Biomedical Momentum

The curtain has begun to lift on Harvard's growing commitment to life sciences, particularly those involving biomedical research. Three events early in the academic year highlighted the enormous economic implications of developing biomedical technology; the role of university research in underpinning such advances; and some of the new programs Harvard hopes to launch to advance basic and applied scholarship in these realms.

On September 12, Lawrence University Professor Michael E. Porter, a scholar of corporate strategy and of enterprise "clusters," convened a "Massachusetts Life Sciences Summit" at Harvard Business School. Attendees included education leaders, corporate executives, trade association officers, and elected officials, each with a distinct perspective on what President Lawrence H. Summers called a moment of "unique promise" in life sciences.

Porter detailed what he called the world's preeminent life-sciences center in a single metropolitan area, as measured by research funding, patents, share of local employment, and other indicators. The Greater Boston cluster, he demonstrated, encompasses research universities, academic hospitals, 300 biomedical companies—from start-ups to established manufacturers of pharmaceuticals and medical devices—and supporting services such as venture funding and legal counsel. He estimated that the industry could create 100,000 new jobs in Massachusetts, the largest economic opportunity available to the Commonwealth, and declared that "It's ours to lose." Lest Massachusetts reprise the collapse of the minicomputer industry (as electronic technology migrated to semiconductor chips and the personal computer, the engine of growth in Silicon Valley), he urged participants to join forces to address inadequacies in housing, clinical-testing infrastructure, and workforce skills so as to ensure success.

Michael E. Porter

JUSTIN IDE/HARVARD NEWS OFFICE

Porter's presentation followed speeches by Summers and by MIT's president, Charles M. Vest, and a whirlwind overview of genomics by Eric S. Lander, who will direct the Broad Institute, a Harvard-MIT-Whitehead Institute collaboration to develop new tools for medicine (see "Genomic Joint Venture," September-October, page 75).

Summers, outlining Harvard's role, propounded three economic principles. First, he said, in knowledge-based industries, returns increase from new investment (as more scientists come into proximity, generating fresh ideas and avenues for investigation). Second, he observed that some division of labor is in order: universities "are uniquely well-suited" to carry out basic research "because of our endowments, because of our ability to attract philanthropic resources, because of synergies with the scientific mission," but "are very poorly situated" to market

A Bioscience Portfolio

Two recent grants to faculties at the far geographic reaches of the University demonstrate the diversity and scale of Harvard's life-sciences expertise. Each also illustrates the institutional collaborations required for contemporary biological and medical research.

GRAHAM RAMSAY

Dennis L. Kasper

At the applied end of the scientific spectrum, Dennis L. Kasper, Channing professor of medicine and professor of microbiology and molecular genetics, will become scientific director of the New England Center on Biodefense and Emerging Infectious Diseases, based at Harvard Medical School. The center, one of eight established nationwide with a total of $350 million of National Institutes of Health funding during the next five years (roughly $45 million for each venue), will conduct research and training focused on vaccines and therapies for anthrax, botulism, SARS, West Nile, and other infectious diseases. Each center will operate core laboratory facilities for other academic and biotechnology-business researchers in its region, and will assist public officials in case of biodefense or naturally occurring biological emergencies. Boston University, the University of Massachusetts Medical School, and other institutions will conduct four of the center's nine initial research programs. (School of Public Health dean Barry R. Bloom's perspective on the challenges of bioterrorism research in an academic setting appears at page 48.)

In Cambridge, Andrew W. Murray, professor of molecular and cellular biology and director of the Bauer Center for Genomics Research, will lead a new five-year, $15-million study of "modular biology"—collections of genes or proteins that work together to carry out a biological function. The study, funded by the National Institute of General Medical Sciences, creates a "center of excellence in complex biomedical systems research." (A similar center, focused on computational and systems biology, was funded at MIT.) Basing the project at the Bauer Center emphasizes its interdisciplinary nature: the current fellows working there are trained in mathematics, physics, computational biology, and diverse biological disciplines. Other collaborators come from several Harvard departments, including computer science and chemistry and chemical biology; the medical school; and institutions from Stanford to Hebrew University of Jerusalem.

products. Finally, he urged diversification in research projects.

