 2006, to honor Dr. Scully and the donors and to celebrate the initiation of the Scully Professorship (figure 25.5). With the approval of the Trustees and the Dean of HMS, David Louis appointed Robert Young the first incumbent of the Robert E. Scully Professorship in 2007.

The Close of the Colvin Era

On April 12, 2005, in announcing to the faculty his intent to retire after a successor was chosen, Robert Colvin listed a number of departmental accomplishments since 1991, including initiation of full pathology subspecialty practice, now modeled by other academic centers; expansion of the staff by 33 percent and the residents by 25 percent; recruitment of 53 of the present faculty members; promotion of nine professors; addition of one endowed professorship in surgical pathology; tripling of research funds; doubling of research space; creating a new molecular pathology lab; and increasing the departmental reserves and endowment fivefold. Dr. Colvin concluded: “Thank you for making my tenure as chief a wonderful and most exciting experience. We can be proud of what we have accomplished together and more is anticipated in the future. If you give as much energy and devotion to our department and the MGH in the future as you have in the past, we will thrive.”

THE YEARS 2006–PRESENT

David N. Louis became the sixth Chief of the Pathology Service at the Massachusetts General Hospital on September 1, 2006, and the Benjamin Castleman Professor of Pathology at Harvard Medical School later that fall. Dr. Louis was born in London, England, on December 25, 1959, and, after living in England, Israel, and South Africa, was raised in the New York City area. He attended Cornell University, majoring in English, and then the State University of New York at Stony Brook School of Medicine, graduating in 1985. After two years of training in internal medicine at Albany Medical Center, he changed his career path from neurology to neuropathology. Dr. Louis moved to the MGH in 1987 and completed two years of training in Anatomic Pathology and two years in Neuropathology, as well as two years in cancer genetics research in the Molecular Neuro-Oncology Laboratory of Dr. Bernd Seizinger in

Neurosurgery. Dr. Louis joined the faculty in Pathology and Neurosurgery in 1992. When Dr. Seizinger left the institution, Dr. Louis continued the Molecular Neuro-Oncology Laboratory, which joined the Pathology Department partially in late 2001 and fully in 2006.

Dr. Louis's clinical neuropathology practice and research focuses on brain tumors, with an emphasis on the molecular genetic basis of malignant gliomas and the application of molecular diagnostics to malignant glioma classification. His laboratory was the first to demonstrate that molecular approaches could be used to subdivide malignant gliomas in a biologically relevant manner, and that molecular approaches could be used to predict the response of particular malignant gliomas to specific therapies—work that resulted in worldwide adoption of molecular testing for the management of patients with these tumors. As of this writing (2011), he has contributed about 250 original papers to the literature, as well as approximately 100 chapters, reviews, and clinical reports; he has also authored and edited major textbooks in the field of neuropathology, including books for the World Health Organization and Armed Forces Institute of Pathology series.

When Dr. Louis became Chief of the Service, he began a program designed to capitalize on the accomplishments of Dr. Colvin's tenure by utilizing departmental and hospital strengths to address departmental needs. He set programs in place to unify the department in a single operational unit and to develop the three areas of molecular diagnostic pathology, molecular pathology research, and pathology informatics—believing that these three areas represented important directions that the field was taking, and that MGH Pathology was or could be well positioned to take the lead in the next generation of academic pathology departments.

Administrative Unification of the Department

In 2006 the department was large, with over 700 employees and 76 faculty members. The

incorporation of the clinical laboratories approximately 15 years earlier had created a large Clinical Pathology/Laboratory Medicine group, which complemented the already large and renowned Anatomic Pathology division. These two large enterprises, however, remained quite administratively, operationally, and financially independent of one another. Moreover, the research group, which was growing, also remained relatively isolated.

