Building Interdisciplinary Biomedical Research Using Novel Collaboratives

Katya Ravid, DSc, Russell Faux, PhD, Barbara Corkey, PhD, and David Coleman, MD

Abstract

Traditionally, biomedical research has been carried out mainly within departmental boundaries. However, successful biomedical research increasingly relies on development of methods and concepts crossing these boundaries, requiring expertise in different disciplines. Recently, major research institutes have begun experimenting with ways to foster an interdisciplinary ethos. The Evans Center for Interdisciplinary Biomedical Research ("the Evans Center") at Boston University is a new organizational paradigm to address this challenge. The Evans Center is built around interdisciplinary research groups termed *affinity research collaboratives* (ARCs). Each ARC consists of investigators from several academic departments and at least two research disciplines, bound by a common goal to investigate biomedical problems concerning human disease. Novel aspects of the Evans Center include a "bottom-up" approach to identifying areas of ARC research (research vision and strategy are typically initiated by a core group of faculty with input from the center director); a pre-ARC period of faculty affiliation/project(s)' self-selection prior to formation of a peer-reviewed ARC; and Evans Center support for innovative ARCs for up to three years pending yearly metric evaluation, followed by continued administrative support as a group matures into an ARC program.

Since its inception in early 2009, the Evans Center has documented achievements at discovery/publication, grant award, and educational levels. Enhanced interactions between members of individual ARCs, as assessed by quantitative networking analysis, are discussed in the context of high productivity. As universities seek new approaches to stimulate interdisciplinary research, the Evans Center and its ARCs are offered as a productive model for leveraging discovery.

Editor's Note: A commentary by T. O'Brien, K. Yamamoto, and S. Hawgood will appear with this article in the February issue.

The complexity of biologic systems and our growing ability to relate these systems to the study of human disease have transcended traditional scientific disciplines and structures. Discovery generated by one discipline may yield knowledge that is constrained by the limitations of the field. For example, a biologist might apply biochemical tools to understand roles of a cell-surface receptor in cancer promotion but might not be able to follow up on findings by targeting the protein with nanoparticles for therapeutic purposes because he or she would not be familiar with details of such a strategy. Comprehensive exploration of biological mechanisms and the development of new therapeutic approaches require the knowledge and skills of multiple disciplines. In this article, we describe how we have approached this challenge in a new center at Boston University School of Medicine and what has been achieved in the past three years, 2009–2012.

Dr. Ravid is professor of medicine and biochemistry and founding director, Evans Center for Interdisciplinary Biomedical Research, Boston University School of Medicine, Boston, Massachusetts.

Dr. Faux is researcher associate and statistician, Davis Square Research Associates, Cambridge, Massachusetts.

Dr. Corkey is professor of medicine and vice chair of research, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.

Dr. Coleman is professor of medicine and chairman, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.

Correspondence should be addressed to Dr. Ravid, Boston University School of Medicine, 700 Albany St., CVI, W-601, Boston, MA 02118; telephone: (617) 638-5053; e-mail: kravid@bu.edu.

Acad Med. 2013;88:00–00.
First published online
doi: 10.1097/ACM.0b013e31827c0f79

The Problem and Our and Others' Solutions

As traditional academic departments focus on discrete disciplines, the rapidly accumulating volume of data, the accelerated development of technologies, and abilities to relate those to complex biomedical systems may limit the potential application of those data and technologies to human disease. A recent study, focused on the reorganization of basic science departments at U.S. medical schools across 20 years (1980–1999),[1] showed a decreasing number of traditional departments (biochemistry, pharmacology, etc.), which have been replaced by new departments or newly named departments reflecting newer trends in science. However, the study concluded that in many cases these transitions were not fundamental; the most common change was the renaming of a department to reflect intent for renewed focus and/or to attract trainees and faculty. Advanced biomedical research clearly mandates effective integration of physical and life sciences disciplines as well as the development of infrastructures that facilitate communication between disciplines accustomed to speaking their own disciplinary "languages."

In their recent publication, Sharp et al[2] propose a new term—*convergence*—that they describe as "the merging of distinct technologies, processing disciplines, or devices into a unified whole that creates a host of new pathways and opportunities." Although convergence among disciplines is critical for innovation, several barriers to interdisciplinary collaboration have been identified, including conceptual differences, short-term career considerations, incompatibilities of the various science cultures, and financial disincentives.[3] In an editorial in *Science* in 2011, Dr. Alan I. Leshner[4] encouraged institutions pursuing high-risk research

to rethink criteria for rewarding performance toward the goals of building transformative research programs.

