

Energetic Contribution of Residues in the RNA3 Stem Domain to DNA Binding

PAPER

Understanding the energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.

The energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.

The energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.

The energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.

The energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.

The energetic contribution of RNA3 residues to DNA binding is essential for understanding the mechanism of action of the RNA3 domain of the HIV-1 Rev protein. We have used a combination of site-directed mutagenesis and thermodynamic analysis to determine the energetic contribution of residues in the RNA3 stem domain to DNA binding. The results show that the RNA3 stem domain is a highly conserved region of the Rev protein and that residues in the stem domain are essential for DNA binding. The energetic contribution of residues in the RNA3 stem domain to DNA binding is discussed in terms of the mechanism of action of the Rev protein.



CUTS

It's a double whammy," says William Garrity, director of Dartmouth's Biomedical Libraries. It's the libraries' job to supply clinicians and researchers in the Dartmouth medical community with the information they need to do their jobs. But these days that means not only picking carefully from among an ever-increasing number of print journals, plus a multitude of online periodicals and reference databases, but also paying more for the resources that make the cut.

Call it what you wish—a double whammy, a catch-22, or a pretty pickle. The financial challenges facing biomedical research libraries throughout the nation are enormous and complex. Double-digit percentage increases in journal subscription prices have dramatically reduced libraries' purchasing power. A 2004 study in the *Journal of the Medical Library Association* determined that biomedical journal prices jumped 52% from 1996 to 1999, and another 32% from 1999 to 2002. Furthermore, the proliferation of journals serving ever more narrow specialties and of innovative nonprint resources has compounded the cost squeeze.

At Dartmouth Medical School and Dartmouth-Hitchcock Medical Center, the demand for more journals and for increasingly sophisticated but costly online reference tools, such as Up-to-Date and MD Consult, is on the rise. New scientific subdisciplines require new resources. Newly hired faculty and newly created departments often request new sources of information.

But as a result of soaring serials costs, the Dartmouth Biomedical Libraries have had to eliminate 11% of their journal subscriptions since fiscal year 2000—canceling 48 in 2004 alone. And Dartmouth is not alone in this struggle. Research libraries across the country are also canceling journal subscriptions. Tufts, for example, dropped 51 titles in 2003. Cornell, Duke, Harvard, and the University of California at Berkeley are among the many other institutions that have trimmed their journal offerings.

The implications of such cuts reach well beyond libraries and threaten the core of scientific discovery and advancement. Peer review—the examination and critique of a study by the author's scientific peers—has long been the accepted system by which new research is evaluated, and it's new research that drives improvements in patient care and public health. As Harold Sox, Jr., M.D., editor of the *Annals of Internal Medicine* (AIM) and former chair of medicine at Dartmouth, puts it: "It isn't science until it's been peer-reviewed." So getting

one's research published—validated by the peer-review system—is essential to academic promotion, to securing research grants, and to developing a reputation in one's field. It's thus no surprise that the future of biomedical publishing is being debated passionately among librarians, scientists, and clinicians alike.

One might therefore expect officials at Dartmouth's Biomedical Libraries, faced with such tremendous obstacles, to be begging for more money from the administration. However, their attitude suggests a broader understanding of the institution and its mission and of just how out-of-control biomedical publishing has become. Although their journal budget has risen from about \$875,000 in '99-00 to \$1 million in '04-05, the increase hasn't been enough to keep pace with soaring subscription prices.

"I could easily spend, this year, \$150,000 more than I am going to spend and have it be worthwhile, used material—not fringe stuff," says Margaret Sleeth, associate director for information resources. "The Medical School doesn't have that much money to give me, but let's say they did. Two years from now, I'd still be crying for more money because the cost of what I just committed to will have gone up."

The dollars add up quickly. For example, DMS pays \$24,000 a year for restricted access (meaning only five people at a time can use it) to the online resource MD Consult, and the *Journal of Comparative Neurology* costs \$19,500 a year.

