Nurturing interdisciplinary research

Thomas R Cech & Gerald M Rubin

The research in biology has been transformed by the products of interdisciplinary research. Here we explore why it is challenging for universities to bring biologists together with engineers, physicists and computer scientists for productive collaboration, and we evaluate alternative solutions. In particular, we describe how the new Janelia Farm Research Campus of Howard Hughes Medical Institute aims to provide a home for creative scientists from different disciplines to attack major biomedical research problems.

Every now and then I receive visits from earnest men and women armed with questionnaires and tape recorders who… seek their Holy Grail in interdisciplinary organization. [But] creativity in science, as in the arts, cannot be organized. It arises spontaneously from individual talent. Well-run laboratories can foster it, but hierarchical organization, inflexible, bureaucratic rules, and mounds of futile paperwork can kill it. Discoveries cannot be planned; they pop up, like Puck, in unexpected corners.

Max Perutz, in
I Wish I'd Made You Angry Earlier
(Cold Spring Harbor Laboratory Press,
Cold Spring Harbor, New York, 2000).

For the Howard Hughes Medical Institute (HHMI), the establishment of the Janelia Farm Research Campus offers an unfettered opportunity to create an environment that will bring biomedical scientists together with computational scientists and instrument builders. The goal is to develop new technologies and apply them to challenging biomedical problems that may have a low probability of short-term success but a high potential impact. An additional goal is to foster this research in a manner complementary to and synergistic with HHMI's existing programs and those of the 70 US research institutions that host the research groups of our 320 investigators.

Scientific research is currently conducted in a wide variety of organizational "cultures," and no single culture is unambiguously the best. Two main factors define these cultures—the conditions attached to the research funding and the career structures available to the participants. In planning its interdisciplinary Janelia Farm Research Campus (http://www.hhmi.org/janelia/), HHMI has had the benefit of being able to look at past models and trying to identify the best elements of each, and of not being constrained by inertia, convention or the need to obtain funding from an outside source. (To put it another way, if it doesn't work we will have no one but ourselves to blame.) In this article we describe our view of some of the challenges confronting those who want to nurture interdisciplinary research and how we anticipate addressing them at Janelia Farm. A more extensive discussion of these issues, as well as detailed architectural plans for the Janelia Farm campus, can be found in ref. 1 (also available at http://www.hhmi.org/janelia).

The authors are at Howard Hughes Medical Institute, 4000 Jones Bridge Road, Chevy Chase, Maryland 20815, USA.
e-mail: President@hhmi.org

Why this interest in interdisciplinarity?

Interdisciplinary science entails the collaboration of scientists with largely nonoverlapping training and core expertise to solve a problem that lies outside the grasp of the individual scientists. For example, a researcher in the Rubin lab develops a computer algorithm to search for a DNA sequence pattern in the *Drosophila melanogaster* genome and then recruits a genetics student to test the function of the predicted DNA element. The goal is similar to that of multidisciplinary research, where the same person masters two or more fields that are traditionally separate—for example, when the same researcher in the Cech lab synthesizes a novel organic chemical compound and then uses it to evaluate the mechanism of a ribozyme. The long period required to become trained in a new discipline and the specialized expertise and expensive equipment unique to each discipline often make interdisciplinary collaborations the only practical pathway. Although interdisciplinary and multidisciplinary research each have their challenges, some of which are shared, we focus on interdisciplinary research in this article.

The movement toward interdisciplinarity is driven by the science itself. Both materials science and nanotechnology require the integration of ideas and techniques from chemistry, physics and engineering, and if biologists want to apply these materials to their problems, so much the better. The various genome projects and the complexity of neurocircuits have made computer sciences more and more empowering for biology—hence 'computational biology.' Chemistry and biology have been compatible bedfellows for an entire century, but the realization that chemical agonists and antagonists of biological processes can be isolated from large combinatorial arrays has sparked new interfaces such as 'chemical genetics.' And the importance of imaging—at the atomic, cellular, and organ levels—has forced a marriage of convenience between physicists and engineers, who know

HHMI's Janelia farm research Campus. Left, architect's model. The S-shaped building set into the landscape comprises laboratories and offices (square structures). the C-shaped building below is conference housing. Right, aerial view of construction in mid-2004.

how to design the tools, and the biologists who hunger to picture their favorite processes at ever greater spatial and temporal resolution.

