JCI The Journal of Clinical Investigation

It takes a village: lessons from collaborative science

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J Clin Invest. 2021;131(2):e145962. https://doi.org/10.1172/JCI145962.

Viewpoint

My story Like many physician-scientists, I started my research career in earnest during my fellowship training, which for me was an endocrinology fellowship in the 1990s. These were relatively early days in the era of using mouse genetics to elucidate in vivo biology and to model disease. The expectation was to obtain a K08 clinical investigator award and then leverage that work into an R01 grant. The traditional approach at that time was to focus on a scientific question that could be used to define your reputation in the field. In my case, my research centered on glucose transport (1, 2) and insulin signaling in the heart (3), largely based on insights gained from my prior work generating cardiomyocyte-restricted deletions of these metabolic regulators. I made the case that these murine models could inform the pathophysiology of diabetic cardiomyopathy, which at the time was beginning to be recognized as a distinct cardiovascular complication of diabetes. When I moved to the University of Utah in 2000 as an assistant professor, I presented a vision of developing a research program based on elucidating the contribution of changes in insulin signaling and glucose metabolism to diabetes-related heart failure and obtained individual grant funding from the NIH, the American Diabetes Association, and the American Heart Association to continue these studies as the sole principal […]

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My story

Like many physician-scientists, I started my research career in earnest during my fellowship training, which for me was an endocrinology fellowship in the 1990s. These were relatively early days in the era of using mouse genetics to elucidate in vivo biology and to model disease. The expectation was to obtain a K08 clinical investigator award and then leverage that work into an R01 grant. The traditional approach at that time was to focus on a scientific question that could be used to define your reputation in the field. In my case, my research centered on glucose transport (1, 2) and insulin signaling in the heart (3), largely based on insights gained from my prior work generating cardiomyocyte-restricted deletions of these metabolic regulators. I made the case that these murine models could inform the pathophysiology of diabetic cardiomyopathy, which at the time was beginning to be recognized as a distinct cardiovascular complication of diabetes. When I moved to the University of Utah in 2000 as an assistant professor, I presented a vision of developing a research program based on elucidating the contribution of changes in insulin signaling and glucose metabolism to diabetes-related heart failure and obtained individual grant funding from the NIH, the American Diabetes Association, and the American Heart Association to continue these studies as the sole principal investigator.

From silos to consortia

Shortly after arriving at the University of Utah, I had my first encounter with a collaborative funding mechanism. My friend Henry Ginsburg at Columbia University once told me, "There never was an RFA [request for applications] that he would not take out on a date!" My first RFA "date" presented itself in October of 2000. My division chief and academic mentor, Don McClain, had an uncanny knack (that continues to this date) for identifying collaborative funding mechanisms to build and support resources. He shared with me an RFA for a consortium to study mouse models of diabetic complications. The goal of this RFA was to use the U01 cooperative research grant mechanism to bring together up to six centers to assemble a crossdisciplinary Mouse Models of Diabetic Complications (MMDC) Consortium to develop innovative mouse models that closely mimic the diverse human complications of diabetes. We thought it was a long shot, but went for it. I would not be writing this if we had not become members of this initial consortium that brought together groups from the University of Utah, the University of Michigan, Vanderbilt University, Mount Sinai, Rockefeller University, Columbia University, Duke University, and UCLA.

The U01 program required collaborative interactions among the centers to advance the missions of the consortium. I initially chafed at the idea of science by committee, but quickly came to understand the value of openly sharing data and obtaining consensus that was based on our best understanding of the strengths and weaknesses of each model. Moreover, these interactions led to the formation of meaningful collaborations, many of which continue to this day. After the first five years of the MMDC, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) renewed the RFA to broaden the scope into animal models of diabetes complications. We competed again and remained in the Consortium, which had expanded to include additional institutions such as the University of North Carolina, the University of California, San Diego, Case Western, the University of Washington, and others. At the end of this second five-year cycle, this consortium was restructured as the Diabetes Complications Consortium, which now focuses on supporting novel research into modeling diabetes complications via a pilot grant program. The impact of this collaborative network has been immense, with more than 1000 publications, sharing and dissemination of animal models and standardized protocols, and sponsorship of scientific meetings. Collectively, these efforts significantly advanced our understanding of diabetic complications to a much greater extent than could have been achieved on the basis of individual groups working in silos.

