Research Technologies: Fulfilling the Promise[1]

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Today's biomedical research requires advanced technology such as mass spectrometry, analysis of macromolecular complexes, genomic analysis and gene expression, bioinformatics, biological imaging, and animal models. These technologies challenge us with their sophistication and complexity and with their rapid pace of evolution. Most support technology at nonprofit research institutions resides in shared resource or 'core' laboratories, which provide not merely investigative tools, but a competitive edge to their users in attracting research funds. Highly skilled scientists and advanced instrumentation are two essential components for a successful shared resource. Scientists in these laboratories make complex experiments possible, provide advanced problem-based experimentation, and create a mechanism for acquisition of new methodologies. Sufficient support of both intellectual and technical components of research infrastructure is essential to be competitive in today's research environment. Remarkably, adequate mechanisms to guarantee this support are often not set in place, perhaps because the requirements for maintaining a productive facility are not well understood by the general academic community.

Scientific opportunities to explore and exploit genomes, to probe the details of protein structure and function, and to achieve a molecular understanding of physiology require funding to provide for the needed technological resources. Although targeted funding areas and new programs are indeed important, opportunities will be missed for established and new programs if resources are either neglected or not shared. Inadequate investment is not only a problem facing technology resource scientists; it is an issue that concerns all experimental biologists. Availability of a group of resource laboratories providing access to focused expertise and instrumentation is essential to the needs of many evolving research programs.

Few studies have focused, or even touched on, the challenges of maintaining technology resources (1–3). None have addressed the needs of local resource laboratories, those available to essentially all investigators. The main problems faced are *1*) high-quality research facilities are costly; *2*) the intellectual infrastructure requires support; and *3*) academic institutions must make long-term commitments. A cooperative partnership of scientists, administration, and funding agencies is needed to make shared resources work. The issues are outlined below, together with explanation of the effects of policies and practices found to be both harmful and helpful to these laboratories and to the research communities that depend on them.

QUALITY COSTS

Issues

The raison d'être of resource laboratories is to enhance the scope and quality of research. In our competitive, peer-reviewed research grant system, quality is rewarded with financial support. This individual grant funding rarely reflects the cost of shared resources, especially for junior and new faculty users. Core laboratory operations often use cost recovery mechanisms, in the form of fees, to share expenses.

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However, imposition of a high fee structure on the resource laboratory erects a barrier against the novel and opportunistic applications that are the strength of technology resources. Furthermore, researchers cannot utilize the full benefits of the resource laboratory if decisions are based on cost rather than scientific outcome.

Application of the most advanced methodologies is often demanding and time-consuming. Development of new research opportunities may require trying different experimental approaches, testing and choosing among alternatives, taking risks. Adequate institutional support then becomes essential to sustain staff in the pursuit of new methods and to obtain equipment of the highest performance, sensitivity, and versatility. New technologies and instruments with powerful new applications for biology are constantly being developed.

Core laboratories with new equipment but without long-range plans for instrumentation upgrades, staff training, and financial support are fated to become obsolete in only a few years.

What are the costs?

Salaries and benefits, together with instrumentation costs, are the largest expenses of any resource laboratory (4). As detailed in **Table 1**, the responsibilities of the scientific staff encompass a breadth of activities not always obvious to the outsider, ranging from experimental design and data analysis to education.

Supplies, reagents, parts, and instrument maintenance are additional hard costs. Because advances are made so rapidly, instruments must be upgraded frequently and replaced as newer ones become available. Small instruments that cannot be purchased through instrument grant mechanisms must be budgeted. To acquire new technology, an institution may have to make an initial investment in expensive equipment, since a track record of experience is a prerequisite for shared instrumentation awards.

Education is one aspect that may be overlooked in planning resource laboratories. Courses and advanced technology meetings for resource laboratory scientists provide professional development for the staff and also benefit the institution, facilitating acquisition of new methods and technologies. Furthermore, resource scientists help local research scientists adapt new experimental approaches to their research programs via seminars, workshops, small group tutorials and individual discussion sessions, as well as teaching in courses.

Personnel, instruments, supplies, and education are all required for a successful, productive core laboratory.

Harmful policies

Problems arise when universities impose high fee requirements on resource laboratories, forcing them to operate like businesses. No matter how fiscally sound this may seem, it is scientifically and intellectually shortsighted. The cost savings of a local resource laboratory do not lie in obtaining inexpensive piecework. Rather, the major benefits lie in preventing unnecessary replication of instrumentation and expertise and in circumventing obstacles and delays in obtaining access to technologies needed for funded research projects.

