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Collaborative Models for Translational Neuroscience and Rehabilitation Research

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Abstract

Little formal research has been conducted on strategies to structure basic, preclinical, and clinical research to increase the likelihood of discovering efficacious interventions for patients with neurological diseases. How academic research is organized and funded by government agencies and foundations seems likely to affect the quality and rate of production of valued therapeutic agents. Few models for translational biomedical research, however, have been defined and no strategies have been compared. Given the narrow width of expertise and laboratory capacity of individual investigators, the complexity of identifying and manipulating mechanisms of disease components over time, and the demand for solutions from society, our continued reliance on funding therapeutic discovery through standalone investigators and projects seems counterproductive. Models are described for funding collaborations of basic and clinical scientists to work in iterative, adaptable, cross-disciplinary interactions around key progress-limiting questions. Problem-oriented collaborations require leadership, incentives, trust, ongoing assessment, and an efficient infrastructure that overcomes barriers. These models are as testable as the hypotheses that drive scientific research.

Keywords

Qualitative methodologies; Collaborative research; Neurologic rehabilitation; Peer review; Transdisciplinary research; Neural repair; Plasticity; NIH Blueprint; Research funding

State and federal governments, biomedical and pharmaceutical companies, universities, foundations, and research scientists justify the \$120 billion spent yearly on medical research in the United States¹ as being the lubricant for the discovery of treatments for diseases. The search for robust therapies for neurological diseases over the past 25 years, however, has been expensive and remarkably unproductive.² This relative failure extends to the paucity of robust effects of interventions for neurological rehabilitation.³ Do the methods of bench-to-bedside research bear some fault, or is the basic and translational science too complex for breakthrough discoveries? The Health Research Alliance,¹ a working group of foundations, expressed frustration with the “misaligned priorities and culture of many academic health centers. . . . The incentives work against translational studies, creating competitive

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environments that foster unnecessary duplication of effort and result in breakthroughs that fill journals rather than medicine chests.” The “mismatch between financial support of neurological research and its yield” has drawn specific scrutiny.⁴ Indeed, Horrobin claimed that pharmaceutical research is failing in its ability to deliver new drugs; as much as pharmaceutical research draws on the wider biomedical research community, academia too may be failing.⁵

The Problem

The scientific method for proof of a hypothesis guides experiments but does not guide the organization of research that seeks to understand mechanisms of disease and develop treatments. In addition, scientists, clinicians, foundations, and government agencies have not pressed for an examination of the validity of their models of intended translational research. One recent recommendation to enhance the likelihood of finding therapies was the call to pull researchers out of their silos and into collaborations. The director of the National Institutes of Health (NIH), Zerhouni,⁶ wrote, “Effective scientific teams of the future will require closer working relationships among basic, translational, and clinical scientists. Traditional disciplinary, departmental, and other artificial or organizational barriers will have to be breached in an era of scientific convergence.” Johnston and Hauser added, “We can, however, increase the chances of serendipity by putting highly productive people together in environments that maximize interactions across disciplines, and that shorten the time between innovation, recognition of its importance, and application.”⁷ A recent consensus statement emphasized the need for collaborative strategies to move neurological rehabilitation interventions forward.⁸

A far more collaborative interaction, then, rather than cloistered scientists and compartmentalized disciplines, sounds reasonable and necessary for progress toward patient-valued therapies. Fruitful collaboration, however, takes practice, coordination, and adaptable mechanisms of funding. No rules of engagement for collaborative translational medical science have been tested, especially for moving from basic neuroscience discoveries into neural repair and rehabilitation. A handful of models that aim at collaborative interactions exist, but most do not define the problems best suited for collaboration, suggest the necessary infrastructure, or offer solutions to the perceived barriers that keep academic mom-and-pop shops from merging their expertise. Thus, experiments with models for research that foster collaborations of experts will have to be conducted.

