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Risky Business: Meeting the Structural Needs of Transdisciplinary Science

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Academic institutions are facing a fundamental challenge. Their infrastructure, systems of rewards, and indeed, claims to authority, are rooted in the pursuit of deep, highly specialized knowledge. At the same time, however, the needs of society are increasingly demanding solutions to problems that are so complex that they require research initiatives that draw simultaneously on diverse arenas of expertise.[1,2] The potential of this "convergence" or "transdisciplinary" science to address major biomedical challenges has recently been reiterated.[3,4] However, as suggested by a 2014 National Research Council report entitled, *Convergence: Facilitating Transdisciplinary Integration of Life Sciences, Physical Sciences, Engineering, and Beyond*, current academic structures and research funding mechanisms may not easily facilitate such innovative investigative collaborations.[1] There remain concerns that the increasing competitiveness of biomedical funding may be exacerbating conservative funding decisions that are less likely to invest in younger investigators and high risk projects.[4,5] Levitt and Levitt recently documented a substantial bias in National Institutes of Health (NIH) funding in favor of older investigators[6]; the percentage of NIH independent grant recipients younger than 36 years of age has fallen from 18% to 3% over the past 3 decades.[7] The NIH's High Risk/High Reward, Pioneer, and New Innovator Award and related programs designed to encourage higher risk but higher potential impact research support, although generally considered successful,[8] account for less than 5% of all NIH research funding.[9] In addition, the evaluation of several NIH-funded research networks explicitly created to advance transdisciplinary research have underscored the role of traditional academic reward and funding systems as potential barriers to convergent, transdisciplinary collaboration.[10-12]

This commentary reflects our experience within the national network of March of Dimes (MOD) Prematurity Research Centers (PRCs). Preterm birth is the leading cause of mortality of young children globally and is characterized by profound social disparities. Despite years of traditional research, its causes have remained largely unknown.[13,14] It became apparent to the MOD and many of us working in prematurity research that a new research strategy was needed, one that would take greater investigational risk and cross traditional disciplinary boundaries. The MOD initiated a transdisciplinary research program in 2011 at Stanford University that has now become a network of 5 university-based centers, involving more than 200 researchers, clinicians, and policymakers.[15] This commentary cannot claim that this strategy has already proven to be highly beneficial, because the network is still relatively immature. Rather, this discussion is directed at conveying our experience developing the kind of complex, transdisciplinary research initiative that has received growing attention.[4,5] In turn, both the scientific opportunities and organizational obstacles this effort has encountered are described in relation to the structural strengths and weaknesses of different forms of collaborative networks.

MOD	March of Dimes
NIH	National Institutes of Health
PRC	Prematurity Research Center

Facilitating Convergent Science

Although the Center at Stanford has initiated a variety of basic and applied research activities, it has focused its efforts on using emerging, and creating new technical and computational capabilities to understand and prevent premature birth. Of special importance has been the elucidation of the fetomaternal immune interface during pregnancy and the detection of differences in inflammatory and immune signatures between preterm and term pregnancies with disparate sociodemographic characteristics. This effort has included a variety of basic and applied approaches to the examination of large, population-based clinical and social datasets.

These research efforts were developed within an institutional infrastructure specifically created to facilitate and sustain

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cross-disciplinary interaction. Center leadership has had to act as knowledge brokers,[16] "translating" highly specialized language of one discipline into another and supporting the crafting of new, shared, "creole" languages of integrated methods.[17] The center's research activities have also been heavily dependent on investing in innovative computational and statistical strategies that have been purposely tasked to identify previously inaccessible etiologic patterns and to integrate data from across different analytic platforms.