Learning from the giants

The type of interdisciplinary research organization that we are contemplating for Janelia Farm has been successfully implemented. Two well-known and highly regarded examples are the Medical Research Council Laboratory of Molecular Biology (MRC LMB) and the former AT&T Bell Laboratories. We have attempted to understand the cultural, organizational and management features critical to their success. Despite the fact that one of these institutions was a small public-sector biological research laboratory and one a large private-sector electronics enterprise, they share a surprisingly wide range of operating principles.

Individual research groups were small, generally composed of fewer than six individuals. Small group size was considered essential to promote collaboration and communication between groups, as well as good mentoring. Larger projects were often conducted by self-assemblies of smaller groups. Excellent support facilities and infrastructure were provided, enabling individuals and small groups to function effectively and to focus on creative activities. Internal sources provided dependable and generous funding; outside grant applications were not permitted, nor was there any obvious pressure for the work to be of immediate medical relevance or commercial value.

The time made available by the lack of formal teaching, administrative or fund-raising activities, as well as the high level of staff support, made it possible for group leaders to carry out experimental work with their own hands. Experienced scientists were also much more approachable and available to discuss scientific ideas and mentor junior scientists. In contrast, it is increasingly rare for a tenured faculty member in a US research university or medical school to spend substantial time working at the bench[2] or even engaging in unscheduled interactions with their colleagues.

At both the MRC LMB and Bell Labs, 'success' was defined as solving difficult and important research problems, as opposed to more typical criteria such as publication number, service on editorial boards or speaking invitations. The management of both institutions felt it was their responsibility to be familiar enough with the work of their scientists to be able to evaluate their potential and their accomplishments. They were patient with those who were considered to be very good, but had not yet achieved external recognition. At both institutions, turnover of group leaders was high and tenure was either absent or limited; most group leaders moved on to university positions after five to ten years.

No institution in operation today fully fits the above description. We have, however, identified and learned from several current institutions, including the European Molecular Biology Laboratory, Carnegie Institution of Washington Department of Embryology, and Cold Spring Harbor Laboratory. All three demonstrate that it is possible for a freestanding research institution to be highly successful without granting tenure. Cold Spring Harbor Laboratory also provides a useful role model of how to overcome physical and intellectual isolation, as well as provide a service to the scientific community, by means of an extensive program of scientific conferences and training courses.

At the universities

The success of interdisciplinary research centers such as those described above has prompted universities around the world to develop their own mechanisms to encourage stronger interactions between the disciplines. The Deutsche Forschungsgemeinschaft funds collaborative research centers (SFBs) that bring together university scientists located within 50 kilometers of one another. For example, an SFB centered at the University of Frankfurt unites organic chemists, theoreticians, spectroscopists, informaticists, X-ray crystallographers, geneticists, microbiologists and physicians in studies of RNA science. In the United States, the W.M. Keck Foundation has kindled vibrant multidisciplinary projects such as the Laboratory for Functional Brain Imaging and Behavior at the University of Wisconsin-Madison, whereas the Whitaker Foundation funds research at the interface of engineering, biology and medicine. Additional examples abound.

Despite this progress, the universities find it challenging to bring down their internal walls between disciplines. Their biologists are in separate buildings from their physicists; their engineers work in a separate college of engineering; and the nearest medical school may even reside in a different city (University of California Berkeley versus University of California San Francisco; Harvard College in Cambridge versus Harvard Medical School in Boston). Such geographical separation presents a considerable challenge. The spark of transdisciplinary approaches and insights requires 'productive collisions' between people in different disciplines, just as atoms and molecules must undergo productive collisions to react. If engineers, biologists and computer scientists live apart, they need to make an appointment in order to 'collide.' And individuals are often so highly scheduled that such collisions, even when they occur, are usually of short duration.