There are several factors driving up the cost of journals. One is the dwindling pool of subscribers. It's estimated that the number of scientists in the United States has increased from 1.9 million in 1965 to nearly 6.8 million in 2000. Yet fewer and fewer individual scientists are subscribing to journals. Instead, they access those they need via their institutions' electronic site licenses—allowing them to read their favorite journals online from the comfort of their office or lab or home. This holds true in the private sector as well, where, for example, several physicians in a group practice may share a single print or online subscription.

"It used to be that every doctor in a practice group took the [top] journals," says William Morain, M.D., a former DMS faculty member who is now editor in chief of the *Annals of Plastic Surgery*. "But now, only one copy is taken" by the entire group.

The resulting cost-shift, says DMS's Bill Garrity, has been borne largely by libraries. For all the wonders of the advent of digital publishing—such as interactive features, searchability, and remote access—this shift has been one of its major drawbacks.

The pages of peer-reviewed scientific journals may not be very colorful, but they're the lifeblood of an academic medical center. The information in journals is essential to clinicians and researchers alike, and journals are the medium through which discoveries made at Dartmouth are spread around the world. That's why both librarians and academics are worried about changes in scientific publishing.

By Jennifer Durgin

Jennifer Durgin is DARTMOUTH MEDICINE's senior writer. She joined the magazine's staff this past June.

It's a common misconception that electronic subscriptions—which function more like leases—are cheaper than print subscriptions. Actually, the cost is often much greater. For example, Dartmouth can buy a print subscription to the *New England Journal of Medicine* for about \$400, while an online site license costs the library \$5,800.

The Dartmouth Biomedical Libraries' two locations—one on the Medical School's Hanover campus and one on the Medical Center campus in Lebanon—currently subscribe to about 1,100 journals. About 47% of those titles are purchased only in digital form, meaning Dartmouth no longer gets the print version, and 80% have some digital component. Over the past two years—for various reasons, including to offer 24/7 service to their geographically scattered clients—DMS librarians have switched nearly 500 titles from print or print-with-digital to digital-only.

It's a common misconception that electronic subscriptions—which function more like leases—are cheaper than print subscriptions. Actually, the cost is often much greater. For example, Dartmouth can buy a print subscription to the *New England Journal of Medicine* (NEJM) for about \$400, while a site license—which allows Dartmouth faculty and staff to access the NEJM online, from home or work—costs the library \$5,800. Similarly, the American Association of Cancer Research has a package of five journals that costs Dartmouth \$2,000 in print form. The price for the same package in digital form would be \$11,000, but that's an expenditure DMS has chosen not to make.

The archival implications of digital access are also worrisome. “For the length of your agreement, your contract, you have access [to the journal]. But if, at the end of the contract, both parties walk away, you may not have anything to show for it. Whereas if you stop a print subscription, nobody's going to come and take the paper copies away from you,” Sleeth explains. “If the world were perfect, we'd buy both print and digital.”

The administration has been “hugely cognizant and supportive” of the libraries' struggle, Sleeth and Garrity emphasize. “They've done, I think, whatever they can. They've granted us a lot of discretion in how we fund for information,” says Garrity.

“Like all of us, they don't have an answer either,” adds Sleeth.

But some librarians and academics believe they *do* have an answer—in a concept called the open-access initiative, which aims to provide readers with no-cost access to published research.

“In the age of print, open access was physically and economically impossible,” reads a report by the Scholarly Publishing and Academic Resources Coalition (SPARC), a group formed by the Association of Research Libraries to “correct market dysfunctions” in scholarly publishing. “But thanks to the Internet, it's an emerging reality. Now, the tradition of producing journal articles without expectation of payment combined with electronic pub-



lishing offers an unprecedented public good: the free online availability of peer-reviewed scientific and scholarly journal articles.”

But even if putting an article on the Internet is less expensive than printing it, preparing peer-reviewed articles is still time-intensive and costly. The top medical journals—such as NEJM, AIM, and the *Journal of the American Medical Association*—employ large editorial staffs. Sox, for example, works full-time as the AIM's editor. The journal, published twice a month, also employs more than a dozen full- and part-time deputy and associate editors—all of them physicians who must be paid competitively—plus a statistician. Add printing, distribution, and administrative costs to the equation and, Sox estimates, it costs between \$10,000 and \$12,000 to evaluate and prepare each published article.