In addition to the time needed to perform those analyses easily charged as fees, resource staff scientists also require time to implement new methodologies that will benefit their research environment. The experimental goals of complicated, technically demanding projects often require iterative work during their start-up phases, when sample preparation protocols and other variables must be modified in order to be successful. During this critical developmental period, full cost recovery is a barrier preventing realization of the experimental goals.

Even for mature projects, data acquisition and analysis require extensive time commitments—the most costly resource. If the time of a resource

TABLE 1. *Costs of research resource laboratories*

Skills and activities of resource staff
Planning and performing experiments
Setting up and calibrating instruments
Performing tests and controls
Troubleshooting problems, instruments, experiments, and methods
Method and instrument validation
Instrument maintenance
Discussing experimental design and data with research scientists
Instructing students and postdoctoral fellows in operation of community-use instruments
Teaching data analysis and interpretation skills
Maintaining databases
Optimizing experimental conditions for new projects
Setting up and testing new methods and technologies
Evaluating new instruments
Accounting, billing, and secretarial work
Instruments
Large instruments
Mid-range instruments and laboratory support apparatus
Computers and programs
Instrument updates
Parts
Preventive and routine maintenance
Service calls and service contracts
Downtime, depreciation
Consumables
High-purity organic chemicals and water
Specialty reagents and enzymes
Calibration standards
HPLC and other columns
Education
Technology courses and advanced technology meetings for resource staff
Books, journals, memberships
Seminars, workshops, tutorials, and personal discussion sessions for research scientists

scientist is fully calculated into fees, few research laboratories could afford these experimental approaches. Furthermore, when cost recovery from recharges includes large portions of salaries and benefits for all scientific staff at whatever academic level, salaries are often not maintained at adequate levels. High staff turnover may result, with loss of technological edge and investment in training.

High fees are a disincentive to good science and sidetrack scientific opportunities.

Helpful policies

Policies fostering productive use of core laboratories have been identified at many institutions, and more need to be developed (**Table 2**). A special fund established for each resource laboratory to encourage young investigators to use advanced technologies helps their scientific careers off to a sound beginning. For example, only one-half the amount of each cost-sharing fee might be paid by an assistant professor's research funds, with the other half paid from the special fund. Another mechanism for stimulating use of resource laboratories by young investigators is the inclusion of 'gift certificates' for core facility use in start-up packages. Often during the course of research projects, unanticipated opportunities arise in which a novel technology enables a scientific breakthrough and provides possibilities for new funding. One way to stimulate these novel projects is to eliminate the cost-sharing fee or to charge the fee to a small fund set aside for this purpose, after review by the core laboratory's director and an expert advisory committee. Similarly, projects of investigators on crisis support could be internally reviewed and approved to obtain data critical to their research proposals.

Obtaining salaries for key scientific staff from center grants, program projects, or biomedical research support grants is an established mechanism for providing support for resource facilities and removing personnel expenses from cost-sharing calculations. However, it is important that the savings not simply be translated into discounts to obtain cheap work, but instead be used to provide staff scientists with the time to establish new methodologies and develop investigators' projects. At smaller colleges or universities that may not have such large programs, several researchers can pool their resources to pay for salaries and supplies.

TABLE 2. *Policies that stimulate use of resource technologies*

Partial cost-sharing funds for use of resource laboratories by assistant professors
'Gift certificates' for resource lab activities as part of start-up packages
Funds for unanticipated opportunities, internally peer reviewed
Access for researchers on crisis support to obtain preliminary data for proposals
Minimize cost-sharing fees by direct support for resource scientist salaries

On a practical level, institutions with effective purchasing directors can often negotiate bulk discounts on supplies and service contracts. Teamwork between resource laboratories and administration serves the interests of both. There may also be other ways in which administrators can help improve the financial situation of the core laboratory so as to improve the scientific output, but such relationships require an investment of time.

Special funds set aside for developing research programs, direct support of staff salaries, and pragmatic economies can keep fees low and stimulate research.

SUPPORTING THE INTELLECTUAL INFRASTRUCTURE

Issues

Core laboratories usually include a range of faculty and professional scientists with career positions, a staff composition intrinsically distinct from the transient student/postdoctoral environment of academic research laboratories. Resource scientists, like their fellow researchers, also need continuous professional and career development to maintain their skills in developing technology. Compensation and professional development of nonfaculty staff must compete with the private sector, since the intellectual and technical demands of research institutions are at least equivalent. Research scientists who come to resource laboratories expect high-quality technological guidance, possible only with trained staff.