Advocates of convergent or transdisciplinary research stress the need for creativity and responsiveness to unanticipated opportunity. These needs can limit the ability to develop precise timelines and meet long-specified product milestones that are often key requirements in consideration for research funding. Most current research structures tend to prize efficiency and bureaucratic control, either by fidelity to an approved protocol or the dictates of a funder or its advisory proxy. The development of the center's facilitative elements, so essential to its convergent, transdisciplinary intentions, would have generally fallen outside of traditional projects and would not likely have been funded through traditional channels. Moreover, many of the most important scientific opportunities generated by the center were largely unanticipated, emerging not from a highly specific and formally approved methodology, but from productive, convergent interaction among diverse arenas of expertise. For example, a center rapid seed grant allowed innovative cell-free RNA techniques developed for the early identification of organ transplant rejection to be focused on the exploration of a possible transcriptomic "clock" during pregnancy and its potential disruptions leading to preterm birth.[18] Another rapid seed grant supported the repurposing of mass cytometry technology from the investigation of surgical outcomes to the exploration of complex immune signatures associated with preterm birth. In addition, innovative computational techniques are being developed to link these and related data with the dynamics of the microbiome during pregnancy.

Although these research initiatives seem to be highly promising, a willingness to pursue relatively high-risk research paths can also generate failures, or at least results that do not warrant continued investment at the current time. For example, an effort to use sophisticated, machine learning techniques to analyze epidemiologic patterns of preterm birth in the US, although yielding intriguing results, was put on hold because investment in other collaborations was felt to be more promising at the time.[19]

The function of collaborative infrastructures has been the subject of both theoretical and applied examination. Weber's classic discussion of bureaucracy recognized the tension between the need for intense creativity and close fidelity to prescribed, accountable procedures, noting that a growing insistence on highly standardized processes, although perhaps efficient, can "dehumanize" collaborative or hierarchical relationships.[20] This tension has been described as choosing between 2, perhaps oversimplified, visions: the scientist as autonomous craftsperson with the tools and freedom needed to create new knowledge versus the scientist as factory worker with confined, specialized expertise within a larger, managed organization. Cross et al[21] have examined different collaborative structures and suggest that applied networks (ie, those developed to generate a product directed at solving a real-world problem) can be grouped into three broad categories: customized, modular, and routine.

Customized networks are best suited for settings in which both the problems and solutions are ambiguous. The premium here is on flexible, collaborative structures that can identify and respond quickly to new insights and directions for research. Customized networks require academic structures that facilitate the development of research teams that draw on different disciplines but that also remain consistently focused on a common, applied goal. Creativity and innovation are emphasized in customized networks. Early stage drug development or the search for the etiologies of complex disorders with heterogeneous phenotypes are the kinds of research challenges that are likely to require customized, flexible research structures.

Modular networks are deemed best when the components of a problem and solution are known but the combination or sequence of components has yet to be determined. The premium here is on the manipulation of identified technical expertise. Modular networks, therefore, tend to be organized to connect distinct teams efficiently, each with a responsibility to generate a specified product that contributes to the overall goal of the network. Accordingly, modular networks require that the goal and the necessary components be relatively well-identified. An example of this sort of network would be the integration of distinct surgical teams, each with a unique role in addressing a known but complex surgical problem.[21]

Routine networks are deemed best when problems and solutions are well-known and the component activities are highly standardized. The premium here is on predictability and efficiency. Routine networks tend to function on the basis of established protocols that reduce discretionary decision making. An example of a routine network would be linked call centers or the routine processing of a laboratory test, such as newborn genetic screenings, each completing a designated task based on standardized protocols.

The distinction between customized and modular strategies begins to articulate the inherent difficulties of developing convergent, transdisciplinary science within current research infrastructures. In many respects, convergent, transdisciplinary science requires highly flexible, customized networks of interaction. The problem, however, is that many biomedical academic and funding structures are rooted in modular designs. These modular approaches seek consistent conformity to intensely scrutinized and specific aims and methodologies. Even within multisite research networks, proposed projects must run a gauntlet of highly bureaucratized approval procedures. Calls for a greater tolerance of investigative risk and the establishment of intensely, cross-disciplinary research initiatives, therefore, question the underlying incentives shaping current modular approaches and confine highly customized strategies to relatively few, purposefully organized, biomedical research funding and academic infrastructures.[4,5] Nevertheless, as scientific insight accumulates, the creative usefulness of a customized network may give way to the efficiency of a more modular design. Again, the structural requirements of a research initiative should reflect the specific demands of the scientific challenge, a challenge that can be transformed by new knowledge.