Most journals do not have quite so much overhead. Rarely are deputy and associate editors paid, and often even the editor in chief receives a small honorarium instead of a salary. Still, many fixed costs remain. “Publishers have had to purchase equipment and design the platforms necessary for the electronic distribution and searchability of STM [science, technology, and medical] journals,” according to a study in the *Journal of the Medical Library Association*. “This includes the cost of archival storage, a new responsibility for publishers, because libraries have historically provided that function for print journals. These investments have created added value for libraries and their users, but they

have been in addition to the fixed costs of continuing to publish the print versions.”

While the concept of open access is appealing from the reader's perspective, one looming question remains: who will bear the costs that can't be eliminated? Proponents of open access say there are many ways to fund such a publishing plan. Yet the only models currently in use are ones in which study authors—the researchers—pay. For example, BioMed Central (BMC), a for-profit publishing company, charges authors between \$525 and \$1,500 per accepted article. The fee is waived, however, if the researcher's institution holds a BMC membership, which costs between \$1,612 and \$8,060, depending on the size of the institution. Dartmouth is not a BMC member but does subscribe to two of the company's subscription-based products—a journal called *Genome Biology* and a database of scientific illustrations called Images.MD.

Another open-access publisher is the Public Library of Science (PLOS). A nonprofit organization, it charges authors \$1,500 to publish in its two journals—*PLoS Biology*, launched in October 2003, and *PLoS Medicine*, launched in October 2004. The group was funded by a \$9-million start-up grant from the Gordon and Betty Moore Foundation.

Garrity and Sleeth question the long-term sustainability of ventures like BMC and PLOS, however. “Are junior faculty going to be so confident that this new model is good that they're going to publish in these less-than-prominent journals?” Garrity wonders. “Your career can be made or broken by having that article in *Science*. Are junior faculty going to be confident enough to ‘experiment’? Are tenure committees going to consider a publication in Journal X as prestigious as a publication in *Science*?”

Many librarians support open access, adds Sleeth, in order to build momentum for the creation of institutional repositories where a university's own research papers would be archived and made freely available. “I think that's where people dream of being, but getting from here to there is the hard part.”

In addition, as AIM editor Hal Sox notes, open access could have implications for professional societies that depend on the revenue generated by the journals they publish. “I'm not sure what kind of business model they're going to adopt once those grants run out,” says Sox. He notes that a typical peer-reviewed article for the AIM costs several times more than the author fees that BMC and PLOS charge. “A publishing model that doesn't pay the full cost of peer review—I see that as a real threat to the public interest,” he says. “Clinical

journals that can't do the kind of peer review that the major journals do run the risk of publishing things that aren't right. And when you're talking about new treatments, getting it wrong is a big-scale mistake.”

Another concern for Sox (who is based in Philadelphia but continues to hold an appointment on the Dartmouth faculty) is “that members of the American College of Physicians might find less reason to be members if they could get free access to the *Annals*. *Annals* is consistently, far and away, the top-rated benefit of being a member of the College in surveys that we do periodically. So organizations like ours have good reason to be concerned about the potential impact of free access.”

Dartmouth vascular surgeon Jack Cronenwett, M.D., coeditor of the *Journal of Vascular Surgery*, is also critical of the author-pays concept. “I would question any model in which authors were required to pay for publication, because theoretically that implies discrimination on the front end,” he says. “What we have now potentially is discrimination on the back end, where access may be limited but is at least possible. Any individual can go to [a library]; it may be inconvenient, but one can get there.”

Author-pays models also disadvantage major research institutions, Cronenwett points out. For example, if DMS's 877 faculty members published an average of two papers apiece per year in journals that charge \$1,500 per paper, the tab would be \$2.6 million. Meanwhile, undergraduate schools that do not conduct much research would have access to all those results at no charge.

The fact that scientific publishing has both nonprofit and for-profit players is also a complicating factor. Even many society-owned journals are actually published by for-profit companies. Such firms “have the people right there who are capable of doing all the copyediting and the publishing. And they ship it out and they bind it and they mail it,” explains Ann Barry Flood, Ph.D. She is a professor of community and family medicine at DMS as well as the coeditor of *Health Services Research*, a journal published by the for-profit firm Blackwell. Open access has “the potential of taking away the rationale and reason behind Blackwell wanting to do this,” she continues. “They have to at least make [some] money.”