Collaborative translational neuroscience will be used to mean that 5 or more basic and clinical scientists and clinicians from at least several institutions seek plausible, mechanistically novel therapies by tackling progress-limiting questions that can reach across diseases (Figure 1). The investigators’ background knowledge, experimental choices, and preclinical models should inform and be informed by potential clinical targets. These laboratories, each a branch with limited knowledge, must develop as a tree of knowledge by growing within their cross-disciplinary planning of objectives, back-and-forth trading of information, and assistance with each other’s conceptual and experimental needs. Incoming data should continuously influence the directions of the team. Their neurobiology experiments and insights, preclinical models of disease, and probing clinical pilot studies

should aim to develop proofs of concepts that can lead to randomized clinical trials of high potential yield. The researchers may be prospectively recruited by a sponsor or spontaneously merge their interests in pursuit of science and funding. Partnerships can include academics, industry, government, and foundations that align around scientific opportunities. Participants are encouraged to leverage each other's talents and resources.

Multidisciplinary, interdisciplinary, or transdisciplinary collaboration should benefit all participants (Table 1). Researchers routinely limit the scope of their experiments due to short-term funding and finite laboratory resources. Indeed, they compete with each other for dwindling resources. In a collaboration, individuals enrich their own work by accessing the thoughts and tools of other experts. A team is likely to define problems and potential solutions better than any one player, by developing more inclusive and meaningful narratives about what is known and not known. Participants will also draw on past experiences of their peers, including data that never reached publication. The collaboration can become a spirited and focused scientific incubator rather than the gradual and meandering accretion of knowledge that evolves across multiple single laboratories. Diverse, but not divisive, input among participants helps prioritize questions and experimental steps. Discussion about data continuously reframes scientific paths. Even hypothesis-generating experiments, sometimes referred to by NIH grant reviewers as fishing expeditions, can be encouraged if the group plans to cast for big fish.

Universities also benefit. Departments may not always have to recruit new faculty and purchase major instruments to bring certain expertise onto the campus—scientists can be “borrowed” from another university to enable the work of faculty and share training opportunities. Also, a collaborative milieu will help develop needed physician-scientists. Donors may become more excited about philanthropy that fields a team of players who are the best at their positions across institutions. Indeed, disease-oriented foundations and granting agencies may be especially interested in the sweeping interaction from preclinical to clinical studies.³ Most important, industry may have a higher level of confidence in therapeutic pathways and clinical pilot studies reported by outstanding scientific collaborators.⁴ Companies gain far more expertise from a collaboration than they can hire. They may anticipate that drug development and clinical trials will be safer investments than what an academic mom-and-pop shop can offer.

Solutions

The impetus for biomedical collaborations across institutions and progress-limiting challenges arises not only from the increasing complexity of scientific problems, society's frustration with the cost and burden of diseases, and the common pathways that are being recognized across a variety of diseases, but also from the expanding feasibility of interactions among scientists. Accessible databases, Internet communications, and diverse expert knowledge and skills now reside on every continent.⁹ Attempts to merge separate subfields of expertise around specific medical problems have taken a handful of forms. Networks were recently sponsored by the American Association for Cancer Research through “Dream Teams” of 8 or more collaborators around 1 type of cancer; the Howard Hughes Medical Institute uses Collaborative Innovation Awards for 3 to 6 scientists around

1 topic such as toxic proteins in neurodegenerative diseases; the Myelin Repair Foundation funds 4 to 5 scientists at different institutions for multiple sclerosis studies using a strategy that emphasizes delivering patents and working with pharma; the Packard Foundation sponsors a motor neuron disease consortium; the Reeve Foundation aims to achieve interactions in spinal cord injury; and the Wellcome Trust, the MacArthur Foundation, and the Robert Wood Johnson Foundation have a record in cross-discipline projects. The California Institute for Regenerative Medicine has begun to consider collaborative projects for neural repair. The NIH funds Collaborative Translational Science Awards (CTSA) to create infrastructure for interactions within a university. A stated goal is a consortium (CTSC) of 60 university sites that works together on clinical studies. Other federal programs include a multi-principal investigator R01 and a \$50 000 R01 supplement per investigator from the NINDS Administrative Supplements for Collaborative Activities to Promote Translational Research. Interactions are also encouraged through Program Project grants (P01) and Center grants (P50), such as the Specialized Programs in Research Excellence (SPORE) for cancer at 1 site. The SPOREs are also expected to interact. A confounder of cross-institution interactions is that the NIH allows each of the institutions to take their full indirect costs from funds that are transferred from one to another (http://grants.nih.gov/grants/multi_pi/index.htm). No assessment has been published about the results of these models.²

