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Establishment of a Private Foundation-Academic Partnership to Promote Careers of Early-Stage Investigators Examining the Influence of Sex and Gender on Health and Health Care

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Abstract

Biological sex and gender-based constructs contribute significantly to the diversity of disease outcomes and treatment responses across the life course. To promote research considering sex and gender, the National Institutes of Health (NIH) Office of Research on Women's Health (ORWH) launched the Specialized Centers of Research Excellence (SCORE) on sex differences program. The Career Enhancement Core (CEC) of the Johns Hopkins SCORE on Sex and Age Differences in Immunity to Influenza (SADII) partnered with the Foundation for Gender-Specific Medicine, which matched NIH funding to support seed grants. Over 3 years we awarded 12 (10 were women faculty) seed grants to early-stage investigators. One year after the award, the seed grant awardees highlighted their progress, including publications, grant applications, and abstracts. All awardees noted challenges with their progress related to the COVID-19 pandemic and supply chain delays and shared suggestions for improving the programming of the CEC. They also highlighted the multiple ways the awards had helped them gain pilot data toward larger grants, build collaborative relationships, and present at the annual SCORE symposium. We describe a model and evidence supporting a private–academic collaboration to support the careers of early-stage investigators conducting research related to sex and gender.

Keywords: private-academic partnership, early-stage investigators, sex as a biological variable, pilot grants

Introduction

E VIDENCE SHOWS THAT both biological sex and gender matter when it comes to a wide variety of biological and clinical outcomes, including intervention or drug effects, health behaviors, and health care utilization.^{1–3} Many preclinical studies, however, either use only one sex or do not report on the biological sex of the animals or primary cells,⁴ and clinical studies often fail to disaggregate results by sex.⁵ In 2016, the National Institutes of Health (NIH) implemented a policy that requires NIH grant proposals to include plans for including male and female cells and animals in preclinical investigations.⁶ Guidelines also exist for journal publishers to ensure that sex and gender are appropriately reported in peer-reviewed literature.³

To further promote consideration of sex and gender in biomedical research and foster career development for women in science and medicine, $^{1,2,7-9}$ in 2018 the NIH Office of

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PROMOTING CAREERS IN SEX AND GENDER RESEARCH

Research on Women's Health (ORWH) launched the Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 [RFA-OD-19-013U54]).¹ The Career Enhancement Core (CEC) was a required feature of the SCORE program that aimed to support pilot research and train the next generation of scientists in the study of sex differences. The CEC was required to support pilot studies for a minimum of 12 months (maximum of 3 years) consistent with the research scope of the SCORE program.

The Johns Hopkins SCORE on Sex and Age Differences in Immunity to Influenza (SADII, pronounced sādē) was one of six funded SCOREs in 2018, followed by five more Centers in 2019. A major strength of the SADII CEC is its close partnership and matched funding from the Foundation for Gender-Specific Medicine (hereafter referred to as the "Foundation"). The Foundation, led by academic cardiologist, researcher and author,^{10,11} Dr. Marianne Legato, was launched over 25 years ago, with private donations and academic partners. The mission of the Foundation is to educate health professionals and researchers, and ultimately integrate sex and gender-specific medicine into the routine practice of science and medicine.¹² Dr. Legato was a faculty mentee of the Chairman of the Department of Medicine at Johns Hopkins. He introduced her to the leaders of The Johns Hopkins Center for Women's Health, Sex, and Gender Research (W.L.B. and S.L.K.) to identify collaborative opportunities.

In this article, we describe the private foundationacademic partnership that has supported our pilot grant program and report on the results of the evaluation of the CEC program participants. We also highlight strategies for furthering the promotion research and research careers on the influence of sex and gender on health and health care.