The public sector is also wrestling with all these issues surrounding access to scientific information. In July 2004, the House Committee on Appropriations ordered the National Institutes of Health (NIH) to “make the complete text of [peer-reviewed] articles and supplemental materials gener-

“A publishing model that doesn't pay the full cost of peer review—I see that as a real threat to the public interest,” says Harold Sox. “Clinical journals that can't do the kind of peer review that the major journals do run the risk of publishing things that aren't right. And when you're talking about new treatments, getting it wrong is a big-scale mistake.”

But there is one matter on which there is agreement: the current cost of biomedical journals is too high and not in the best interests of medicine, science, or the public. In a 2002 report, financial services giant Morgan Stanley estimated that science, technology, and medical publishing worldwide was a \$7-billion industry.

ated by NIH-funded research available on PubMed Central,” a digital library maintained by the National Library of Medicine.

Congress told the NIH that such a system must be implemented in 2005. It will ensure that any published peer-reviewed paper resulting—even in part—from NIH funding will be freely available online six months after its publication. Proponents of the concept, including patient-advocacy groups and 25 Nobel laureates, argue that the latest scientific findings should be accessible to the average citizen. “When a woman goes online to find what treatment options are available to battle breast cancer, the cutting-edge, peer-reviewed research remains behind a high-fee barrier,” the Nobelists wrote in an August 2004 letter to Congress. “Families looking to read clinical trial updates for a loved one with Huntington’s disease search in vain because they do not have a journal subscription.”

But, wonders Ethan Dmitrovsky, M.D., chair of pharmacology and toxicology at DMS, “what would be the mechanism for support of the journals if they do not have revenue from subscription fees or page charges?” (Some journals charge authors a fee for each page of their article.) Dmitrovsky is associate editor of four prominent cancer journals, and he also chairs an NIH peer-review committee and routinely serves on NIH review panels. “There’s greater pressure on the research dollar today than ever,” he continues, “given the fact that we’re expecting the consequences of the flattening of the NIH budget to be evident. And, again, that raises the question, how will we support the publication process?”

Opponents of the NIH initiative maintain that taxpayers will bear the burden because the NIH will have to spend an additional \$2 million to \$4 million to post and archive the articles. In late October 2004, several publishers met with the NIH to argue against the plan. They said a delay longer than six months was needed in order for them to recoup their investment on an article. “Publishers say the U.S. would lose a valuable export since overseas buyers represent a significant slice of sales,” reported the *Wall Street Journal*. Despite intensive lobbying by opponents, as of mid-December the NIH was moving forward with the plan and was expected to make a final decision in January of 2005.

But there is one matter on which research librarians, academicians, government officials, open-access proponents, and journal editors are in agreement: the current cost of biomedical journals is too high and not in the best interests of medicine, science, or the public.

In a September 2002 report entitled “Scientific



Dollars and sense

Since 1986, the average price of science, technology, and medical journals has risen by 215%.

—Morgan Stanley (2002)

Between 1994-95 and 2001-02, the typical U.S. research library’s expenditures on electronic resources increased nearly 400%, to almost \$1.4 million.

—Association of Research Libraries

Scientific, medical, and technical journals have been the fastest growing sub-sector of the media business over the past 15 years.

—Morgan Stanley (2002)

Because of a weak dollar in some years, U.S. research libraries have had to bear price increases of 20% or more for some overseas journals.

—Library Journal

Publishing: Knowledge is Power,” financial services giant Morgan Stanley estimated that science, technology, and medical (STM) publishing worldwide was a \$7-billion industry, with U.S. academic libraries accounting for 60% of the market. The report, aimed at investors, focused specifically on Reed Elsevier (the parent company of Elsevier, the world’s largest publisher of STM journals). “Market leader Reed should outperform the market . . . as libraries trim peripheral suppliers who can’t bundle journals as effectively,” predicted the report. Furthermore, “STM publishing accounts for 37% of Reed’s profits and 40% of its cash flows.”