Disease-related foundations may express the desire to fund a truly collaborative translational model but quickly recognize potential barriers (eg, intellectual property rights, ownership of data, authorship) and inertia (eg, lack of leadership, need to revise styles of review and funding). Also, most foundations are not organized to interactively engage their grant recipients, which is essential for successful team science.

The AMRF Model

An opportunity to fund a collaborative model for research was provided by the Dr Miriam and Sheldon G. Adelson Medical Research Foundation (AMRF) in 2006. Six programs were developed over several years with planned participation of approximately 140 scientists from 60 universities. Each program included 3 to 12 collaborations of 4 to 12 basic and clinical scientists. Each program examined the fundamental components of a set of diseases that might share pathological common denominators over time, considered key confounders of progress, and planned to identify and validate targets for therapy. For example, the initial program, the Adelson Program in Neural Repair and Rehabilitation (APNRR), tested the concept of organizing collaborations to find treatments across neurological diseases that cause sensorimotor impairments and disability. The team aimed at a proof of principle to regenerate clinically important central nervous system and peripheral nervous system axons (see Sidebar).

The clinician-scientists who worked with patients and disease models drew from the fundamental insights of basic scientists who studied axon transport, regeneration-associated genes, mechanisms of myelination and conduction, synaptogenesis, and the bases for learning and memory. They looked for opportunities in subgroups of patient pathologies to apply both a repair and a subsequent rehabilitation intervention that optimized the repair

strategy. Targets included, for example, the motor complete spinal cord injury patient to regenerate axons and improve function 2 levels below the lesion; after stroke to reinstate motor control in a hemiplegic upper extremity or restore language in an aphasic patient by a cellular or remyelination strategy; for a traumatic root or plexus lesion at the junction of the spinal cord, to reimplant the proximal nerve segment into the cord at or above the level of avulsion or compression; after cord trauma or amyotrophic lateral sclerosis, use cells to replace motor or dorsal horn neurons; and for a traumatic or progressive sensorimotor neuropathy, modulate regeneration-associated genes and prevent distal myelin degradation. Investigators resonated with the intellectual challenges, networking, peer support, and trust that grew over time (see RAND working paper at www.adelsonfoundation.org).³⁵ The international financial crash in 2008 interfered with the ability of the AMRF to fund its programs, but lessons learned may offer insights to stimulate foundations and agencies to explore ways to develop and manage models for collaboration.

Barriers to manage—Many potential barriers may limit the enthusiasm for collaborative research across laboratories in the same and different institutions. The NIH Office of Ombudsman suggests 10 questions to discuss before individuals collaborate (Table 2). The AMRF aimed to resolve these questions and then developed common guidelines with universities (and some drug companies) to protect the rights of investigators and institutions in a rational way. The key element was to build trust within everyone's self-interest. After coming to understand the logic and goodness of collaboration, university legal and administrative staffs often suggested ways to go beyond what prior constraints had allowed. For example, the president's office at the University of California system quickly negotiated a letter of agreement for all University of California schools in regard to intellectual property, licensing, publication rights, indirect costs, and other matters. This contract was to be presented to other sites as a format for a master collaborative agreement.

Organizational principles—Formal planning, management, and infrastructure are essential for collaborations that are large enough to enable productive preclinical and clinical innovation. Table 3 connects some of the key components recognized by an independent RAND Corporation review of the AMRF.