Dr. Louis, believing that the department and field of Pathology could grow only through combining its various strengths, undertook a rapid integration of the different elements of the department (the divisions of Anatomic Pathology, Clinical Pathology, and Molecular Pathology and Research), and began a nearly yearlong process of reorganizing the departmental administration and operations. A matrixlike organizational approach was designed to encourage each unit (Surgical Pathology, Autopsy Pathology, Microbiology, Immunology, etc.) to achieve all three of its missions: clinical service, teaching and education, and research. He then created five Associate Chief positions, each responsible for a specific element of facilitating those missions. The five Associate Chief-level positions were in Clinical Services, Teaching and Education, Research, Informatics, and Finance and Administration. Following a strategic plan completed in March 2008, a sixth Associate Chief position was added, for Quality and Safety. In September 2006 Dr. Kent Lewandrowski, a clinical and anatomic pathologist who had excelled in the department in clinical chemistry and in operational issues relating to laboratory medicine, assumed the role of Associate Chief of Pathology for Clinical Services; Dr. Stephen Black-Schaffer, who had successfully directed the residency and fellowship training programs under Dr. Colvin, continued this role as the Associate Chief of Pathology for Teaching and Education; and Dr. Louis continued being temporarily in charge of the Research Program. William Hynes, the Executive Director

of Pathology, continued his role, directing the group in charge of Administration and Finance. In the fall of 2006 Dr. Louis recruited Dr. John Gilbertson from the University of Pittsburgh and Case Western University to become Associate Chief of Pathology for Informatics; Dr. Gilbertson had extensive experience in pathology informatics, particularly in the digital imaging applications. In January 2009, Dr. J. Keith Joung was appointed Associate Chief of Pathology for Research; Dr. Joung had trained at the MGH and had been an early recruit to the rebuilt Molecular Pathology Unit; he had built a successful research career in the field of zinc finger biology. And in July 2009, Dr. Jennifer Hunt joined the department as Associate Chief of Pathology for Quality and Safety; Dr. Hunt was recruited from the Cleveland Clinic and was nationally known for her work in ENT pathology, molecular diagnostics, and pathology operations. Two additional changes in 2009 completed the reorganization of the department: (1) an administrative consolidation of the various laboratories into six groups: the Blood Transfusion Service, directed by Drs. Christopher Stowell and Sunny Dzik; Core Laboratory, led by Dr. Anand Dighe; Cytopathology, under the leadership of Dr. David C. Wilbur; Histopathology Services, encompassing Surgical Pathology and Autopsy Pathology, under Dr. Gregory Y. Lauwers; Microbiology, led by Dr. Mary Jane Ferraro; and the growing research laboratories in Charlestown and at the main campus, overseen by Dr. Keith Joung; (2) creation of the Pathology Senior Management Group, which meets weekly for ongoing management of the department. This group complements the Pathology Leadership Council, which Dr. Louis had started in late 2006, as a planning and leadership body within the department.

Molecular Diagnostics

The advent of molecular diagnostics promised to change the field of pathology dramatically, but its implementation proved challenging

in different ways for pathology departments across the country. At the MGH before 2004 molecular diagnostics had grown substantially within Microbiology under the direction of Dr. Eric Rosenberg, an infectious diseases specialist who joined the Microbiology Laboratory in 2001 and who became its codirector in 2009. But molecular diagnostics had made only relatively small inroads in the Clinical Laboratories and Anatomic Pathology. For example, in Anatomic Pathology, selected testing was scattered in mostly research-based laboratories, without centralized billing or reporting. Moreover, since the creation of Partners HealthCare in the mid-1990s, all of clinical cytogenetics was performed in a centralized Partners laboratory at Brigham and Women's Hospital, as was hematopathology molecular diagnostic testing.

Plans to expand and formalize molecular diagnostics came to fruition in 2005 with the development of the Diagnostic Molecular Pathology Laboratory (figure 25.6). Dr. John Iafrate was recruited by Drs. Colvin and Louis to lead this endeavor, having completed an anatomic pathology residency at Brigham and Women's Hospital and the HMS-wide Molecular Genetic Pathology Fellowship Program. The lab started in modest laboratory space in the Charlestown Navy Yard with only one technician. Within two years the lab had moved to Warren 5 and had three technicians as well as a growing test menu that included Sanger sequencing and FISH on formalin-fixed tumor tissue. The new proximity of the laboratory to Surgical Pathology operations was beneficial to both the Molecular Laboratory and the department. In addition, the laboratory began to take on clinical trial work and was beginning to show leadership in the area of prospective genotyping of tumors for clinical trials of new targeted antineoplastic agents.