Research libraries spend more on Elsevier titles than on any other publisher’s journals, according to an August 2004 report from the Association of Research Libraries. That report compared the average expenditures of research libraries on for-profit and nonprofit publishers in 2002. For-profit publishers were far more taxing on libraries’ budgets, with average expenditures per publisher ranging anywhere from two to 20 times more than per nonprofit publisher.

Given these figures, it’s easy to vilify the for-profit companies, which include Blackwell; Elsevier; Kluwer; and Lippincott, Williams & Wilkins. Yet the true picture is more complex. In fact, the size and influence of these huge publishing houses provide some advantages for journal editors and the scientific community as a whole.

Earlier this year, when DMS’s Jack Cronenwett and the *Journal of Vascular Surgery (JVS)* were threatened by a lawsuit from a biotechnology firm, Cronenwett experienced firsthand the benefits of having what he calls “the big kid on the block” behind you. In December of 2003, the *JVS*, which is published by Elsevier, received a scientific manuscript about a device used to treat aneurysms. The paper—written by four FDA scientists—concluded that the device might result in higher mortality rates than open-surgery procedures. The *JVS* reviewed the article and, in March, accepted it for publication. On May 7, the journal posted the copyedited and author-approved paper in the pre-publication area of the *JVS* Web site. The manufacturer of the device, Medtronic, was not pleased. A September editorial in the *JVS* written by Cronenwett and his coeditor, James Seeger, M.D., recounts the events that followed:

“On May 20, 2004, the authors contacted the *Journal* to request that this accepted article be removed from the *Journal* Web site so that changes could be made prior to print publication. They related that Medtronic, Inc., had raised major concerns about the content of the article, which had

prompted a rereview of this submission by the FDA Center for Devices and Radiologic Health, from which the article originated. Subsequently, on May 21, the *Journal* was contacted by an attorney at Medtronic, Inc., who alleged that the authors had used confidential and proprietary data to write the article without the permission of Medtronic. . . .

“On May 25, the editors and publisher received a ‘request to cease and desist unauthorized publication of Medtronic, Inc.’s Confidential Data,’ from the law firm King & Spaulding, LLP, representing Medtronic, Inc. This letter indicated that Medtronic, Inc., strongly objected to the publication of analyses of post-market approval study data, which had been submitted to the FDA by Medtronic under the confidentiality provisions of the Federal Food, Drug, and Cosmetic Act and the Freedom of Information Act. The letter also alleged that public release of such information would constitute both criminal and civil violations under these acts, and indicated that if the *Journal* chose to ignore this request, Medtronic would pursue all available legal remedies against the *Journal* and protect its interests in court if necessary.”

Despite the fact that the data contained in the study had been posted since December 2003 on the FDA’s own Web site, as a Public Health Notification, the agency insisted the article be pulled. Trying to find a way to get the paper to the public, Cronenwett and his coeditor worked closely with Elsevier’s legal council.

“We were all hoping to find a legal way to publish the article,” he says. “When it turned out that we couldn’t, everyone was frustrated.” In general, Elsevier will support its editors and provide legal assistance “for the sake of maintaining the credibility of the scientific process,” he says. “And I think that is potentially an advantage. . . . Without some deep pocket in terms of opposing that type of legal action, it would be difficult for a journal to stand up to that.”

Yet it’s the depth of that pocket that has fueled the access debate. “In 2001, Reed Elsevier’s STM division’s operating profit was 34%,” according to the Association of Research Libraries’ 2004 report. The report also noted that “multiple-year licenses to large bundles of content” force libraries “to cancel titles from smaller publishers to cover price increases of the bundles.”

Even Sleeth and Garrity, who are skeptical about open access, recognize the need for alternative publishing models. Dartmouth benefits from the package deals that group several journals together for one discounted price. But Sleeth expects that to change soon, as the inflexibility of the bundles—which often require multiyear subscription

An August 2004 report compared the average expenditures of research libraries on for-profit and nonprofit publishers in 2002. For-profit publishers were far more taxing on libraries’ budgets, with average expenditures per publisher ranging anywhere from two to 20 times more than per nonprofit publisher.