In programmatic terms, he suggested "greater emphasis on science and technology in everything that we do," from educating undergraduates to equipping scientists with management skills. He also stressed the importance of practice and applied science, underscoring efforts to grow DEAS (the Faculty of Arts and Sciences' Division of Engineering and Applied Sciences), "putting energy behind the two middle initials." He underscored the importance of collaborations, within Harvard, with MIT, and with other institutions. And he encouraged partnerships with business, to which end Provost Steven E. Hyman will review policies on intellectual property, technology licensing, and related issues (all subjects of real passion among academic medical researchers concerned about compromising conflicts of interest).

Vest spoke about the changes in scientific knowledge spawned by genomic tools and the use of high-speed computation and new sampling technologies. He envisioned scientists modeling the dynamics of living cells and teasing out the three-dimensional structure of protein molecules. He insisted, with some concern, that federal support for science must be sustained to maintain the "strongest base of research universities on the planet." And he emphasized the importance of making universities more nimble as research crosses disciplinary lines, so discoveries can progress from bench science to clinical application.

Lander talked about moving medical science from chance observations and clinical trial-and-error testing to a production-line, engineering practice based on automated assays and manipulation of huge data bases—an image he tried to explain by calling "life a library of information" which is only now becoming accessible because the shelving system has been outlined. He projected that scientists could ultimately proceed to tease out variances in individuals' genetic susceptibility to disease, its incidence, and even customized therapies.

Harvard medical school (HMS) put some flesh on these *(please turn to page 58)*

HARVARD PORTRAIT

Timothy Mitchison

"When i came to america, I found that if you could do something or had something to say, people would listen," says Timothy Mitchison, who as a student in his native England encountered occasional obstacles to doing science. The Sabbagh professor of cell biology at Harvard Medical School has been quietly breaking down barriers ever since. As codirector of the Institute of Chemistry and Cell Biology, he has fostered collaborations among academic chemists and biologists and discovered interesting small molecules—drug precursors potentially able to cure disease. A founding faculty member of HMS's new, interdisciplinary department of systems biology (see page 58), his abiding interest is in cells—how they move, divide, and control their shape using a system of muscle-like, dynamic protein filaments. He uses a variety of tools to probe cell secrets. Monastrol, a small molecule he discovered that arrests cell division, facilitates his study of the mechanisms of mitosis in frog eggs and human cancer cells. The bacteria listeria (a common cause of food poisoning in processed meats like hot dogs) sheds light on the biochemistry of cell movement, because it "hijacks the mechanism that lets cells move, using it to spread rapidly from cell to cell in the body." When not administering his Harvard lab, Mitchison and his wife, Christine Field, a fellow biologist, are the "activist parents" of two children adopted from China and Cambodia. A word of advice from the father and listeria expert: When cooking franks, "popping them in the microwave is not enough. Rolling boil, four minutes."

Photograph by Jim Harrison

bones on September 23, announcing the formation of a department of systems biology. The new unit, ultimately planned to support more than 20 new faculty positions, would then rank among the school's largest. Among the disciplines to be represented are mathematics, computer science, physics, and engineering. Collaborations are envisioned with the Bauer Center for Genomics Research (FAS) and with MIT's computational and systems-biology initiative.

The new department's focus on understanding whole cells and then multicellular systems (organs and ultimately organisms) reverses the current reductionist focus on individual genes or molecular interactions. The goal is to gain "a predictive model of physiology," according to Walter professor of cell biology Marc W. Kirschner, the department's founding chair. (For his work on cellular controls and cell morphogenesis, Kirschner has been named the American Society for Cell Biology's Wilson Medalist, its highest scientific honor.)