The year 2007 saw rapid expansion of operations and the hiring of Dr. Dora Dias-Santagata to aid in clinical test development and translational research. Within a few months a major



Figure 25.6 MGH Molecular Diagnostic Pathology, 2010. Seated, left to right: Jennifer Hunt, A. John Iafrate. Standing: Long Le, Dora Dias-Santagata, Miguel Rivera.

expansion of the mission of the laboratory occurred when it had the opportunity to build a new laboratory in the Jackson Building in collaboration with the Cancer Center. Dr. Daniel Haber, Director of the MGH Cancer Center, and David Louis funded a new laboratory dedicated to high-throughput tumor genotyping: the Translational Research Laboratory, under the leadership of John Iafrate and Leif Ellisen, a medical oncologist, and codirected by Dora Dias-Santagata and Darrell Borger. The laboratory has developed a custom clinical cancer genotyping platform, termed SNaPshot, which analyzes archived tumors for over 100 recurrent mutations. This assay is the first of its kind to be applied clinically, and the lab now is a prototype for what many see as the future of cancer diagnostics; indeed, the clinical implementation of this testing received local and national media coverage, both in the

popular press and in scientific venues such as *Nature*. The molecular diagnostics laboratories have also proven key sites for clinical trials, serving as a central resource for at least three major genetic prescreening trials. Perhaps the most successful as of 2011 has been a large screening effort to identify prospectively non-small cell lung carcinoma patients with a rare genetic lesion, the EML4-ALK rearrangement.

As case volumes continued to increase, the laboratory in 2010 hired additional molecular pathologists: Drs. Jennifer Hunt, Miguel Rivera, and Long Le. Dr. Le has begun to introduce several cutting-edge technologies, including DNA microarrays and next-generation sequencing, into clinical practice. As of this writing, hopes are high that the near future will witness deep sequencing of clinical specimens to revolutionize clinical cancer management.

Molecular Pathology Research

In late 2001, during Colvin's tenure, David Louis became the head of the Division of Molecular Pathology and Research. In this capacity he began a process of recruiting additional basic scientists to the Molecular Pathology Unit and restructuring the Pathology departmental research effort. This recruiting strategy continued when Dr. Louis became chief, and, with Dr. Keith Joung's taking over as Associate Chief of Pathology (Research) in 2009, it continues still.

The general outline of the recruiting strategy was to target research related to cancer, given the strengths of the Pathology department in the clinical aspects of cancer and the interests of some of its research faculty, as well as the close relationship that developed between the Molecular Pathology Unit, then on the seventh floor of Building 149 in the Charlestown Navy Yard, and the MGH Center for Cancer Research, also on the seventh floor. Indeed, most of the recruiting undertaken by Pathology over this period was in collaboration with the Cancer Center. In addition to their research relating to cancer, researchers

were selected on the basis of their ability to interact with the clinical arm of the department in a mutually beneficial manner. In general, this involved the hiring of researchers who understood the benefits of working in a pathology department (e.g., pathologist expertise in cancer and in tissue analysis, and tissue access) and whose work would also benefit the more clinically oriented pathologists (e.g., by generating academic projects involving both clinical and research faculty). Numerous conferences and activities were created to encourage more interactions between the clinical and research groups, most notably the Molecular Pathology and Research (MPR) Conference (started in January 2002) and the InterLaboratory Conference (started in the fall of 2009). To facilitate growth in Pathology research,

the hospital administration provided the department with approximately 2,000 square feet of newly renovated research space in the Simches Research Building in 2006. In addition, approximately 13,000 square feet of research space was renovated for Pathology on the sixth floor of Building 149 by the fall of 2008; the new space offered laboratory and office space for 10 principal investigators. Another approximately 3,100 square feet of research space was then renovated for Pathology in the fall of 2010 on the seventh floor of Building 149.

As of the fall of 2001, the Molecular Pathology Unit included David Louis's group (Drs. Louis, Anat O. Stemmer-Rachamimov, and Gayatri Mohapatra; a laboratory shared with Neurosurgery), and Drs. Eveline Schneeberger (pul-



Figure 25.7 MGH Molecular Pathology Unit (MGH East campus), 2010. Seated, left to right: David Langenau, Miguel Rivera, Kevin Haigis. Standing: David Louis, Eveline Schneeberger, Dennis Sgroi, Keith Joung, Atsushi Mizoguchi, Catherine Nutt.