The scientific and medical publishing market is often described as “inelastic” because the “products”—the journals, that is—can’t be substituted for one another. For example, if a researcher needs a specific article from the October 2004 issue of *Nature Genetics*, there is no acceptable alternative.

commitments—force her to make cuts elsewhere.

In essence, says Garrity, DMS faculty “do have open access. There are no barriers for the Dartmouth community to read and use information we provide to them. The barrier is that we can’t afford everything.”

And “everything” is a constantly growing universe. Adding to the problem is the proliferation of new journals. As Sleeth notes, “Ten years ago there was just *Nature*. Now we subscribe to the original *Nature* and several spin-offs, all of which are expensive: *Nature Biotechnology*, *Nature Cell Biology*, *Nature Genetics*, *Nature Immunology*, *Nature Medicine*, *Nature Neuroscience*, *Nature Reviews Cancer*, *Nature Reviews Drug Discovery*, *Nature Reviews Genetics*, *Nature Reviews Immunology*, *Nature Reviews Microbiology*, *Nature Reviews Molecular Cell Biology*, *Nature Reviews Neuroscience*, [and] *Nature Structural Biology*. And that doesn’t count the five new titles they are publishing for 2005 that we can’t afford to add.”

And the burden is only exacerbated, Sleeth says, when “some editorial board” realizes that the cost of biomedical journals “is a big problem. They’ll say, ‘We don’t want to be associated with Elsevier anymore, so we’re going to start a new journal.’”

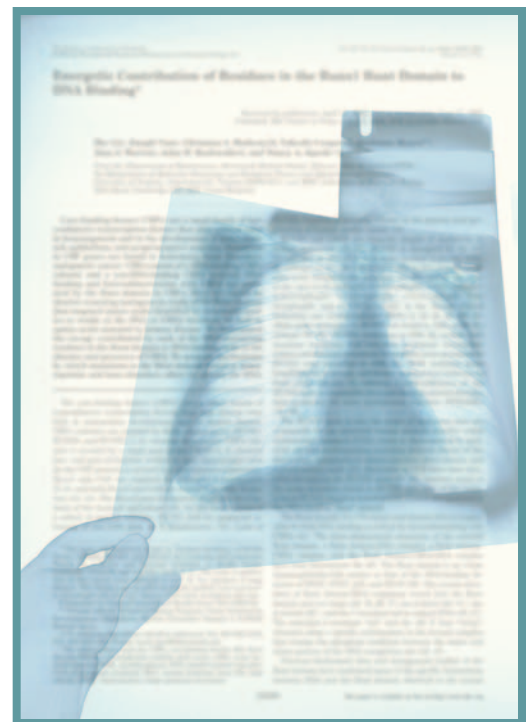
“So the old Elsevier journal still exists,” Garrity chimes in. “People still want it.”

“But now we have a competitor,” continues Sleeth, “which maybe only costs \$500 versus \$2,000, but that’s \$500 more that we’re going to have to come up with. People want the new one, too, but the old one people still want.”

The scientific and medical publishing market is often described as “inelastic” because the “products”—the journals, that is—can’t be substituted for one another. For example, if a researcher needs a specific article from the October 2004 issue of *Nature Genetics*, there is no acceptable alternative.

Dartmouth currently has either a print subscription or licensed online access to 96 of the top 100 science journals. Even so, Sleeth maintains a wish list of journals, many of them quite narrowly focused, that members of the faculty have requested but to which DMS does not subscribe. As of October, the list contained more than 115 titles, which would cost an additional \$95,000 a year. Yet narrowly focused journals play an increasingly essential role in advancing science and medicine.

“There’s a lot to be learned that is important to practitioners of highly specialized and narrow fields,” explains Sox, who was involved with the founding of two relatively small journals, the *Journal of General Internal Medicine* and *Medical Deci-*



sion Making. “Much of this research, the larger journals don’t have room for,” he explains, “and in some cases don’t see as necessarily part of their mission to publish. And yet there’s a need for scientific communication. So, I guess I’m not particularly troubled by the proliferation.”

Although Sox worries about the burden on medical libraries, he also worries about “barriers to communication of valid scientific research that may impact favorably on patient care.”