Two years earlier, the Department of Medicine at Boston University School of Medicine opted to fund a new paradigm for stimulating integrative, interdisciplinary research through the establishment of the Evans Center for Interdisciplinary Biomedical Research (hereafter, "the Evans Center"). The driving principle of the Evans Center was the conviction that a combination of organic, investigator-driven development of research goals, early and rigorous peer review of collaborative visions, and financial and structural support would optimize the Evans Center for success. The Evans Center is built on the following operating principles:

- The structural units of the Evans Center are interdisciplinary research groups entitled *affinity research collaboratives* (ARCs). These groups are formed by a process of self-assembly during a "pre-ARC" period.
- The general area of research is primarily identified by the faculty (e.g., a "bottom-up" approach) and at times by the Evans Center's director, whereas the specific topic areas are selected by ARC members. The director is available to offer insights throughout the process.
- Resources for ARCs are made available on an annual basis using a rigorous peer-review process and are contingent on inclusion of faculty from several departments and at least two disciplines.
- ARC projects and activities include trainees at graduate and postgraduate levels.
- The educational mission of the Evans Center also includes leading or coleading cross-departmental interdisciplinary seminars and developing interdisciplinary graduate courses and workshops.

Although other programs have used some of these guiding principles, the Evans Center's initiative is innovative in basing its endeavors on all five. In particular, the bottom-up approach empowers investigators to develop and own areas of research during the pre-ARC period of meetings, self-assembly, and sorting, prior to forming a peer-reviewed ARC.

Other universities have developed interdisciplinary centers, but these have primarily been in specialized areas, as at Rockefeller University, where several centers have been established with laboratory-based organizational structures that foster interdisciplinary research, including centers for Alzheimer disease research, for biochemistry and structural biology, and for human genetics. Northeastern University also has an array of specialized centers, focusing on areas such as drug discovery or translational neuroimaging. Similarly, the University of Delaware has an interdisciplinary research center in climate and land-surface change, which includes faculty from the departments of geography, geological sciences, civil and environmental engineering, and plant and soil sciences.

One aspect of the Evans Center's structure that is novel is that it does not focus on a general area of research or on one disease but, rather, on providing infrastructure, including rigorous peer review, for intense interdisciplinary approaches to a range of problems. The Evans Center consists of multiple ARCs, each with investigators from different backgrounds and expertise studying a biomedical problem or disease of their choosing. These ARCs provide organizational structures that allow investigators from different departments to jointly study subareas within a larger discipline. For instance, the nanotheranostics ARC aims to develop new diagnostics and drug delivery tools for certain cardiovascular diseases rather than focusing on cardiovascular biology and/or nanomedicine. As further described below, the Evans Center also provides an infrastructure for interactions among different ARCs.

The Evans Center

The Evans Center's structure

The Evans Center was founded in the early spring of 2009 under the leadership of a founding director (K.R.), an administrative assistant, and an interdisciplinary advisory board, comprising faculty from different departments at Boston University and outside of our university (see Figure 1). Although organizationally nested within the Department of Medicine, the Evans Center has actively sought participation by faculty affiliated with different departments and schools at Boston University (medicine, public health, dental medicine, engineering, chemistry, biology) and with the external biomedical research community. Established as a "virtual" center, the Evans Center does not house its participants: Collaborating investigators remain in their existing research spaces.

ARCs: Formation and management

General areas of research are identified primarily by faculty who wish to form an ARC, but also by the Evans Center's founding director. Before forming an ARC, investigators are encouraged to identify colleagues with similar interests and complementary expertise and to undertake preliminary explorations of a particular challenge or area of research. Typical ARCs crystallize from a core of faculty with expertise in a certain area, linked to faculty from other disciplines to form an expanded field of interdisciplinary research.

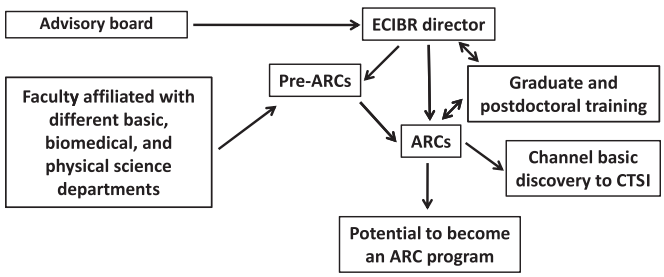

Figure 1 Organizational structure. The scheme depicts the structure of the Evans Center for Interdisciplinary Biomedical Research and its affinity research collaboratives (ARCs), and their interactions with different entities, including with the Clinical and Translational Sciences Institute (CTSI). The transition from a pre-ARC to an ARC status is subject to a review process. Particularly successful ARCs, based on metrics of success outlined in this article, might ultimately achieve program status in the department or school, with advantages and responsibilities dictated by the departmental bylaws for programs.