The next day, Harvard unveiled the medical school's new research building, a huge "scientific instrument" (see page 56). Summers hinted at other life- and biomedical-sciences programs in the offing: "expanding very substantially our capacity to address issues in neuroscience" and ramping up the University's commitment to "global health." The former will no doubt build on the Harvard Center for Neurodegeneration and Repair, launched in 2001 by medical school dean Joseph B. Martin, who is Walker professor of neurobiology and clinical neuroscience, and on other brain research by HMS professors and their counterparts in the arts and sciences (see "Brainy Women," May-June 2002, page 36). By all indications, the nascent global-health initiative will involve the School of Public Health, social scientists and policy analysts from FAS, and others. Still other initiatives are likely in stem-cell research, in computational research and bioengineering (DEAS), and in other promising fields.

Marc W. Kirschner

JEFF CLEARY/HARVARD MEDICAL SCHOOL

All these initiatives, of course, have implications for undergraduate teaching and laboratory experiences; siting of new FAS science facilities in Cambridge; the financing and housing of additional faculty members and their graduate students and postdoctoral research fellows; and use of the future Allston campus to accommodate still more laboratory space (see page 64). Big as the new research building is, Harvard's drive into bioscience clearly means there are bigger things to come.

Barer-Bones Budgets

Greater cost-consciousness will become a part of Harvard's culture in much leaner University budgets for fiscal year 2005, beginning on July 1. Interviewed in her Massachusetts Hall office on the September day when the *Boston Globe* reported "MIT to cut budget, may lay off 200," vice president for finance Ann E. Berman took pains to distinguish Harvard's approach from that of peer institutions, which have imposed spending freezes, halted construction, and laid off employees following three years of endowment losses. But at the same time, the University's chief financial officer made clear that some of Harvard's goals are the same. "Our endowment resources," she said, "allow us to be thoughtful and strategic about this, rather than having an across-the-board cut."

Ann E. Berman

STEPHANIE MITCHELL/HARVARD NEWS OFFICE

Harvard's concerns, Berman said, are "not triggered by any one event or issue. It's about many more things"—one of which clearly is the economic environment. Although Harvard's endowment recovered strongly in the year ended last June 30, after two years of modest declines, the annual report on investment results unusually highlighted the relative decline in endowment purchasing power since 2000 (see page 59). During fiscal year 2003, the "spending rate" (funds distributed divided by endowment value at the beginning of the year) rose to 5.15 percent, at the upper limit of the Corporation's goal, and the highest level in two decades. (Income provided from the endowment includes about $770 million for academic operations, and $80 million for a special limited-term assessment for the costs of assembling land in Allston—together, much the largest source of University revenue.)

Berman also cited constraints on sponsored-research funding, the University's next most important source of revenue. Grants from the National Institutes of Health, the principal source for Harvard, are leveling off, she said, and "Some people probably aren't worrying enough—it's not automatic that Harvard's brilliant faculty will get an increasing piece of that smaller pie."

Intersecting with those limits on income are factors that propel spending. Although Harvard's annual financial report is published after Thanksgiving, Berman disclosed that expense growth in the fiscal year ended June 30 again outpaced revenue growth. (In fiscal year 2002, expenses rose 10.8 percent and revenues 5.8 percent; see "Tighter Times," January-February, page 58.) The "most striking" factors were higher healthcare and pension costs. Space and occupancy costs also rose as new facilities opened. Utilities were "dramatically" higher, reflecting energy prices and the cold winter.

In this context, four issues make timely "a strategic review of what we are doing" to enhance efficiency and control costs. First, Berman noted, alumni donors and other supporters regularly ask, "How do I know that the University is well managed?" That interest becomes more important as the University plans its next capital campaign (see page 69). Second, families are struggling with escalating tuition bills. Third, given the priorities

President Lawrence H. Summers and Provost Steven E. Hyman have enunciated—investments in curricular revision, public service, life sciences, and the future Allston campus—"We want to be able to say we are pushing as many of the resources in that direction as we can." Finally, after the years of growth enabled by the University Campaign and strong endowment returns during the late 1990s, a review of accreted "nice to do" functions is warranted.

That review is taking place in three concentric rings from Massachusetts Hall, encompassing central administrative functions, University services (dining, facilities, and so on), and the schools.