Methods

Origin of the foundation-academic partnership

The Johns Hopkins Center for Women's Health, Sex, and Gender Research began in 2008 as an interdisciplinary program, including faculty and trainees in three biomedical schools at Johns Hopkins University: School of Medicine, Bloomberg School of Public Health, and the School of Nursing. Its mission is to increase opportunities for mentorship and capacity for high-impact research in women's health, sex and gender at Johns Hopkins. In the 4 years before receiving SCORE and CEC funding, the Center was growing its collaborations. We fostered a close collaboration with the Foundation around the common goal of promoting innovative research and supporting junior faculty's careers in sex and gender research. Altogether, we launched a collaborative Request for Applications (RFA) process to offer seed grants (\$25,000 each) and awarded a total of four before the SCORE funding. With the launch of the SADII CEC Seed Grant Program, we were able to expand this existing collaboration and leverage the infrastructure of our grant selection process.

Overview of the Johns Hopkins SADII SCORE

The SADII SCORE focuses on improving our understanding of the role of biological sex and aging on the immune responses to influenza vaccination (Fig. 1). Components include three Cores: Leadership Administration, Sex and Gender Analysis, Immunology Response and the CEC. SADII SCORE also supports three research projects. Figure 1 shows the SADII SCORE's organizational structure and close collaboration across Johns Hopkins and with the Foundation for Gender-Specific Medicine, studying sex differences at Johns Hopkins and beyond.

Design of the seed grant program for research on sex and gender differences

The goals of the SADII CEC Seed Grant Program for Research on Sex and Gender Differences are (1) To promote research examining sex and gender differences and the intersection between sex and gender; (2) To facilitate the research careers of junior faculty across Johns Hopkins University and enable them to use pilot data to generate grant applications; and (3) To foster interdisciplinary research collaborations.

We designed an RFA specific to the SADII CEC Seed Grant Program, as the NIH grant mechanism specified that the area of research was required to align with the theme of our SCORE grant. In our case, the applications were required to broadly involve the "immune system or inflammatory conditions and could include, but are not limited to aging, allergy, asthma, cancer, inflammatory diseases of diverse tissues and health conditions, autoimmunity, intersectionality, infectious diseases, pregnancy, and vaccinology." We sought proposals across the translational spectrum: basic biomedical, clinical, epidemiological, health services, qualitative, or social sciences research.

In an effort to diversify and incorporate junior investigators studying women's health and gender-related research, we expanded the RFA beyond biological sex differences, to promote more diverse research, including gender analyses. To be eligible, the principal investigator must be an instructor or assistant professor (no more than 6 years post-training) from any Johns Hopkins School. Collaborations involving faculty from at least two schools were preferred. We decided to restrict project timelines to 12 months to maximize the number of investigators and projects we could support.

In addition to the seed grant program, the CEC programming included an annual jointly sponsored SCORE-Center for Women's Health, Sex, and Gender Research symposium, hosting visiting professors and methods workshop for incorporating sex as a biological variable (SABV) and gender considerations when planning, analyzing, and reporting data, and research dissemination activities. One of our collaborative symposia focused on COVID-19 through a gender lens and resulted in a published commentary.¹³

Review and selection process

We invited SCORE faculty and other reviewers from our Institution who had content and methodologic expertise and then assigned three reviewers per proposal. Reviewers completed their reviews electronically and rated applications based on the same criteria as an NIH independent research award. The group of reviewers met to discuss and then chose the awardees, who were announced at the annual Center for Women's Health, Sex, and Gender Research symposium FIG. 1. Organization of and collaborations with the SADII SCORE at Johns Hopkins. SADII, Sex and Age Differences in Immunity to Influenza; SCORE, Specialized Centers of Research Excellence,



each May. Awardees committed to completing their projects and spending the funds in 1 year, completing an evaluation at 1 year and presenting at the annual symposium.