New resource technologies coupled with experimental biology have the potential to generate long-term projects that may exceed the capacity of the resource laboratory staff. This presents excellent opportunities for graduate students and postdoctoral fellows to work within the resource laboratory, learning to perform and evaluate technology-based experiments. This form of joint effort enhances the scientific outcome of research projects. Furthermore, students and fellows who train either part- or full-time in resource laboratories gain excellent opportunities for scientific careers in academia or industry, particularly in biotechnology research and development.

Intellectual interactions between resource and research scientists are essential to the success of each project. When this success results in publication, a citation in the acknowledgments section of a manuscript may be appropriate for routine analysis. However, contributions from resource scientists that involve novel resource laboratory work and insight, experimental design, or advanced data analysis that make a publication possible or significantly enhance its value require coauthorship as the appropriate acknowledgment.

Core facilities are specialized research laboratories with staff scientists who contribute to research programs and whose careers must be nurtured.

Who are the essential personnel in a resource laboratory and what are their qualifications?

The number and type of personnel in a resource laboratory will depend on the type of technology and the size of the institution (**Table 3**). A resource laboratory director who works together with experienced staff scientists and postdoctoral fellows helps to form a productive and interactive laboratory environment. A senior faculty member or administrator conversant in the technology can be a helpful liaison to the decision-makers of the institution. A faculty committee advisory to the core facility can help with planning and problem solving, reviewing projects, buffering the resource laboratory against problems anticipated and unanticipated, providing support in requests for funds from the administration and research grants, but should be careful not to micromanage laboratory operations.

Depth of technology experience and good communications skills are required for resource staff scientists at every level. Integrated approaches are now required in all experimental biology disciplines (5). For example, to appropriately address each project, a core protein laboratory can no longer focus narrowly on one technology, but must include multiple protein technologies in a problems approach such as Edman sequencing, mass spectrometry, 2-dimensional gel electrophoresis, both on-line and off-line HPLC, biosensor instruments, and instrumentation to analyze biomolecular interactions. Since early stages of sample preparation dramatically affect the success or failure of the experiments, the resource laboratory staff needs to interact with the research laboratory staff, providing advice on protein purification or design of cell culture experiments, for example. Other technologies and disciplines have similar demands, where communication and partnership between research and resource scientists benefit research.

Willingness and ability to learn and to incorporate new technologies at a rapid pace on a continuing basis are required of all resource scientists, and are critical to a successful shared resource laboratory. If it is meeting the needs of modern experimental biology, the core laboratory of today is not the core laboratory of 10 years ago, or even 2 years ago.

The final component underlying all successful resource laboratories is the ability to share (1). Those who are active in resource laboratory operations know that sharing is a prerequisite of their daily lives. A major finding of the Institute of Medicine's 1996 study of six National Center for Research Resources-funded national resource laboratories was that sharing is a significant factor in the success or failure of these laboratories as resources. This report was the first time that scientists outside the walls of shared resource laboratories recognized this fundamental principle.

Successful resource laboratories require a variety of scientists with specialized expertise, communication skills, a lifelong interest in learning, and the ability to share.

TABLE 3. *Essential qualities and types of personnel in resource laboratories*

Qualities
Technology expertise
Communications skills
Willingness and ability to learn new technologies on a continuing basis
Ability to share
Personnel
Director
Senior staff scientists (data collection, analysis, and investigator interactions)
Junior staff scientists (focused technologies, teaching, etc.)
Postdoctoral fellows from research laboratories
Postdoctoral fellows in resource laboratory for special projects
Faculty or administrative liaison to decision-makers
Advisory committee
Office and accounting staff

Harmful policies

The lack of incentives to share is a crucial barrier in access to and success of resource laboratories. Indeed, academic science often rewards those who do not share. Despite its essential nature, there are few professional rewards for providing technological expertise and insight. If resource scientists are expected to share their knowledge and experience, then academic institutions must also share, providing them a full place in academic life.

Professional and career development for resource scientists commensurate with their skills and experience is lacking at many universities. Furthermore, graduate and postgraduate training in biomedical technologies has also been neglected. Disregarding these needs of our essential, highly trained resource scientists will risk losing them from existing university facilities, deter young scientists from training in the critical biomedical research areas, and certainly discourage them from seeking employment in universities.