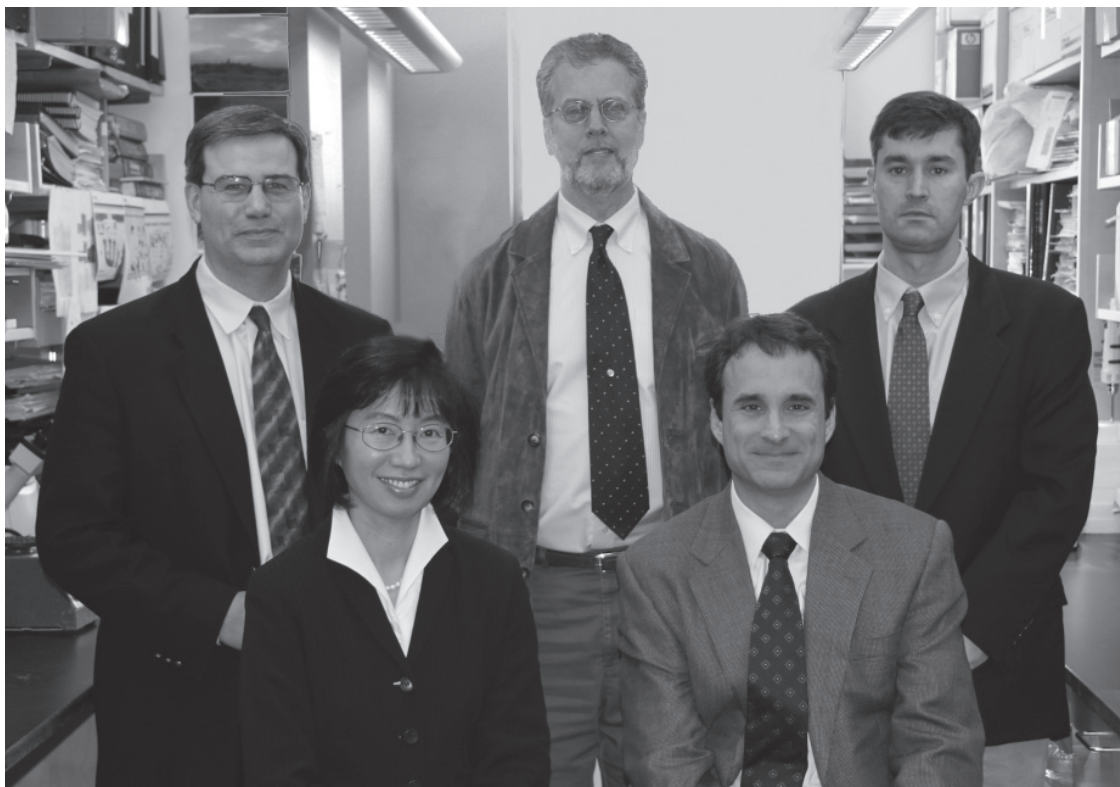


Figure 25.8 MGH Molecular Pathology Unit (Simches Building) and associated investigators, 2010. Seated, left to right: Jeannie Lee, Bradley Bernstein. Standing: James Stone, Fred Preffer, John Higgins.

monary biology) and Dennis Sgroi (breast cancer genetics). Recruits to the Molecular Pathology Unit over the 2001–2010 period were (figure 25.7):

- J. Keith Joung, M.D., Ph.D. (2001): protein and genome engineering
- Sandra Orsulic, Ph.D. (2002): mouse models of ovarian cancer
- Bradley Bernstein, M.D., Ph.D. (2005): epigenetics
- Kevin Haigis, Ph.D. (2007): mouse models of gastrointestinal cancer
- Catherine Nutt, Ph.D. (2007): molecular neuro-oncology
- David N. Lengenau, Ph.D. (2008): cancer modeling in zebrafish
- Miguel N. Rivera, M.D. (2009): pediatric cancer genetics