The administrative and service categories, comprising about one-third of a billion dollars of Harvard expense (see chart), are more immediately under Berman's "influence and control" than the autonomous schools. She hopes to realize savings by sorting out what functions might be done better, or not at all. Rather than setting a numerical goal for expenses or personnel, central administrative units have been asked to prepare alternative 2005 budgets level with current spending and 5 percent smaller. If adopted, either course would force some downsizing or abandonment of functions, given the likely increase in employee-benefit costs.

The service units are undergoing what Berman called "peer review," asking their University customers whether they would prefer cost savings that might accrue from curtailed service. At the same time, she said, the staff will examine outsourcing (to realize lower costs available on the market) and opportunities to reduce internal unit costs from gains in volume (perhaps achievable if the schools combined back-office or service functions). All proposals will be reviewed by a task force, vetted for impacts on customers, and winnowed for the 2005 budget by next spring.

Extending across the University, Berman said, the central administration seeks further savings from new purchasing agreements (like those in place for office furniture, computers, travel, etc.) for photocopiers and for paper. Larger savings are being pursued for big-ticket building-related expenses, including systems, supplies, and construction.

The financial pressure on the schools—personnel costs, tighter research funding, greater student need for financial aid—comes internally through the endowment spigot. After double-digit boosts in the endowment distribution earlier in the decade, the faculties have geared down to 2 percent increases for two years now. The Corporation will not set the fiscal year 2005 distribution until late autumn, but Berman said signals are being sent: "We've been a bit more pessimistic. We've said, 'We're thinking about zero.'"

In response, there have been publicized reductions in staff at the Kennedy School, Graduate School of Education, and Radcliffe Institute; rumors of reductions at the Harvard University Art Museums; proposed savings in the library system from reducing services at Hilles; and still "more happening by attrition," Berman said, plus decisions not to fill empty positions and deferral or cancellation of future capital projects.

Looking ahead, Berman "would love to see revenue increase faster than costs" by the time the books are closed on fiscal year 2005. Given the time required to reach purchasing agreements and have users adopt them, she forecast that goal would more likely be realized in the following year. A realistic aim, therefore, is for revenue and expense to grow only in tandem in the year that begins on July 1—an outcome that clearly requires a change from recent Harvard spending habits.

University Expenses

Fiscal year ended June 30, 2002

(Dollars in millions, total after rounding)

Faculty of Arts and Sciences	$ 658.2
Business School	278.6
Graduate School of Design	30.9
Divinity School	20.4
Graduate School of Education	59.1
Kennedy School of Government	117.8
Law School	103.7
Medical School	417.4
School of Public Health	189.6
Dental School	22.1
Radcliffe Institute	20.7
Service Departments	216.6
Central Administration	108.6
Other	44.0
Total	**$ 2287.7**

Rebounding Returns

A powerful fourth-quarter rally led by fixed-income portfolios yielded a total return of 12.5 percent on endowment assets for the fiscal year ended June 30. The strong returns, after all investment expenses, raised the value of the endowment to a new peak of approximately $19.3 billion. That sum was up from $17.5 billion a year earlier, and slightly above the endowment value of $19.1 billion recorded at the end of fiscal year 2000. Modestly negative investment returns and rising distributions from the endowment to support Harvard's operations and programs (offset somewhat by capital gifts received) reduced the value of the endowment in each of the ensuing two years.

"Practically the whole return came in the fourth quarter, and a good portion of our value added came in the fourth quarter as well," said an obviously pleased Jack R. Meyer, M.B.A. '69, president of Harvard Management Company (HMC). HMC's in-house fund managers and the outside professionals who invest some of the assets had handily outperformed their benchmarks (the market results for each class of assets, measured by standard indexes) and peer institutions' endowments in the prior two fiscal years. Yet they couldn't take much pleasure from the absolute result: returns, respectively, of -2.7 percent and -0.5 percent.

Fixed-income investments, about one-quarter of the endowment assets and a mainstay in fiscal year 2002, contributed even more in the year just past. "It's a