

Building Research Capacity in Vascular Biology in Rhode Island

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ABSTRACT

The CardioPulmonary Vascular Biology Center for Biomedical Research Excellence (CPVB COBRE) was funded in 2013 by the National Institute for General Medical Sciences to establish a collaborative center for research excellence in vascular biology in Rhode Island. The CPVB COBRE has funded successful junior faculty investigators and pilot projects spanning the research spectrum from basic vascular development mechanisms using zebrafish to clinical research on pulmonary hypertension to the effects of mindfulness on hypertension in pregnancy. The Administrative Core has united the group with an active seminar program with visiting experts, a focus on career development, and the use of evaluation to support continuous improvement. The Cell Isolation and Organ Function Core has provided high-quality research services and expertise. Most importantly, hard-working and creative physicians and basic scientist investigators and mentors have worked together to expand the spectrum of vascular biology research in Rhode Island.

KEYWORDS: vascular biology, pulmonary, cardiology, interdisciplinary

INTRODUCTION

Cardiovascular and pulmonary diseases are among the leading causes of morbidity and mortality in the US and the world.¹ Coronary artery disease (CAD) is the leading cause of morbidity and mortality globally, with greater than 8 million deaths in 2019. Chronic obstructive pulmonary disease and lower respiratory diseases are the 3rd and 4th leading causes of death worldwide, respectively, with greater than 5 million deaths in 2019, and are frequently complicated by pulmonary vasculopathy and cardiovascular co-morbidities that markedly worsen prognosis. In 2020, COVID-19, caused by the SARS-CoV-2 virus, has become the 3rd leading cause of death for persons aged 45 through 84 years and the 2nd leading cause of death for those aged 85 years or older, as compared to other leading deaths in 2018.² Most patients with COVID-19 die from respiratory failure or vascular complications, including stroke, myocardial infarction, or thromboembolism, and COVID-19 is recognized as a disease

directly impacting the endothelium.³ In addition, deaths due to cardiopulmonary vascular diseases manifest health inequity and are increased in lower socio-economic populations and settings.^{1,4} Thus, cardiopulmonary vascular diseases are important causes of human suffering, for which more effective treatments and prevention are needed.

VISION AND PROGRAMS OF THE CPVB COBRE

In 2013, the CardioPulmonary Vascular Biology (CPVB) Center of Biomedical Research Excellence (COBRE) was established through funding from the National Institutes of Health, National Institute of General Medicine and Sciences (NIH, NIGMS) and is currently in Phase 2 of funding. This center's visions are to unite clinical and basic scientific investigators from multiple disciplines and foster research career development of those who have not yet established an independent research program (**Figure 1**). The goals are to enhance understanding of vascular cell injury mechanisms and develop and strengthen an interdisciplinary collaborative research center with strong technical support and career development activities across Rhode Island institutions. The CPVB COBRE has brought together investigators from the Vascular Research Laboratory at Providence VA Medical Center (PVAMC), the Surgical Research Laboratory, Cardiovascular Research Center, Cardiothoracic Surgery Research Laboratory, and the Division of Pulmonary/Critical Care/Sleep Medicine at Rhode Island Hospital (RIH), as well as

Figure 1. Schematic representation of strategies used by the CardioPulmonary Vascular Biology COBRE in accomplishing the vision of the center.

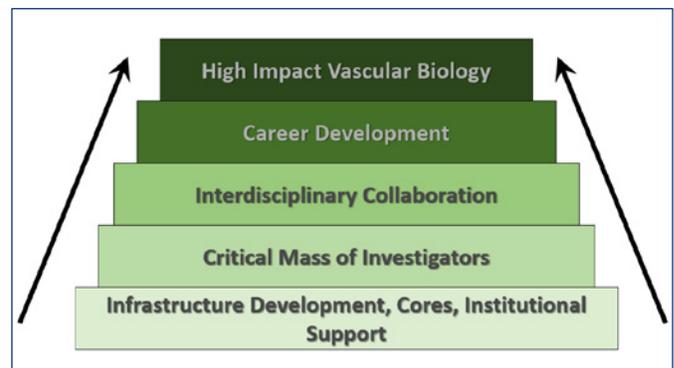
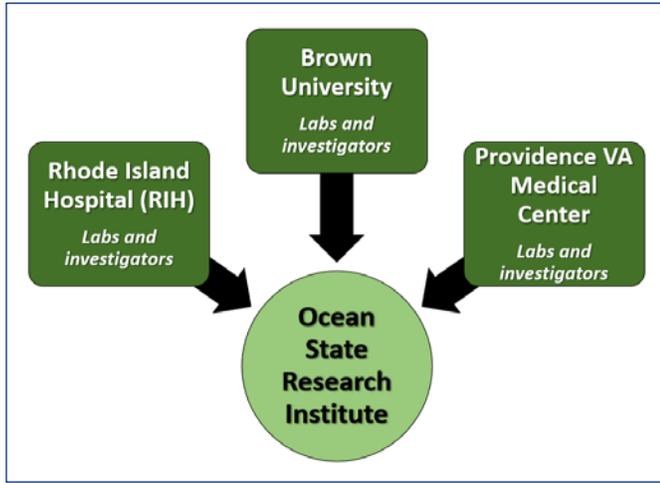