Joint participation by both research and resource scientists in resource planning is essential for their success, but is not common. Disappointment can be substantial when technology facilities are relocated to beautiful new laboratories ill-suited for their experimental discipline, designed by well-meaning individuals or architects who had no notion of what is required to carry out the work. Frustration mounts when resource scientists are instructed by administrators that they must not set up advanced technologies, but should restrict themselves to more routine or conventional technologies of the sort that could be supplied by commercial vendors.

Lack of incentives to share, lack of professional opportunities, plus exclusion from long-range planning can disable resource laboratories.

Helpful policies

At the end of a recent article on the next phase of the human genome project, Francis Collins and colleagues (6) called for establishing academic career paths for resource technology scientists. The impact on the local scientific community resulting from the activities of their core facilities should be considered in faculty promotions. Career needs of nonfaculty resource scientists should also be addressed. As discussed earlier, resource laboratory budgets can also provide the support for scientific staff to attend professional meetings or specialized courses. These professional activities clearly provide technical and intellectual benefits not only for the staff member, but also for their home institution. New methods and technologies are imported to the resource laboratory, and the staff develops a network of associates familiar with related problems that can aid in their solutions.

Mechanisms for upgrading instrumentation must be implemented. Working with outdated technologies frustrates both resource and research scientists. Resource laboratory scientists must drive planning; they have the most expertise in the future of the technology. Resource scientists should be involved in planning core facilities for basic and clinical research from their inception, before the first blueprints are drawn or the first steps taken. Institutional funds and government agencies could support research opportunities associated with resource technologies. Education and training programs at all academic levels should be introduced, updated, and revitalized. Young scientists encouraged by expanded opportunities and a more receptive environment will nourish the science of the future (6). These are win-win solutions that benefit everyone, encourage sharing, and nurture excellent science.

Career development, investment in postgraduate education, plus involvement in resource planning will strengthen shared resources.

COMMITMENT FOR TECHNOLOGY RESOURCES

Issues

Technology resources are an investment in the faculty and future of the university. They should not be a competing priority, but a priority complementary to direct investment in faculty recruitment and faculty research programs. The level of institutional commitment is a key criterion in evaluating grants for expensive shared instruments from both the National Institutes of Health (NIH) and the National Science Foundation, who insist that the institution have a stake in the success of their shared resource laboratories. A one-time contribution to the purchase of instrumentation and remodeling of facilities without continuing staff support and equipment upgrades will produce a self-terminating facility. Institutions that provide initial operating support, but expect their facilities to be self-supporting, are destined for the same fate.

Government investment in creative technological development and in enhanced shared instrumentation and resource laboratory programs will allow researchers improved access to essential technologies and encourage additional investment by research institutions.

The success of shared resources requires long-term investment and commitment.

What special commitments are needed?

To have successful core laboratories and research infrastructure, academic institutions must invest in resource scientists, instruments, operational budgets, and space. These are listed in the order of priority (see Table 1). Instruments are important, but qualified people are required to operate them and perform the complex scientific work lest equipment remain underutilized or new experimental approaches be poorly implemented. Once the technical and intellectual components are taken care of, adequate supplies and space are more easily identified.

Academic institutions must make shared resources a top priority not only to create them, but also to sustain them.

Harmful policies

Overemphasis on cost savings instead of research excellence and productivity is the policy that most damages resource laboratories. It is surprising that even government agencies with strong commitments to research technologies and the research centers they fund have local *ad hoc* policies that contradict their own philosophies. Perhaps overinterpretation of guidelines by both agency and academic administrators and accountants has led to these unintended consequences.

A recent Life Sciences Forum article in this journal briefly described the frequent deterioration of infrastructure and the neglect of this infrastructure by deans (7). This report also decried the lack of faculty involvement in long-range planning. Repairing this rupture between faculty and administration when it exists may be the first step in revitalizing research infrastructure. Divisive or selfish faculty behavior can also create an environment in which academic administrations choose to emphasize other priorities, perceiving their faculty as not being committed to the development of research technology laboratories.

When shared resources are not set as a priority and high-cost recovery is demanded of them, these laboratories will struggle. As a consequence, science will suffer.

Helpful policies

Scientific excellence and fiscal responsibility are not competing goals. Investment in resources brings returns in research funding, recognition, and scientific breakthroughs. When funds are not limiting, finding support is simply a matter of recognizing and placing priority on the needed technological infrastructure. When financial constraints exist, planning and cooperation are important for implementing what is currently possible and defining strategies to meet future needs. Support of resource technologies is a means to invest in all faculty research programs.