This process is aided by well-developed university-wide and medical school databases of faculty research foci and affiliations. For instance, a group of geneticists and experts in the study of neurodegenerative disease assembled a team of biostatisticians, computational biologists, biochemists, and a pharmacologist. Together, they are studying the biochemistry of cellular protein trafficking in the context of several neurodegenerative diseases, based on target genes identified in human population studies. During several months of meetings, this group—which we term a *pre-ARC*—selects members, hones goals, and decides whether to submit an ARC application. ARC research applications include information similar in content to that required by a National Institutes of Health (NIH) RO1 grant proposal, in abbreviated form.

Each ARC must consist of at least five investigators with representation from at least two disciplines. Members of an ARC can work with previous collaborators but must attract and include new collaborators into their ARC. Thirteen ARCs have been approved to date (2012), representing approximately 75% of ARC applications. All approved ARCs are also subject to a yearly review by a panel of 8 to 10 investigators from inside the university (appointed by the ARC director). This review follows the NIH scoring system with additional criteria relating to the interdisciplinary growth potential of the ARC. In addition to scientific merit, review criteria include novelty, cohesion, interdisciplinary approaches, relevance to disease, and training opportunities. Each approved ARC is provided with $40,000 to $75,000 per year to cover research supplies or partial support of trainees to carry out pilot studies. The use of these funds is determined by the ARC director(s) in consultation with ARC members. Once funded, ARC members meet as a group at least once a month, and all ARC directors meet quarterly with the Evans Center's director to discuss research and translational potential. The incentives for forming an ARC include not only financial research support but also access to shared knowledge, ideas, and technologies.

The Evans Center is independent of the institutional Clinical and Translational Science Institute (CTSI) at Boston University; however, the ARC's basic discoveries can be further developed using the CTSI infrastructure for technology and translational research (see an example in the Evans Center Outcomes section). As the collaborative networks in the ARCs continue to mature, we envision that they will become largely self-sufficient through extramural funding. Particularly successful ARCs might ultimately achieve program status within a department or school (Figure 1). Thus, the Evans Center serves as an incubator of sorts, providing additional financial and scientific support as well as rigorous peer review of ideas in the early stages of a new endeavor.

Participation in the Evans Center is open and does not mandate affiliation with an ARC, although over 85% of the approximately 150 Evans Center members (to date; 2012) are linked to an ARC. Participation grants access to the workshops, technologies, symposia, and other research and educational activities described in the next section. About half of current Evans Center members are from the Department of Medicine, but just 30 months after launch, the Evans Center had participating faculty from the following programs: 28 from other basic science and clinical departments at Boston University School of Medicine, 3 from the Boston University School of Dental Medicine, 7 from the Boston University School of Public Health, 18 from physical sciences and engineering departments (Boston University Charles River campus), and 14 collaborators from outside of Boston University. Faculty of all ranks are represented in each of the ARCs, and about 25% of members self-identified as clinical investigators.

Research and educational activities

From 2009 until this article was submitted for publication in 2012, the Evans Center has coalesced the following ARCs (see also www.bumc.bu.edu/evanscenteribr/):

- Protein Trafficking and Neurodegenerative Diseases
- Sex Differences in Adipose Tissue: Mechanisms and Role in Disease Risk Associated With Obesity
- Mitochondrial Dynamics in Health and Disease
- Regenerative Medicine: The Boston University Induced Pluripotent Stem Cell (iPSC) Bank
- Blood Microbiome
- Cardiovascular Consequences of Metabolic Disease
- Atrial Fibrillation Initiative
- Biomarkers of Disease: A Proteomics Approach
- Calcium Homeostasis in Health and Disease
- Mechanisms and Treatment of Arterial Stiffness
- Obesity, Cancer and Inflammation
- Metabolic Disease and Adipose Tissue Biology in Patients Undergoing Bariatric Surgery
- Nanotheranostics

Of these, one has received an NIH-funded program project based on ARC work and no longer requires Evans Center support; one dissolved as an ARC, with three of its leading members continuing efforts within a recently refunded National Heart, Lung, and Blood Institute–supported Cardiovascular Proteomics Center; and a few were initiated only in 2012.