Initiation of collaborative teams—Collaborations can be self-organized by investigators who find each other or may be prospectively developed by an outside sponsor. If the collaboration is successful, these approaches otherwise merge by the end of the first year of support. The prospective strategy requires considerable preparation by the sponsor, especially for a foundation or biomedical company. The focus of one or more collaborations around large lingering questions will gradually evolve from small group discussions among the experts in pertinent disciplines. For a foundation, these initial discussions also serve as auditions in search of creative team players who possess scientific and social intelligence. A symposium with presentations by potential participants will also reveal important directions. Then, 6 to 15 participants who represent the scope of the translational problem are brought together by video conferences to discuss directions for research, led by a short list of questions raised in earlier interactions. The core researchers may tilt toward the greater experience of associate and full professors with a record of influential publications relevant

to the topics at hand. Several who have already worked together can promote a template of collaboration for others. These meetings inform investigators about their range of interests and laboratory skills beyond their publications, tools they can access, and their lab's capacity for additional endeavors. This exchange also serves as an audition of potential players by each other. As ideas and names are brought up by subsequent e-mail and phone conferences, a sense of who is willing to play one or more key team positions evolves. At this stage, the group is less like an all-star baseball team and more like accomplished jazz musicians playing without a conductor but able to take cues and influence each other.

A 2-day workshop with no more than 15 to 20 potential collaborators and facilitators and an agenda drawn by the funder's staff and participants should follow. This format is most efficient if each researcher has already presented a 30-minute, interactive Web-based lecture about personal research activities and lab tools. Additional 10-minute presentations at the workshop help construct concepts and key experiments that could initiate complementary studies. Experiential games can be played to promote awareness of how to listen and grow comfortable in a new undertaking that demands mutual trust and agile adaptation. Openness and contrarian or alternative points of view about directions for research and for the interpretation of past studies should be encouraged and solicited by group leaders. Unstructured time and long meals allow peers to discuss opportunities and develop a social network. The workshop is followed by frequent phone meetings until proposals are written.

Size—An individual collaboration or a network of collaborations within a program must be calibrated to a critical mass of researchers with complementary capabilities to address the problems they have identified. The optimal size of a focused academic team will vary with the level of available funding, the complexity of the undertaking, and the desired pace of progress. In general, 6 to 12 primary investigators per collaboration offers an efficient start. More than 15 will overwhelm personal interactions during meetings, especially if postdoctoral students attend, and make it difficult for the group to keep track of its mutual experiments. Affinity groups of 4 to 8 investigators who also interact across the collaborations of a larger program may be more efficient than a single group dynamic with more than 15 principal investigators. Once established, a collaboration must agree to an open process for considering, vetting, and adding peers.

Proposals—By the time grant proposals have been written, the group should have vetted most of the aims and methods that will be incorporated into the collaboration. Thus, a 5-page overview of the collaboration to describe specific interactions and primary milestones ought to be sufficient. This document reinforces the planning process and the search for clinical targets. In addition, a 5-page submission from each component project of the collaboration (usually 1 laboratory) to describe its aims, collaborative roles, and any nonstandard methods should be sufficient for evaluation. If technology platforms are included, these labs should explain how they will be integrated and how data will be disseminated. A timeline for 1 to 2 years can then be drawn with columns showing the interactive experimental studies and their milestones, interim clinical goals, and long-term opportunities that will depend on acquired data. These charts become visual touchstones for

the investigators and sponsor from year to year—a means to assess progress and changes in direction elicited by new information.

Review process—Procedures for reviewing proposals and funding must include transparent checks and balances. The AMRF chose genuine peer review by the collaborators themselves. This approach challenged the NIH process, in which a primary reviewer may highly bias scoring.¹⁰ The rationale was that, for collaborative science, the investigators chosen because of their expertise and vetted by these peer experts are best positioned to evaluate each other's contributions. The group itself will also best appreciate the team dynamic, which may include players who hit sacrifice fly balls and bunts to move others along the bases. The members of each program anonymously reviewed all collaborative projects, except their own in that collaboration, and scored them on a Likert scale (Table 4). This review process allows critiques that peers may not comfortably provide during workshops and conference calls. More so, the interactive review process adds to the understanding of what each lab aims to do, often leading to new ideas and interactions. An executive committee of a few investigators drawn from the program, the program leader, and the scientific leader from the foundation provide oversight, as well as help make compelling ideas feasible. This committee then recommends adjustments to research plans and budgets that are immediately discussed with the contributing scientists, to avoid delays created by formal resubmissions of proposals. Outside experts or a scientific advisory committee can be brought in to further assess and shape projects, but they must calibrate their critiques to the innovative strategies of the team. Consensus within an AMRF program was nearly always attained for recommended, revised, and not recommended projects.