Figure 2. Institutional structure of the CardioPulmonary Vascular Biology COBRE.



from Brown University departments within the Division of Biology & Medicine (Figure 2). Investigators are supported as either Project PIs for 2–5 years or as Pilot Project PIs for 1–2 years, with funding prioritized by scientific review in the manner of NIH study sections. A key feature of the CPVB COBRE program is fostering interactions among clinicians and biologists, in the strong belief that interdisciplinary research is most likely to successfully translate discoveries to patient care.

Each CPVB COBRE junior faculty investigator is supported by a mentoring team of experienced senior researchers who provide scientific expertise and guidance, career advice, leadership skills, professional development, organizational advancement, networking opportunities, and examples of work-life balance. In addition, institutional and administrative support from the PVAMC, Ocean State Research Institute (OSRI), RIH, and Brown University has provided an infrastructure for CPVB COBRE investigators, enabling them to focus their efforts on establishing a productive research program.

The CPVB COBRE has two core facilities that are available to all investigators and mentors. These include an Administrative Core and a Cell Isolation/ Organ Function (Cell/Organ) Core (Table 1). The Administrative Core facilitates the research activities and career development of junior investigators by providing fiscal assistance, organizing career development opportunities, managing mentorship committee meetings, organizing meetings with our external and internal advisory committees and other activities, as described in Table 1. The Cell Isolation and Organ Function Core is a scientific core that focuses on cultured cells and whole organ structure and function to investigate vascular injury and repair. The Cell/Organ Core provides a unique skill set and expertise to Rhode Island vascular biologists by providing high-quality cell isolation, characterization, and propagation of vascular-derived cells; tissue morphometry

and image analysis; and heart and lung function. The Cell/Organ Core services are described in Table 1. A new scientific core to assess Respiratory Function is in the planning stages.

A vigorous program of research seminars provided by visiting speakers and local experts is a critical aspect of the CPVB COBRE program. The CPVB COBRE sponsors twice-monthly seminars. Each project and pilot project investigator presents results of “work-in-progress” and research and professional achievements at least twice per year. In addition, the CPVB COBRE seminar series is complemented by the monthly Brown Investigators in Respiratory Diseases (BIRDS) lecture series and (in 2020) the “Decoding COVID” and “Decoding Disparities” seminar series, sponsored by the Division of Biology and Medicine. These seminars feature both local experts and visiting speakers. Junior faculty investigators serve as the primary host for guest lecturers, providing them with an opportunity to become acquainted with the distinguished visiting researcher, thereby increasing their professional network. Indeed, these visits have led to scientific collaborations for some junior investigators. To

Table 1. Services provided by CPVB COBRE Cores

Core	Service
Administrative	Junior Investigator fiscal assistance
	Organize and manage career development opportunities
	Managing mentorship committee meetings
	Manage meetings with our internal and external advisory and executive committees
	Maintains the cpvb.org website
	Provides financial management of entire program
	Tracks investigator outcomes
	Manages evaluations of the mentor-mentee teams
	Assesses scientific core efficiency and program effectiveness
	Manages seminar series and guest lecturers
Manages intramural and extramural progress reports	
Cell Isolation & Organ Function	Provides high quality cell isolation, characterization, propagation and functional assessment of vascular-derived cells; including endothelial cells from heart, lung, and other organs, cardiomyocytes, fibroblasts, and epithelial cells
	Provides tissue morphometry and image analysis
	Assessment of heart, lung, vessel structure and function and angiogenesis
	Transient gene manipulation in vivo
	Acquire, establish, and disseminate technologies and instrumentation to provide state of the art research tools for vascular biology research in Rhode Island
Establish processes and procedures that support the sustainability of the Cell/Organ Core	

leverage resources, the CPVB COBRE has co-sponsored lectures with other research seminar series at Brown, including the Pathobiology; Molecular Pharmacology and Physiology; and Grand Rounds in Cardiology, Pulmonary, and Internal Medicine. With funding partners, the CPVB COBRE and BIRDS seminar series have sponsored 70 visiting speakers from 29 universities since 2013.