Another problem is that the academic culture and promotion system often actively discourage collaboration among research scientists. When scientists collaborate, their unique contributions are often not apparent, a situation that adversely affects their performance review and career advancement. So often we hear of an assistant professor being denied tenure because he or she was a middle author rather than first or last author on too many publications. But order of authorship, necessarily determined in one-dimensional space, does not adequately depict contributions in a multidimensional collaboration. This situation is compounded in the case of interdisciplinary research where the research advance itself may not be seen as being at the forefront of any of the individual disciplines, the standard-bearers for which generally reside in separate departments that are competing for resources such as new faculty appointments. For example, the development of the field of bioinformatics was greatly delayed because neither biology nor computer science departments saw bioinformatics as an appropriate area of research for their faculty.

In response to these challenges, American universities have constructed buildings for collaborative research separate from the traditional departments. JILA (the Joint Institute for Laboratory Astrophysics) at the University of Colorado at Boulder brings together physicists, chemists and superb instrument engineers and fabricators[3], and has garnered two recent Nobel Prizes. BIO-X at Stanford University has equal doses of biology, physics and engineering. Princeton University's Center for Integrative Genomics merges molecular biology, chemistry and physics. The Skaggs Institute of the Scripps Research Institute is especially strong at the interface of chemistry and biology, whereas the new Broad Institute will bring Massachusetts Institute of Technology, Whitehead Institute and Harvard scientists together to apply genomics and chemistry to problems of medicine. Of course, when you bring energetic, creative people together, it is not surprising that great things happen. But the measure of success for these interdisciplinary institutes needs to be "Is the whole greater than the sum of the parts? And, if so, by how much?"

The challenges of promoting innovative interdisciplinary biological research are routinely solved—not in academia, but in biotechnology companies. There, if product development requires a team of bioinformaticists, chemists, cell biologists, pharmacologists and chemical engineers, the company wastes no time in bringing them together. Because they live under a single roof, the challenge of dealing with geographic separation is mitigated. And the team benefits from being faced with a well-defined target for their work. Perhaps academic institutions, which currently select and train their scientists to be fiercely independent, could benefit from adopting a bit of this attitude in their interdisciplinary science.

Back to the farm

The Janelia Farm Research Campus in northern Virginia will aim to identify important biomedical problems for which future progress requires technological innovation and then foster the self-assembly of integrated teams of biologists and tool builders who seek to break through the existing barriers. This in turn will require a much stronger focus on developing new tools—experimental methods, computer software and scientific instruments—than is typical in most academic research centers. The scientific problems we choose to pursue will drive the choices of tools we seek to develop; the software and instrument development activities will work in close concert with, and support, the ongoing experimental work. The group leaders will be recruited through an open international competition. Individual research groups will be capped at six people, mostly postdoctoral fellows and technicians, but extensive shared core facilities will be provided; group leaders will be able, even expected, to continue to work at the bench. A single laboratory building will allow about 400 individuals from different disciplines to work together without departmental walls.

We believe that having HHMI provide all, or nearly all, funding for activities at Janelia Farm is essential for creating the interactive, interdisciplinary and collaborative research environment we envision. Only in this way can we provide scientists with the freedom from distractions that will allow them to participate directly in experimental work and the freedom to tackle important problems that might have too low a probability of success—or not yet be well-enough defined—for a typical grant application.

An assistant professor's freedom to select a research problem is generally limited to problems that can garner external research support. Not only are grant-giving agencies notoriously risk-averse, but the work will probably be carried out by postdoctoral fellows and graduate students who are under pressure to obtain publishable results within a short time span. Thus much emphasis is placed on quantity and certainty of output at the expense of originality and potential impact. Similarly, research in biotechnology companies must support the business plan. Although these funding models are appropriate for the vast majority of biomedical research, they have two major limitations. First, proposals for more adventuresome projects, even those that may have enormous impact if successful, have traditionally fared poorly. This is especially true for non-hypothesis-driven research aimed at developing new research tools. Second, the ability to move quickly to take advantage of unforeseen targets of opportunity is severely constrained.