Funding—Funds that are sufficient for each lab's scientific contribution, in relation to the whole collaboration's aims, must be discussed openly during grant preparation and reviews. A successful group learns to restrain self-interest. After trying a few variations, the favored schedule for duration of AMRF funding became 2 years, with written progress reports at 18 months following one of the twice-a-year formal program workshops. Continuing renewal requests included an overview of progress, as well as new plans from the collaboration and its component projects. This approach allows investigators to iteratively interact to develop the directions for their collaboration almost yearly, based on new information and milestones within a feasible budget. Another approach is to fund for 3 to 5 years but build in yearly interim reviews by the collaboration and the funding organization. In this scenario, the investigators should be permitted to shift or add to the original funds in a modest way to undertake new opportunities. Funds are best directed from the sponsor to each institution, not subcontracted to other sites by one institution. Refunding should also depend on good citizenship, such as attendance and participation in workshops and Web-based seminars, along with a record of sharing wisdom and data with peers.

Facilitation and Consolidation of Collaborations

Collaborations require preparation, practice, socialization, and trust among investigators, which takes time to cultivate. A team may take 6 to 12 months after initiation to grow resilient, or fail. Leadership, infrastructure, and assessment, along with workshops and analyzing data and writing journal articles together, help cement the collaborative process.

Leadership—Appropriate leadership enhances the overall effectiveness of teams and increases the satisfaction of team members.¹¹ A collaboration leader serves as a liaison, gatekeeper, fellow expert, consultant, and coordinator whose access to a wide array of information from participants helps stimulate interactions and encourages both creative thinking and integrity. An influential leader promotes divergent thinking and risk taking, while envisioning and discussing with everyone how various disciplines and investigators can work in constructive ways.

The initial and ongoing organization of a collaboration should include leadership by a basic or clinical scientist or clinician with a background in academia or industry who does not participate in the experimental work. This scientific officer, paid for part-time or full-time assistance to the collaboration by the funder, must be opportunistic and systematic in identifying complementary players, as well as scientific and translational strategies. A program director who is a clinical scientist drawn from the initial group of participants should be designated by peers or the sponsor as the group leader. This leader serves as a key facilitator of the vision of the collaboration but may occasionally have to manage its personalities. A program director should rotate after 2 years of service to reduce personal burdens and to promote fairness.

Infrastructure—Setting up infrastructure for a team is important but does not directly promote collaboration. Rather than having a university or foundation create its impression of the optimal collaborative infrastructure (eg, genomic and high-throughput facility cores, drug libraries, or staff to run clinical trials), the investigators should continuously assess their requirements and work with the sponsor and universities to realize needs. Certain highly valued supports, however, are essential by the time a team begins its first season:

1. The scientists should not be burdened with new administrative responsibilities. Embed into the collaboration the leadership of a senior scientific officer who helps develop the collaboration and serves as an ombudsman for the group and the sponsor. As noted earlier, this MD or PhD should have credentials in the field of study and translational research. Indeed, this advisor ought to be able to play the role of a scientific or clinical utility player for the team while serving as a coach and occasional umpire. In addition, a program manager for the team should be hired to direct operational and administrative requirements that affect productivity. This PhD should be knowledgeable about the science most relevant to the collaboration, so as to best provide technical and logistic resources for research, maximize communications, enable synergies, manage details for scientific meetings and Web seminars, visit participating labs, and provide feedback to the team, scientific officer, and sponsor. Someone trained in skills for collaboration, rather than simply drawn from an investigator's lab, will be most valued. A foundation may prefer to have these positions filled from its staff.
2. Continuously seek solutions. The collaborators and staff should monitor new publications and symposia for ideas and potential new participants. A disease-related foundation can draw on the work of its past and present recipients. A CTSC can draw on faculty at participating sites. In addition, collaborative assistance by

subcontracting or by so-called crowd sourcing (eg, modeled by www.InnoCentive.com) can engage peripheral problem solvers for a specific task.