I was hooked! As a result of insights gained in our laboratory linking mitochondrial dysfunction with diabetic cardiomyopathy and knowledge gleaned from the MMDC about the intersection of obesity and diabetes in the pathophysiology of heart failure in diabetes, another RFA came to my attention in 2002 on the pathophysiologic mechanisms of obesity-associated cardiovascular disease. Although this was not a U01 grant, the program leadership at the National Heart, Lung, and Blood Institute (NHLBI) fostered and encouraged interactions between other grant awardees that, like my experience with the AMDCC, continued to lead to productive collaborations that truly advanced our understanding of diabetes and obesity-related heart failure. Since that time, I have taken multiple other RFAs on "dates" and have participated in five collaborative research initiatives sponsored by the NIH (including grants focused on thrombotic and hemostatic disorders; sex hormone–induced thromboembolism; and collaborative interdisciplinary team science in diabetes, endocrinology, and metabolic diseases) and strategically focused research networks sponsored by the American Heart Association. I have subsequently been funded in three multi-PI R01s. It should be clear by this track record that my personal research journey has benefitted immensely by participation in collaborative research

Conflict of interest: The author has declared that no conflict of interest exists.
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Reference information: *J Clin Invest*. 2021;131(2):e145962. https://doi.org/10.1172/JCI145962.

networks, and a small sampling of publications arising from these experiences are referenced below (4–10).

Collaborative science fuels research progress

What have I learned from my work in consortium-based research projects? These networks have been powerful platforms for expanding the professional networks of their participants in ways that by far exceed what would normally occur via the customary channels, such as scientific meetings. Many of these collaborative networks have had robust training and mentoring components, and as such, they have provided trainees invaluable opportunities for professional and scientific development. These networks have fostered new collaborations outside of the parameters of the original consortium, thereby amplifying the impact of the science. They have generated valuable resources and reagents that are easily shared with limited restrictions. They have harmonized methodologies, standardized assays and protocols, and promoted best practices, all of which have increased scientific rigor and reproducibility. Collaborative networks have catalyzed the development of shared resources and expanded the reach of sophisticated platforms, such as mass spectrometry and single-cell genomics analysis, to groups that lacked either the resources or expertise to establish these tools independently.

Interdisciplinary networks bring together groups with seemingly disparate interests to advance a field of inquiry. A notable example for me personally is my collaboration with Andrew Weyrich at the University of Utah across two consortia involving the intersection of metabolism and platelet biology. When we started the journey, Andy shared with me an RFA seeking to understand the increased risk of thrombosis in diabetes. His lab had preliminary data indicating changes in the metabolome of platelets in diabetes, and we had generated (for other purposes) mice harboring floxed alleles that could affect platelet metabolism. The rest is history (11–14)! Thus, the ability to share expertise across diverse fields represented a powerful tool for advancing knowledge and refining our collective understanding of complex systems and pathways.

As chair of a research-intensive department of medicine and director of an interdepartmental research center, some of the greatest successes, both in terms of scientific productivity and opportunities to train the next generation of scientists, have been anchored in collaborative research networks. Three notable examples (among many) in my department have been the impact of longstanding program project grants in cardiovascular pathobiology initiated by Francois Abboud; our interdisciplinary program in lung biology spearheaded by Michael Welsh; and the Center for Access and Delivery Research and Evaluation (CADRE), a Health Services Research program funded by the Department of Veterans Affairs, led by Eli Perencevich. A common characteristic of these networks has been their ability to spawn entire generations of successful investigators in their respective fields.

Perspectives

The integrity of science is based on rigorous peer review of our work and ideas. An important consequence of participation in collaborative scientific networks has been the opportunity to have colleagues within the network actively participate in the evolution of a project. Their input during project updates has refined projects, consequentially increasing the rigor of findings once they are reported. My experiences in multiple collaborative scientific networks have shaped a perspective that it is far more important to collaborate to get our science right than to get our findings published first. Let me share with you one recent experience that speaks to that ethos. Through our participation in the Strategically Focused Research Network on heart failure, we generated mice with loss of pyruvate transporters in the heart and observed an interesting effect on ventricular remodeling. I came to learn through a mutual collaborator that another laboratory had obtained similar findings, so we got in touch and agreed to openly share and discuss our findings with a view toward coordinating the submissions of our initial research findings. A few months later at an international meeting after giving a talk where I discussed some of our findings, a postdoctoral fellow from a laboratory in the UK approached me and asked me to visit her poster, where she shared with me similar studies that they were undertaking. Having learned this, to me the issue was clear. The twosome had to become a threesome. We therefore openly shared our findings and collaborated on joint submissions, which culminated in a recently published trifecta (10, 15, 16). I believe that our decision to collaborate and to publish independent findings that support a common hypothesis is a powerful representation of the impact of collaborative research in promoting rigor and reproducibility. There will now be little doubt regarding the mechanisms linking mitochondrial pyruvate import with cardiac remodeling. Long live collaborative networks!

Acknowledgments

Work in my laboratory over the years has been supported by the following collaborative awards: U01 HL70525, RO1 HL73167, U01 HL087947, R24 DK092784, U54 HL112311, and R61HL141783 (NIH); and 16SFRN31810000, and 20SFRN35120123 (American Heart Association).

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