With small individual groups, Janelia scientists will have to collaborate to tackle a big project. The group leaders will be valued and evaluated on the basis of their contribution to collaborations, supportive interactions, and mentoring of other scientists as well as their individual achievement, overcoming the most pervasive obstacles to collaboration in academia. Decisions about renewal of appointments every five to six years will include an evaluation by an external panel of experts who will interact with the scientist being reviewed, rather than simply judging from publications and written reports. The process and the expected level of performance will be similar to those now applied to the review of HHMI investigator appointments. The external opinion will be weighed along with an internal evaluation of the contributions to collaborations and mentoring. Although group leader appointments will be untenured, there will be no limit on the number of terms for which a scientist can be reappointed.

It is critical that Janelia Farm be able to evolve as science evolves. Thus, some group leaders will be asked to leave not because the quality of their work has slipped, but because their expertise no longer fits with the mission of the campus. Such group leaders will be allowed to transfer their HHMI appointment to any of our host institutions that wishes to receive them, and after another five years they will be evaluated on an equal footing with the other investigators. This 'soft landing' should make having an untenured position quite palatable.

Academic institutions have one key resource that biotech companies do not share: an abundant supply of graduate and undergraduate students as well as postdoctoral fellows. Interdisciplinary research benefits greatly from students and postdocs, who are not so mired in disciplinary dogma and transgress boundaries rather effortlessly. From the other side, students benefit greatly from interdisciplinary research; they find it intellectually invigorating, they enjoy the social dynamics of a team approach to problems, and they derive excellent preparation for a possible future in a more interdisciplinary academic environment or in the biotech industry. Thus, although Janelia Farm will not be a degree-granting academic institution, it will provide opportunities for students from partnering universities throughout the world to carry out all, or part, of their thesis research on site. Furthermore, a robust visiting scientist program will allow visitors with appropriate interests and expertise to participate in ongoing projects with Janelia's resident scientists and also serve to make the tools created at the farm broadly accessible and promote their dissemination.

Another area where Janelia Farm aims to have an impact is increasing the participation rate of women in the highest-level biological research. Unlike the case of underrepresented minorities, the pipeline of talented young female biologists is full, yet women still make up less than 15% of full professors in departments of biological sciences at research universities. It is widely agreed that a major factor in the declining participation of women is the conflict between an academic career in science and the demands of assuming primary childcare responsibilities. Janelia Farm is well positioned to provide a supportive environment for women scientists. Most importantly, the lack of nearly all professional obligations not directly related to research, and the provision of high-quality on-site infant and child care, should allow the time needed for both high-level research and family life.

The majority of scientists at Janelia will be focused around two or three broad goals or missions. We call these '1,000 person-year projects,' and ask what biological goal would be worth the effort of 100 scientists working for 10 years with abundant resources, with instrumentation and computational tools being created in-house to further the project. A series of workshops held earlier this year, each with about 30 participants, has helped evaluate potential initial research objectives (see http://www.hhmi.org/janelia for a current description of these workshops). We are particularly interested in identifying research areas that may be underpopulated not because they are seen as unimportant, but because they are considered too challenging for traditional funding mechanisms and career structures or because they require an interdisciplinary approach not feasible in a university setting. It is important to emphasize that the initial objectives are meant to provide some focus but not to constrain the creativity of individual scientists to follow opportunities as they arise.

Clearly, interdisciplinary research will take many forms over the coming decades as more scientists and institutions become committed to this approach. A key related issue is whether undergraduate and graduate school curricula will be able to change to support a more integrated approach to biological research problems[4–6].

1. Howard Hughes Medical Institute. Janelia Farm Research Campus report on program development (Howard Hughes Medical Institute, Chevy Chase, Maryland, USA, 2003).
2. Pines, M. No time for the bench. *HHMI Bulletin* **16**, 28 (2003).
3. Aldhous, P. Rocky Mountain high. *Nature* **423**, 915–916 (2003).
4. Committee on Undergraduate Biology Education to Prepare Research Scientists for the 21st Century. BIO2010: transforming undergraduate education for future research biologists (National Research Council, National Academies Press, Washington, DC, 2003).
5. Bialek, W. & Botstein, D. Introductory science and mathematics education for 21st-century biologists. *Science* **303**, 788–790 (2004).
6. Ares, M. Interdisciplinary research and the undergraduate biology student. *Nat. Struct. Mol. Biol.* **11**: 1170 –1172 (2004).