These investigators have enjoyed considerable successes, in scientific discovery and in

funding. For example, grant support in the department reached \$10 million by 2010 and was associated with cutting-edge publications in top-quality journals, including the *Nature* family, *Cell* family, and *Science* family journals. Notably, Pathology investigators developed strong ties and affiliations with a number of other centers and institutes. For example, in addition to the multiple cross-appointments with the MGH Center for Cancer Research, Drs. Bernstein and Rivera were members of the Broad Institute of MIT and Harvard; Dr. Lengenau, the Harvard Stem Cell Institute; Dr. Joung, the MGH Center for Computational and Integrative Biology; Dr. Bernstein, the MGH Center for Systems Biology. The group also quickly proved successful at recruiting Ph.D. candidate graduate students in the Harvard Biological and Biomedical Sciences program. Moreover, the long-standing departmental T32 Training Grant was increased to seven

slots per year and was populated by even more pathologist-scientist trainees graduating from the residency program and going into laboratories in Molecular Pathology. By 2010 the research group was vibrant, interactive, and highly productive, poised to make further advances in conjunction with the clinical arm of the department.

Bradley Bernstein's laboratory became part of the Howard Hughes Medical Institute in the summer of 2009, with a concomitant move to Pathology space on the eighth floor of the Simches Building (figure 25.8). In this regard, Dr. Bernstein joined Dr. Jeannie Lee, a graduate of the Clinical Pathology training program in the early 1990s, who went on to become a highly successful Howard Hughes Medical Institute investigator in the department of Molecular Biology at MGH, also in the Simches Building, with a focus on the biological basis of X chromosome inactivation. Other investigators in the Simches Building included Drs. James Stone in cardiovascular pathology, Atsushi Mizoguchi in inflammatory bowel disease research (who would move to the Molecular Pathology Unit in Charlestown in 2009), and Robert B. Colvin in transplant immunopathology.

The rapidly growing Pathology Informatics group (see below) had also developed extensive research activities, centered on digital imaging, and occupied newly renovated space on nearby Merrimac Street in 2010. The robust cross-appointments of pathologist-scientists in other departments also continued, as individuals such as Guillermo (Gary) Tearney pursued his cutting-edge imaging technology development in the Wellman Center for Photomedicine, Matthew P. Frosch studied mouse models of neurodegeneration in the MassGeneral Institute for Neurodegenerative Disease, and Chin-Lee Wu focused on prostate cancer in Urology.

Pathology Informatics

When David Louis became chief, informatics was one of his major concerns. The goal was to

incorporate the use of digital information and digital information systems into all aspects of the practice of pathology and to make MGH a national leader in the field. This was to be accomplished in two related ways: the recruitment or internal advancement of skilled diagnostic pathologists, laboratory technical directors, and technicians with understanding and strong interest in informatics; and a set of initiatives that would focus the department on informatics and the use of information systems.

By 2010 the department had a nationally recognized Associate Chief of Pathology in charge of informatics (John Gilbertson) as well informatics directors in anatomic pathology (Thomas Gudewicz), laboratory medicine (Anand Dighe), molecular pathology (Long P. Le), and clinical imaging (David C. Wilbur), many of whom were nationally recognized in their areas (figure 25.9). It also had a group of highly respected independent researchers with major interests relating to informatics and digital imaging (Kamran Badizadegan, Leo Cheng, John Higgins, James Michaelson, Guillermo Tearney, and Yukako Yagi), a fellowship program that had already become one of the strongest and largest in the country, and a growing number of young pathologists for whom informatics would most probably be a large part of their careers.

To complement these clinical informatics physicians, and to give them a platform on which to work and develop, the department entered into industrial collaborations and enterprise initiatives. Some of the most important in 2011 include a provider order-entry system and robotic line for the Core Laboratory; imaging research collaborations with a number of companies, including NEC, Olympus, Philips, and Sony; developmental initiatives in clinical molecular sequencing for broad-based cancer genotyping with the sequencing pioneer Ion Torrent; and a 10-year codevelopment agreement with Sunquest Information Systems for the development of a modular anatomic pathology laboratory information system



Figure 25.9 MGH Pathology Informatics, 2010 (not all pictured). Seated, left to right: Anand Dighe, John Gilbertson, Yukako Yagi. Standing: David Wilbur, Thomas Gudewicz, James Michaelson

integrated with the clinical laboratory information system. Also important were the establishment of research facilities for pathology imaging and operations (moving into newly renovated space on Merrimac Street in the spring of 2010), the implementation of a new laboratory information system in Anatomic Pathology and a related, department-wide initiative to measure and redesign the workflow, data management, and laboratory practice in anatomic pathology.