As with any great conundrum, close examination of the issue raises more questions than conclusions. For now, Sleeth and Garrity are stretching their budgets as far as they can to maintain the high quality of Dartmouth’s biomedical journal collection, while educating faculty and administrators about the issues. “We’re hanging on by our fingernails,” says Garrity. “We’ve been really good and doing what we can and buffering the faculty and the researchers and the clinicians and educators from these tensions, but it’s going to implode at some point.” No one’s quite sure what that implosion will look like. But it’s likely to be composed of many more journal cancellations. Further cuts will “seriously erode” quality, they say.

“We’re just librarians,” Garrity concedes. “At the end of the day, it’s the faculty who are publishing the information. . . . We’re the handmaidens to the research and clinical enterprise.”

“I’m not sure that librarians are going to be the people that solve this,” adds Sleeth. “I think it’s going to be the institution and the academy.” ■

Journal publishing: A peerless process

Biomedical journals have long been the hub of information-sharing in the health sciences. And behind every influential journal is a team of editors, reviewers, statisticians, and support staff. As the gatekeepers of the peer-review process—by which research papers are critiqued by experts in the same field as the authors—journal editors bear tremendous responsibility. A number of DMS faculty members hold top editorial posts at leading journals. Here are insights into the peer-review process from a few of them.

Why are you a journal editor?

"I believe strongly in service—service to your academic community, both at your institution and also nationally. What drives me when I am asked to serve as an associate editor is to serve the scientific community."

—Ethan Dmitrovsky, M.D.
Associate Editor, *Journal of the National Cancer Institute*; *Cancer Research*; *Clinical Cancer Research*; *Molecular Cancer Therapeutics*

What is your opinion of peer review as a system of evaluating research?

"When you are dealing with peer review, you are dealing with a process that has checks and balances built into it. Peer review is not perfect. Lord knows, it's got its problems. But it's like what Churchill said about democracy—it's the worst thing ever contrived except for everything else that's been contrived. So you have to accept peer review and do your damndest to make sure that you're applying it honestly, without bias."

—William Morain, M.D.
Editor in Chief,
Annals of Plastic Surgery

What can editors do to minimize the potential for bias in the peer-review process?

"We have policies in place to minimize the chance that friendship can play any role in decisions about an article. We have what we call the 'holiday card rule,' which basically is a series of conditions, such as having worked with an author in the recent past or if the author is part of the same division. . . . The holiday card

[is a way] of defining an ongoing personal relationship—if you exchange holiday cards, then you should remove yourself from any discussion [about a paper by that person]."

—Harold Sox, Jr., M.D.
Editor, *Annals of Internal Medicine*

Are there improvements that could be made in the peer-review process?

"We've tried very hard for everybody's sake to take the mystery out of peer review, including its warts as well as its strengths, because we would like both the reviewers and the authors to know what we do and how we do it. So we have deliberately tried to look at our own process. We've done data analysis on our process. We compare the senior associate editors to each other. We compare the two editors to each other, both in terms of time and apparent likelihood of dropping a manuscript before sending it out for review. So we are continuously monitoring our own process as much as we can."

—Ann Barry Flood, Ph.D.
Editor, *Health Services Research*

What do you enjoy about being a journal editor?

"We gain so much from study designs and methods in the literature and it helps us keep up [with our field]. . . . The reason I really continue to edit is it keeps me up with my profession probably better than anything else. That's what I love about it."

—James Weinstein, D.O., M.S.
Editor, *Spine Journal*

Are there any parts of the job that you dread?

"There's no time that I sit down to write an editorial that I don't have a lump in my throat, because I realize that I am very exposed. What I'm sitting there and musing is something that a lot of very opinionated people are going to be reading. I can embarrass myself with colleagues if I don't do well. . . . Every month I have this pre-editorial syndrome that I go through. I get irritable and I don't sleep well. . . . That's the only part I dislike about the journal."

—William Morain, M.D.
Editor in Chief,
Annals of Plastic Surgery

"When you are dealing with peer review, you are dealing with a process that has checks and balances built into it. Peer review is not perfect . . . it's got its problems. But it's like what Churchill said about democracy—it's the worst thing ever contrived except for everything else that's been contrived."