ARCs hold monthly meetings to report findings and discuss plans. Research interactions within and between ARCs are further facilitated via open seminars, workshops, and discussion forums initiated and led either by ARC directors or the Evans Center's leadership. An example is the newly developed collaboration between the ARCs entitled "Mitochondrial Dynamics in Health and Disease" and "The Boston University iPSC Bank," in which the role of mitochondrial homeostasis is being explored in the context of iPS development and differentiation into various lineages. Examples of educational workshops include "Methodologies: Mitochondrial Membrane Potential and Oxygen Consumption" and "Calcium Homeostasis and Measurement." Evans Center–supported interdisciplinary mini-symposia include "Nanomedicine: Bridging Nanoscience and Biomedical Research," "Controlling Hypertension: From Basic Research to the Clinic," "New Frontiers in Molecular Medicine," "A Bird's-Eye View Into the Mitochondria

Dual Role in Life and Energy: Basic Scientist and Clinicians' Perspectives," and "Obesity, Inflammation and Cancer."

Yearly research retreats organized by the Evans Center bring together all ARC and Evans Center members to present data and discuss collective plans. In addition, schoolwide interdisciplinary, thematic seminars, and research receptions co-led by the Evans Center and other departments bring together an array of faculty. Finally, the Evans Center also contributes to graduate studies, including the codevelopment by the Evans Center's director of a new interdisciplinary graduate course, "Biological Core Technologies" (which focuses on principles and applications of an array of research cores), and a course entitled "Nanomedicine: Principles and Applications" (covering nanosciences and biomedical research).

Together, the Evans Center's infrastructure and activities promote and support the convergence of research disciplines to advance discovery and education, providing researchers and trainees with opportunities and incentives to use interdisciplinary approaches to problem solving.

Center Outcomes: Bibliography and Research Network Analysis

We evaluated the impact of the ARCs using the following measures: number of publications, number and diversity of participants, extramural funding, and social network analysis (SNA).[5] The data presented in this section are based on our survey of the 41 core participants in the four original ARCs formed when the Evans Center was founded and for which we have nearly three academic years of data (early 2009 to early 2012).

The four original ARCs were (1) "Protein Trafficking and Neurodegenerative Diseases" (with 8 core participants), (2) "Sex Differences in Adipose Tissue: Mechanisms and Role in Disease Risk Associated With Obesity" (with 17 core participants), (3) "Mitochondrial Dynamics in Health and Disease" (with 11 core participants), and (4) "Regenerative Medicine" (the Boston University iPSC Bank, with 5 core participants).

Regarding the number of publications and grants that involved at least two members of an ARC as coauthors or coinvestigators and that focused on topics directly related to the ARC, there were

- 93 coauthored publications,
- 63 grants applied for,
- 33 grants funded (RO1, R21, or PPG), and
- 15 grants pending.

There were also

- 97 presentations at meetings, and
- 57 predoctoral and 27 postdoctoral trainees affiliated with ARC activities.

These data indicate a notable record of collaborative grant and publication achievements; also, each ARC includes pre- and postdoctoral trainees. The success rate of grant applications—33 (52%) funded from a total of 63—is quite high relative to current NIH funding rates. At a research level, the productivity of ARC research efforts has been high, as indicated by the large number of coauthored publications. As indicated above, from early 2009 to early 2012, the four original ARCs produced 93 coauthored publications, compared with 15 published by similar coauthors during the three years prior to ARC development.

Qualitative outcomes enabled by Evans Center infrastructure and funding include the development of new research resources shared at, and beyond, our school. For instance, in the "Mitochondrial Dynamics in Health and Disease" ARC, biologists, biomedical engineers, and cardiologists collaborated to develop new mitochondrial function readouts of distinct diseases, now available to the university at large and to researchers outside the university (e.g., to members of the NIH-funded Boston Nutrition Obesity Center). Another example is the "Boston University Induced iPSC Bank" ARC, which created an international iPSC bank of more than 100 high-quality cell lines generated from patients with inherited diseases, including cystic fibrosis, alpha 1 antitrypsin emphysema, scleroderma, amyloidosis, and sickle cell anemia. The support of the ARC also allowed the group to provide iPSC lines and reagents free of charge to the nonprofit research community to accelerate the discovery of new drugs and novel therapies to treat genetic disease. This "open source" philosophy—a commitment to sharing reagents, ideas, databases, and expertise with the larger research community—is at the center of our charge of advancing basic science toward therapeutic developments. In addition, with the assistance of the Boston University CTSI, the Evans Center, and the Boston University Office of Technology Development, the iPSC Bank ARC is developing leads to an iPS-based personalized medicine initiative.