Global Health

The department has been fortunate to have a number of faculty active in global health projects, primarily in Africa. These have included, among others, Sunny Dzik working to supply

laboratories and carry out research in Uganda; Drucilla Roberts developing a clinic and an international pathology course in Ethiopia; Aliyah Sohani organizing telepathology teaching activities in Tanzania and Kenya; Richard L. Kradin undertaking training in tropical disease pathology; and participation by several faculty members in the Global Scholars Program in Pathology for Laboratory Professionals. A number of MGH Pathology trainees have also been involved in trips to Africa with Dr. Dzik and to Vietnam with Dr. Martin Mihm. The faculty and trainee group has recently focused on planning additional educational and training ventures, in association with the MGH Center for Global Health.

OVERVIEW OF THE CURRENT DEPARTMENT

MGH Pathology continues its success in its missions of excellence in clinical care, teaching, and research. Its current mission statement reads:

To deliver the highest quality pathology services and to move the field of pathology forward.

The clinical services are completely subspecialized: each organ system has a dedicated team of specialist pathologists, in many cases combining clinical and research interests—a structure that optimizes clinical expertise, teaching, and research productivity across the department. The department is large, comprising 90 faculty members (figure 25.10), 800 employees, 50 residents and clinical fellows, and numerous research fellows; a budget of over \$125 million per year; and test volumes that exceed 10

million clinical laboratory tests, 80,000 surgical specimens, 60,000 cytopathology specimens, and 35,000 red cell transfusions each year. The residency and fellowship programs continue to grow and have been restructured to facilitate and customize subspecialty training tracks as much as possible. The research component continues its rapid growth, as additional investigators are recruited and new programs initiated.

Given that the field of pathology in general has entered an era of exhilarating growth, it is likely that MGH Pathology, poised with strengths in so many areas, will be a major player in the upcoming revolution in personalized medical care that will lead to earlier diagnosis, more precise prognosis, and tailored therapy. We can only hope that those who follow will continue in the remarkable tradition laid down by those who have preceded us.



Figure 25.10 MGH Pathology, 2010, in the Ether Dome, a formal faculty portrait for this book. Front row, left to right: Andrew Rosenberg, Mary Jane Ferraro, Eugene Mark, David Wilbur, Martin Mihm, David Louis, Robert Young, Nancy Harris, Atul Bhan, Eveline Schneeberger. Second row: John Gilbertson, Matthew Frosch, Gregory Lauwers, Stephen Black-Schaffer, Jennifer Hunt, Kent Lewandrowski, Eric Rosenberg, Judith Ferry, Richard Kradin, Petur Nielsen, Keith Joung, Robert Hasserjian, Esther Oliva. Third row: Joseph Misdraji, William Faquin, Lyn Duncan, Chin-Lee Wu, Martha Pitman, Christopher Stowell, Irwin Roth, James Michaelson, John Eichhorn, Mandakolathur Murali, Lawrence Zukerberg, Neal Smith. Fourth row: Anat Stemmer-Rachamimov, Bradley Bernstein, Frederick Koerner, Fred Preffer, Aliyah Sohani, John Grabbe, Katherine Kosinski, Rebecca Osgood, Mari Mino-Kenudson, Aleksandr Vasilyev, James Stone, Elena Brachtel, James Flood, Susan Saidman, Adriano Piris, Abner Louissaint, Peter Sadow, Thomas Gudewicz, John Iafrate. Fifth row: Catherine Nutt, Atsushi Mizoguchi, David Langenau, Miguel Rivera, Lee Zou, Walter Dzik, Yukako Yagi, Anand Dighe, Ronald Balassanian, Rosalyn Nazarian, John Higgins, Kevin Haigis, Elizabeth Lee-Lewandrowski, Diane Brown, Robert Makar, Dora Dias-Santagata, Di Tian, Mai Hoang, Melinda Lerwill, Patrick Sluss, Rosemary Tambouret. (Full-time faculty not available on that day include Robert Colvin, Tessa Hedley-Whyte, Kamran Badizedegan, Drucilla Roberts, Dennis Sgroi, Elizabeth Van Cott, John Branda, Vikram Deshpande, and Long Le.)