Identifying support for resource scientists is important. Finding such support minimizes cost recovery fees and provides time for the complex of activities that underlie effective shared resources. Those responsible for state- or federal government-supported laboratories should be encouraged to seek line-item salaries in their government's budget. Small universities or research institutes with highly focused core laboratories may simply share the costs up front among a set of investigators. Center and program grants can often pay portions of salaries for personnel who support the aims of their research programs. Establishing an endowment fund for resource technologies is another mechanism for upgrading instrumentation or supporting salaries (2). The work of highly technical shared resource laboratories that contribute to the research efforts of many programs can be very appealing to donors as a long-lasting and clearly identifiable tribute.

Institutional funds can provide some flexibility in keeping technologies up to date. However, these funds may be scarce in smaller institutions or those with small endowments. Biomedical research support grants are no longer supported by the NIH, but a limited number are funded by the Howard Hughes Medical Institute. Several groups are seeking reestablishment of the controversial NIH BRS grants, which at their best provided flexible monies to support research goals of the whole institution. Should they be reinstated, it is suggested that they be peer-reviewed grants with periodic review and accountability. These could include not only start-up funds for new investigators and bridge funds for more senior scientists, but funds for partial support of salaries and instrument upgrades for resource laboratories.

Funding agencies are partners in supporting resource technologies. The shared instrumentation grant programs have had great impact, providing state-of-the-art instruments to research institutions (8). After years of diminishing budgets, these programs show promise of renewed support. There is a great unmet need for shared instruments by national resource laboratories (P41) and by large and small academic institutions alike (9). Dramatic increases in shared instrument grants are required to provide broad-based support of American science. Furthermore, setting up and implementing the new research made possible by such instruments is far from trivial. Peer-reviewed funding for advanced instruments should include support for at least a portion of the salary of the experienced person who will interface the new technology with the institution's research programs. Direct peer-reviewed funding for resource laboratories should be evaluated as a mechanism for supporting the nation's basic research enterprise. Improvement in coordinated planning and funding for research and development of emerging technologies is critical.

The Federation of American Societies for Experimental Biology, a coalition of 57,000 scientists in 17 corporate and affiliate societies, recognizes the importance of research infrastructure as a funding priority (10). The Association for Biomolecular Resource Facilities, which the authors of this article represent, is working to increase awareness that advanced technology development and shared resources are important priorities linked to the future of biomedical research.

Despite all these mechanisms for funding resource facilities from extramural sources, however, the first line of commitment must come from an institutional guarantee that their functions will not be compromised in the name of cost recovery.

CONCLUSIONS

Maintaining access to advanced technologies through support of the resource laboratories that provide these services is too important an issue for academic institutions to ignore. In this age of bio-

TABLE 4. *Individual responsibilities for improving technology resource laboratories*

Funding agencies
Enhance shared instrumentation program
Couple salary support to instrumentation awards
Improve coordination and funding for technology research and development
Training programs and postdoctoral fellowships
Administration
Support operating costs and updates in technology and instrumentation
Provide professional advancement for resource scientists
Involve resource scientists in planning
Departments
Incorporate technology resources in all major research plans
Include resource scientists in planning of departmental research and educational programs
Support career development of resource scientists
Research scientists
Plan technology-based experiments with input and expertise of resource lab scientists
Acknowledge contributions of resource lab scientists in publications
Include resource lab scientists in technology planning for research and training programs
Participate in efforts to obtain funds for new instruments and operations costs
Resource scientists
Provide state-of-the-art experimental data
Communicate with research faculty on strengths and limitations of each technology
Incorporate/update new technologies and work with other faculty to plan for future technologies
Participate in technology education

technology, institutions that do not foster the abilities of their resource laboratories to provide cutting-edge equipment, applications, and intellectual infrastructure will suffer in the quality of their research output and in their ability to attract research support. Shared resources are essential, but costly, and require adequate support for capital equipment and personnel. **Table 4** proposes individual responsibilities in achieving the goal of assured access to advanced technologies for modern biomedical research. New creative mechanisms for resource technology support can be found with the joint effort of all concerned. If academic institutions, scientists, and funding agencies regard these facilities as important, are committed to their continued success, set them as a priority, and share the financial burden, the value of these resource facilities and the advice and services they provide will be greatly enhanced as we enter a new period of growth and development in research in the biosciences and medicine.

Note added in proof: After this article was accepted, the NIH issued program announcements both in training (PA-99-028) and faculty development (PA-99-022) for 'genome scientists', embracing a broad category of disciplines.

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