Another important area of evaluation is whether ARCs contribute to networking that enhances research collaboration. It is well known that social relations are critical conduits for the transmission of knowledge, attitudes, and skills.[6] To test our hypothesis that grouping investigators via ARCs provides venues for the interactions that are key to collective achievements (see Table 1), we used a metric evaluation. Systematic examination of the social and research networking required for collaborations is a relatively novel methodology. Thus, we collaborated with Davis Square Research Associates, a local independent research firm, to survey and quantify collaborative networks in the ARCs. The members of the four original ARCs were surveyed. The response rate for the survey was 100%.

The network analyses focused on two metrics: the number and strength of the ties each ARC member claims to have with the other ARC members ("out centrality")[6] and the ties that these other members have with each other ("ego network density"). These ties were further examined by determining the frequency of information exchanges and the number of collaborative activities. The centrality of any given actor is determined by identifying the number of connections that person claims and evaluating the strength of these connections. The density of the respondents' ego networks offers a more fine-grained look into the connectivity of all investigators within the larger network of the ARC. Each researcher in the ARC has a unique set of relationships with other researchers, who may or may not have professional relationships with one another. The ego network densities calculated for the Evans Center study reveal how the observed ego networks compare to maximal values (in which each investigator has the strongest possible relationship with everyone else in the ego network).[6] For example, if Researcher X collaborates with Researchers

Table 1

Mean Numbers of Collaborative and Information-Sharing Activities by 41 Members of Four Affinity-Research Collaboratives (ARCs) Before (Time 1) and After (Time 2) Creation of the ARCs, Boston University School of Medicine, 2007–2011*

	Out centrality†		
Pair‡	Time	Mean number (SD)	Effect size¶
Pair 1§	Time 1 (2007 and 2009)	Collaborativeactivities: 33.1 (17.17)	0.55
	Time 2 (2009–2011)	Collaborativeactivities: 56.76 (21.77)	0.55
Pair 2§	Time 1 (2007 and 2009)	Information-sharingexchanges: 35.19 (22.33)	0.76
	Time 2 (2009–2011)	Information-sharingexchanges: 60.19 (23.39)	0.76
	Ego network density		
Pair‡	Time	Mean number (SD)	Effect size¶
Pair 3§	Time 1 (2007 and 2009)	Collaborativeactivities: 59.30 (27.16)	0.64
	Time 2 (2009–2011)	Collaborativeactivities: 88.16 (7.64)	0.64
Pair 4§	Time 1 (2007 and 2009)	Information-sharingexchanges: 53.63 (34.29)	0.42
	Time 2 (2009–2011)	Information-sharingexchanges: 82.17 (11.68)	0.42

*The table's data are based on ARC members' responses to questions about the number of collaborations and information-sharing exchanges they had before and after creation of the four ARCs. Participants retrospectively recalled what their interactions were before the creation of the ARCs. See the text for the names of the ARCs and details about how the data were processed using social network analysis.
† *Out centrality* refers to the number and strength of the ties that each ARC member claims to have with the other ARC members. *Ego network density* refers to the ties that ARC members have with each other.
‡ Pairs 1 and 2 contrast the changes in *out centrality* when looking at the number of collaborative activities or the number of information-sharing exchanges. Pairs 3 and 4 contrast the changes in the density of the *ego networks* when looking at the number of those same activities and exchanges.
§ Significant at $P < .05$ (paired samples *t* test).
¶ Eta-squared.

Y and Z, these relations are expressed in the centrality value for Researcher X. If Researchers Y and Z also collaborate with one another, then this is reflected in the density of Researcher X's ego network. An increase in both the centrality values for individual ARC investigators and the density of the corresponding ego networks would be a strong indicator that collaboration has increased.

The data from the 41 ARC members' responses were downloaded and configured to create symmetrical matrices that could then be imported into University of California–Irvine (net) for network analysis, with the subsequent network visualizations done in NetDraw.[6] Additional pre–post significance testing was done using the Statistical Package for the Social Sciences outputs for graphical displays of change for the network matrices we considered. Our analysis compared these metrics before ARC formation and after 30 months of ARC operation. The combined data for participants in all four ARCs analyzed showed a significant change (paired samples *t* test, $P < .05$) in pre–post centrality, with effect sizes (eta-squared) of 0.55 for the number of collaborative activities and 0.76 for information exchanges (see Table 1). The eta-squared values are analogous to r^2 values, with 0.55 being a moderate effect and 0.76 signifying a large effect. This indicates that the overall number and strength of the collaborations that ARC members claimed to have with one another have increased significantly.