3. Provide Web-based communications for use at any time by investigators. Design a user-friendly submission and review system that includes overviews of each collaboration, key details of each of its projects, and a utilitarian scoring system. To allow proper credit for work by predoctoral and postdoctoral students and faculty for academic promotions, a Wiki-like writing platform allows documentation of contributions.
4. Provide specific training to managers and investigators in the skills that enable collaborative science, as well as its assessment.
5. Preclinical research, preclinical development of candidate interventions, and phase I clinical studies pose US Food and Drug Administration regulatory challenges that require early support for the investigators.

Assessment of Collaborative Efforts

The effectiveness of collaborative research, either for particular models of interaction or in comparison to other forms of grants making, has to be established by valid techniques of assessment. Evaluation also uncovers deficiencies that can be remedied. Stokols et al¹² stated that “the science of team science encompasses an amalgam of conceptual and methodologic strategies aimed at understanding and enhancing the outcomes of large-scale collaborative research and training programs.”

Assessment of a collaboration can rest on usual modes, such as the number and quality of joint publications or patents and how successful preclinical studies lead to druggable targets, clinical trials, and additional grants from the NIH. Outside experts and the team can grade accomplishments toward planned milestones and their impact. These outcomes, however, do not measure how well a collaborative approach penetrates the actual interactions of participants or how expertise was leveraged. Existing approaches can be applied in novel ways to accomplish this. For example, social network tools that weight interactivity within and across collaborations can serve as sophisticated indicators of the influence that each investigator has on the group.¹³ The AMRF examined the amount and impact of communications among investigators, scientific participation within a collaboration, contributions during workshops and seminars, and data sharing by using social network algorithms. In addition, formal qualitative methods such as case study approaches by an outside assessor, as used in law and business, can reveal the impacts of collaboration. These approaches also chart the agility of adapting to the demands of new information, the consequences of access to tools managed by other experts, and the ability of shared platforms to improve the quality and flow of data.

Conclusions

The recent experience of a handful of foundations suggests that perceived barriers to translational research in neuroscience across universities are surmountable. Collaborative basic and clinical research that is organized around a search for solutions to key disease-

related, progress-limiting questions appears to be a feasible addition to funding isolated investigators in the pursuit of knowledge and therapies. Disease-related foundations, venture-like philanthropy, and undercapitalized biotechnology companies may be especially willing to test models that help fund scientific team work across academic institutions. The NIH could support research on how to best carry out research. By adjusting their traditional ways of soliciting and funding basic and clinical research, by enabling willing experts to work together to identify and achieve essential milestones, and by training leadership and developing infrastructure that best assists the collaborators, everyone who funds biomedical research can begin to test whether they are getting their money's worth.