Hybrid Networks and the Entrepreneurial University

It is important to recognize that, like most academic research initiatives, the investigative infrastructure of the MOD PRCs are not operating in a technical and bureaucratic vacuum. Private donor and other sponsored funds have been sought to continue to support the most creative and facilitative elements of the centers. This strategy has resulted in a kind of hybrid network linking customized, highly participatory strategies to the more bureaucratic, modular structures used by major biomedical funding agencies, including the growing the MOD national network.[22]

Of special importance is the interaction between university-based research, philanthropy, and the private sector.[23] The recent expansion of these relationships has been labeled the "entrepreneurial university" and has attracted considerable scrutiny.[24] Clearly, the expansion of large philanthropic initiatives and commercial ties between university faculty and private interests raises a number of serious ethical and practical challenges. However, although the commercialization of scientific discovery has been viewed as the primary incentive of academic and private sector relationships, these nontraditional research connections may provide collaborative environments that are far more receptive to creative, transdisciplinary interactions. Academic researchers may find the attraction of the private sector funding defined not only by the "pull" of financial reward, but also the "push" of an increasingly confining academic environment dominated by conservative and highly directive funding infrastructures.

Our experience supports recent calls for a creative reconsideration of current biomedical funding policies and processes. Moreover, each organizational strategy possesses its own strengths and weaknesses, and different approaches will be most appropriate for different investigative objectives. Accordingly, there will always be a need for a pluralistic vision of collaborative research arrangements. However, profound mismatches can be created if the fundamental needs of an applied research enterprise are not directly supported by the bureaucratic infrastructure used to manage the enterprise's operations and evaluate its products.

Clearly, the usefulness of the MOD PRC network, as with other transdisciplinary research initiatives, must await careful evaluation. Although the network is too young for synoptic appraisal at this time, several recent reports support the utility of a convergent, transdisciplinary approach.[25,26] First, it is important to recognize that our transdisciplinary efforts have been developed in direct response to the perceived lack of progress in addressing a major health challenge: reducing elevated and disparate rates of preterm birth. This undertaking does not imply a commitment to, or even general tolerance of, cross-disciplinary interaction for its own sake. Rather, our approach is based on the apparent heterogeneity and complexity of our research mandate, and, like many challenges facing the biomedical community today, may require new kinds of investigative frameworks that better couple intense creativity with collaborative discipline, a linkage that may require revisions in traditional academic and funding infrastructure. Such a responsive infrastructure should, in turn, be seen as inherently dynamic, because it must always meet the needs of an evolving science.

Second, if transdisciplinary, convergent research initiatives are to enhance the development of young, innovative investigators, new funding and academic structures are likely to be required.[16] Given the growing competitiveness in biomedical funding, support for young researchers pushing the limits of their respective disciplines early in their career implies some enhanced potential of risk as well as opportunity. Although not confined to transdisciplinary research endeavors, the sustained advancement of promising investigators outside of traditional laboratories or departments working in transdisciplinary collaboratives may be in particular need of purposeful funding and career facilitation. Potentially, the innovative funding infrastructures of transdisciplinary initiatives could provide a particularly flexible and responsive funding and mentoring environment for investigators early in their careers.

Third, universities engaged in efforts that address complex human problems may need to create long-term funding streams that include strategic partnerships with the private sector and large-scale, and sustained philanthropy that are especially willing to support or at least tolerate highly flexible funding allocations.[23] Our experience has underscored the potential need for funding streams that include discretionary capabilities that can quickly address unplanned opportunities and sustain the integrative infrastructure that transdisciplinary initiatives will require. Conservative pressures on research funding mechanisms and a reliance on highly structured, modular strategies may not attend to the deeper utilities of transdisciplinary, convergent approaches. Although the experiences described in this commentary are intended to inform the early development of other transdisciplinary efforts, more formal analysis of the relationship between funding streams, research infrastructures, and scientific progress is required and should be rigorously pursued as transdisciplinary research initiatives such as the MOD PRC network mature.

We recognize that our experience may not be generalizable and that other institutions are struggling with similar challenges. However, our experience does suggest that meeting the demands of transdisciplinary, convergent science may require confronting thoughtfully but boldly potential misalignments between the machinery of mainstream biomedical science and the investigative capacity necessary to address many of the most important health problems of our time. ■

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