Turning to the density of the researchers' ego networks, we found significant (paired samples *t* test, $P < .05$) pre–post gains and effect sizes (eta-squared) of 0.64 for collaborative activities and 0.42 for information exchanges (see Table 1), indicating that ARC members were engaging in more collaborative activities and information exchanges with others who were also more active in the collaborative life of the ARC. The use of the retrospective pretest instrument may inflate effect sizes in some groups because of a possible social desirability response bias—that is, a personal tendency to idealize or minimize past interactions. However, the potential for such errors carries fewer implications than it would in a randomized controlled trial, given the limited generalizability of the findings of the current SNA. Each new initiative would have to apply and evaluate its own analysis, also considering such points.

Summary and Conclusions

We found that the faculty in each of the ARCs had expanded their information-sharing and collaborative activities since the Evans Center began. Each ARC member appears to have used preexisting connections to set the stage for more elaborate collaborative activities relative to the mission of the ARC. Thus, one can reasonably conclude that the ARC approach has been effective in creating a social space within which innovative collaborations have grown. To further examine the effects of the ARCs on their respective scientific areas will require a citation network analysis and survey of new grant funding in a few years. As shown in Table 1, however, the early results are quite remarkable. A second observation concerns the future of the ARCs. Given that the ARCs grew at least partially out of preexisting relationships, it is possible that these could, in the long term, limit the innovative capacities of the group. For the collaborations to be maximally generative, they may need new collaborators introduced at judicious intervals into the groups. Indeed, the Evans Center encourages ARCs to add new partners, as needed, as the projects progress.

The pre-ARC mechanism developed by the Evans Center allows a period of self-assembly and selection. This, of course, implies that other universities that do not apply the same self-aggregative, pre-ARC-type mechanism might obtain different results. Another important aspect to note is that at least 65% of ARC participants occupy laboratory spaces in different buildings (although two of the three building are connected by a bridge). ARC members overcome this potential shortcoming of a "virtual" center by regular

monthly or bimonthly group meetings. It is possible that productivity and networking would have been greater if ARC lab members had been in proximal labs.

Taken together, on the basis of our experience with the new initiative presented here, we propose the Evans Center's structure and content as a new paradigm for promoting interdisciplinary biomedical research.

Acknowledgments: The authors offer their gratitude to the outstanding, enthusiastic faculty of Boston University (BU), who are central to the development of ARCs and research progress. The authors also thank Ms. Robin MacDonald, the administrative manager of the Evans Center, for devoted efforts and skillful help, and the Evans Foundation and its administrators for support. Acknowledgments are also due to Dr. Karen Antman, BU School of Medicine dean and Boston Medical Center provost, as well as Dr. David Center, BU CTSI director, for supporting new concepts developed by the Evans Center's founder and center members. Finally, the authors thank Dr. Andrei Ruckenstein, BU associate provost and vice president for research, Dr. Bennett Goldberg, director of the BU Nanoscience Center, and Dr. Mario Cabodi, deputy director of the BU Nanoscience Center, for indispensable collaboration in developing a nanotheranostics ARC and similar research and educational initiatives.

Funding/Support: None.

Other disclosures: The Evans Center is funded by the Evans Medical Foundation at Boston University School of Medicine.

Ethical approval: Not applicable.

References

1 Mallon WT, Biebuyck JF, Jones RF. The reorganization of basic science departments in U.S. medical schools, 1980–1999. Acad Med. 2003;78:302–306.
2 Sharp PA, Kastener MA, Lees J, et al. The Third Revolution: The Convergence of the Life Sciences, Physical Sciences and Engineering. Cambridge, Mass: MIT Press; 2011.
3 Anderson NB. Levels of analysis in health science. A framework for integrating sociobehavioral and biomedical research. Ann N Y Acad Sci. 1998;840:563–576.
4 Leshner AI. Innovation needs novel thinking. Science. 2011;332:1009.
5 Wasserman S, Faust K. Social Network Analysis: Methods and Applications. New York, NY: Cambridge University Press; 1994.
6 Freeman LC. Centrality in social networks. Conceptual clarification. Soc Networks. 1979;1:215–239.