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One of the APNRR program's collaborations included 10 neuroscientists from 8 universities who had considerable experience related to regeneration of dorsal and ventral root axons. Each had worked with animal and cell culture models using embryonic, early postnatal, juvenile or adult rat, or transgenic mouse dorsal root ganglia, among other experimental models. Injury types included distal and proximal peripheral nerve crush or transection, dorsal and ventral root avulsion, and spinal cord transection or trauma. Each laboratory group had developed a hypothesis about one or more key regenerative genes, transcription factors, and pathways.^{14–19} As a collaboration, they agreed to see where their molecules fit into a schema of axonal regeneration and remyelination by sharing a series of experiments at similar time intervals postinjury. Another lab that had not worked on repair, but had great expertise in neurogenetics, provided standardization of data collection for microarrays, informatics, and sophisticated analyses.²⁰ The informatics group also designed a user-friendly database with the input of the researchers. Other cores provided electron microscopy, magnetic resonance imaging for in vivo imaging, viral vectors, and high-throughput screening of drugs for axonal sprouting. Within 18 months, the group found networks of genes that were expressed in both anticipated and unexpected, but compelling ways within specific time frames. The team added data from other APNRR collaborations—a retinal cell and optic nerve injury model,²¹ regeneration of central nervous system axons,^{22–25} and data about remyelination and neurogenesis.^{26,27} They filled in some time points with microarray data from discrete cell populations that appeared important in several of the models. Simultaneously, they designed upregulation and downregulation gene experiments and obtained transgenic mice from GENSAT that provided further insight into the regulation of axonal growth. Data were also considered within the context of activity-dependent plasticity.^{28–34} The investigators told independent assessors from the RAND Corporation that their rapid progress through diverse approaches, as well as ability to quickly validate results across models, would not have occurred had each worked in isolation.

Figure 1.

Interactive, Iterative Studies in Basic and Clinical Sciences for Neurorehabilitation Interventions

Abbreviations: TBI, traumatic brain injury; SCI, spinal cord injury; MS, multiple sclerosis; ALS, amyotrophic lateral sclerosis.

Table 1

Potential Value of Problem-Oriented, Translational Collaborations

Break down geographical, disciplinary, and intellectual property barriers so that a scientific social network of experts can share research goals and experiments to find solutions.
Resolve important but persisting problems that fall outside the usual capability of one lab for a faster and more robust path to potential therapeutic translation.
Share specialized instruments, techniques, imaging modalities, transgenic mice and other models, reagents, informatics, and access to patients to produce a more comprehensive story in experimental results and publications.
Adapt each other’s diverse models to compensate for less representative models of diseases and therapies.
Present experiments in progress and initial data to peers for early feedback, debate, and discussion of complementary pathways for the group.
Enable rapid availability of positive and negative results, along with validation by reproducing important results in another lab and model.
Foster user-friendly informatics systems to efficiently process, align, and integrate interactome data from experiments and the literature.
Partnerships with clinicians, basic and clinical scientists, and industry enable all to better validate targets and move into trials, with shared attention to potential confounders of preclinical and clinical studies.

Table 2

Questions About Individual Participation in a Collaboration

What do we expect to get out of this?
Who is going to do what and by when?
Who will have access to our data?
Who will give public presentations, and how much data will they reveal?
How will we assign authorship?
How will we decide when to publish?
Who owns the intellectual property?
Will we share our reagents with other labs?
What happens if one of us leaves the project?
What happens if one of us wants to form a separate, but related, collaboration with another lab?

Table 3

General Framework for a Collaborative Model³⁵

Infrastructure Activities	Components of Well-Organized Collaborations				
	Set Expectations	Establish Roles	Create Incentives	Monitor & Evaluate Performance	Build Capacity
Select Programs					
Recruit Participants					
Develop Research Agendas					
Generate Proposals & Milestones					
Evaluate & Fund Proposals					
Support Research Activities					
Disseminate Research Findings					

Table 4

Sample Likert Scale for Review of Component Projects

	Scale: 5	4	3	2	1
	Not at all		Somewhat		Very much so
1	This component project of the collaboration will contribute to the success of the collaboration's scientific goals.				
2	This project will contribute to the milestones necessary to develop a clinically relevant strategy for therapy.				
3	The experimental strategies to achieve the project's aims are appropriate.				
4	The project's methods are feasible within the proposed technology, even if scientifically risky.				
5	The project's experimental outcomes are valid.				
6	The interim milestones of the project are feasible, even if success is uncertain.				
7	The budget for personnel, supplies, and equipment is necessary for the project.				
8	If this is a Platform/Core activity, the service has high value for program collaborators.				
9	If this project is a continuation renewal, the data obtained to date and the progress reported toward milestones that the investigator set for the past year were achieved.				
	(Comments—Please describe strengths and weaknesses and suggest improvements)				