In 2020, the CPVB COBRE Principal Investigators (PIs) partnered with the University of Mississippi Medical Center Cardiorenal and Metabolic Disease Research Center COBRE and the University of Louisville COBRE in Diabetes and Obesity Research PIs to establish a monthly multi-COBRE seminar series. This seminar series features research talks by COBRE investigators and brings together investigators from related disciplines to build a network of collaborations among the COBRE programs.

Finally, the CPVB COBRE has contributed significantly, both administratively and financially, to the Rhode Island IDEa annual symposium since 2015. At these day-long symposia, the junior investigator from each of the Rhode Island INBRE or COBRE programs present their work in short talk or poster format. Thus, the CPVB COBRE has regularly scheduled opportunities to highlight the junior investigator's work both within and outside of Rhode Island, fostering professional growth and career development.

A key element to the CPVB COBRE program and junior investigator successes has been the engagement of the advisory committees, including the executive committee (EC), an internal advisory committee (IAC), and an external advisory committee (EAC). Both the IAC and EAC meet twice annually, while the EC meets every other month. For each meeting, the PIs provide updates, including successes and challenges to the program. While the EC meetings discuss financial expenditures, junior investigator issues, and current and immediate future goals, the IAC and EAC meetings discuss the program's overarching vision. In addition to meeting with the CPVB COBRE PIs, the EAC meets with each junior investigator and mentoring team to discuss achievements, hurdles, and next steps. In these private meetings, the EAC members provide frank feedback to the junior investigators, to help them achieve research independence. The dedication, consistent participation, and wise advice provided by each of the committees have been crucial in the program's ongoing success and junior investigators.

OUTCOMES OF CPVB COBRE

Since 2013 the CPVB COBRE has supported 10 junior faculty investigators from 5 academic departments and 18 pilot project investigators with 24 distinct pilot projects. In addition, the COBRE has supported two administrative personnel and 65 research assistants. Thus, the COBRE has substantially impacted vascular biology research in Rhode Island.

The Administrative Core of the CPVB COBRE supports

on-going quantitative and qualitative program evaluation. More than half (6/10) junior faculty project investigators have achieved RO1 funding, and 5/18 pilot project Investigators have achieved RO1 funding since 2014. CPVB COBRE Junior faculty investigators have also been awarded substantial research support from foundations, such as the Falk Foundation and the Harold S. Geneen Foundation, and other federal sources, such as the Departments of Defense and Veterans Affairs. CPVB COBRE investigators have contributed to the knowledge of vascular biology by publishing 83 publications with CPVB COBRE support. In keeping with our goal of enhancing scientific collaboration, 12 investigators supported by the CPVB COBRE have published manuscripts documenting collaborations with other CPVB investigators and/or mentors.

The CPVB COBRE strongly espouses continuing quality improvement and has therefore used survey methodology to assess program effectiveness. In collaboration with Judy Kimberly, Evaluation Director of the Brown University Division of Biology and Medicine, survey instruments were developed for junior faculty investigators and mentors. The semi-annual surveys address investigator self-efficacy, research mentor interactions, and effectiveness of core support activities. Although generally the program has been considered effective, there continue to be areas for improvement. The content and results of these surveys have been published in the *Journal of Clinical and Translational Science*.⁵

CONCLUSIONS

The CardioPulmonary Vascular Biology COBRE was established in 2013 to develop interdisciplinary research in lung, heart, and vascular diseases in Rhode Island. Critical elements of success include institutional support, interdisciplinary collaborations, a focus on career development and networking, a vigorous program of visiting researchers, and on-going program evaluation. The most important element of success has been the expertise of outstanding, hard-working, and collaborative junior faculty researchers and mentors with whom the CPVB COBRE has been privileged to work.

After 7.5 years of funding, there has been substantial progress toward the ultimate goal of improving outcomes of vascular diseases in Rhode Island. Continued challenges include maintaining a "pipeline" of junior faculty engaged in vascular biology research, sustaining research in difficult pandemic times, and growing sustainability of scientific cores.

Acknowledgments

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