Evaluation of the pilot grant program

To inform the design of a comprehensive evaluation of the pilot grant awardees' progress, we reviewed published tools related to both evaluation of career advancement (*e.g.*, awardees' research grants, publications, and promotion trajectory),¹⁴ as well as research integrating sex and gender (*e.g.*, study design and dissemination methods that consider sex and gender).¹⁵

The evaluation tool that we designed addressed six domains: Section I: Appraisal of SABV/Gender within your research project; Section II: Aims/Outcome of Project to date; Section III: Dissemination (including publications and grant submissions); Section IV: Next Steps in your research; Section V: Career Advancement (promotion and leadership positions); Section VI: How the CEC has helped your work and career. The evaluation instrument is included in Supplementary Data S1.

Analyses

We performed descriptive analyses of the evaluations and provided a qualitative synthesis of comments.

Results

We awarded three \$50,000 seed grants in 2019, four in 2020 because the Foundation donated additional funds for research on COVID-19, three in 2021, and two grants in 2022. Over 3 years, we received a total of 51 applications and 12 junior faculty received awards (5 from the School of Public Health and 7 from the School of Medicine). Of the 12 awardees, 10 identified as women faculty. Table 1 provides the titles of their awards and category of research.

Table 2 summarizes the progress and comments of the 12 awardees at the end of their funding period, that is, 12 months after receipt of the Seed Grant. Awardees highlighted publications in progress and accepted, in-progress grant applications, poster, and oral presentations during the award year. All 12 of the awardees noted challenges with their progress related to the COVID19 pandemic and supply chain delays. They also highlighted the multiple ways the awards had helped them gain pilot data toward larger grants, build collaborative relationships, and that it was helpful to present at the annual symposium. For future help they noted that the CEC could be more proactive with periodic outreach to support their progress and identify barriers to their work, arrange informal "coffee meetings" with experts and peers, and develop a writing accountability group to support their article and grant writing efforts.

Table 1.	TITLES OF	12 Seed	GRANTS,	2019-2022
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	Research category	Proposal title
1	Clinical	Sexual Dimorphism in the Effects of Multiple Sclerosis Genetic Risk Variants on Immune Cell Function
2	Translational	Sex Differences in Response to Immunotherapy and Emergence of Immune-related Adverse Events
3	Clinical	Role of microRNAs in female hearts
4	Clinical	Endogenous Sex Hormones and Respiratory Health in Women with Cystic Fibrosis
5	Clinical	Sex-specific effects of genetic variation in the manganese and zinc transporter ZIP8 and intestinal inflammation
6	Basic	Sex differences and the cytokine storm associated with COVID-19 mortality
7	Population	COVID-19 Impact on Pregnant Women in Ethiopia: Understanding Unmet Needs for a Vulnerable Subpopulation
8	Clinical	Sex Differences in Myocardial Sequelae of COVID-19
9	Basic	Sex differences in the immune response to <i>Trypanosoma brucei</i> infection
10	Population	Examining the relationship between reproductive factors, metabolic syndrome, inflammation, and biological age acceleration in a population-based cohort
11	Basic	Investigating the role of MIP-3 α fused to antigen in sex differences of vaccine-generated immunity in dendritic cells
12	Translational	The Sex Steroid Metabolome and its Effects on Sexual Dimorphism in Pulmonary Arterial Hypertension

Discussion

Using the SCORE mechanism, our CEC has demonstrated a sustained and effective partnership between a private foundation and an academic institution to promote early careers for faculty conducting sex and gender research in biomedical science, public health, and translational science. Over 3 years we awarded and administered 12 grants (8 supported by the foundation funding) and found that awardees were extremely productive with generating pilot data, writing articles, and grant writing, despite challenges due to the co-occurring COVID-19 pandemic.

Importantly, the 3 years of our CEC and pilot awards (2019-2022) encompassed the COVID-19 pandemic and its effects, including limitations to travel, supply chain disruption, and changes in and delays with human subjects' research. Increasing evidence shows that the pandemic will have a lasting impact on the advancement of careers of faculty, and disproportionately impacted women and faculty underrepresented in science and medicine, due to changing work culture, heightened clinical demands, and home care-giving stressors.^{16–18} Our CEC is considering how to "rebuild" the culture of collaboration, support, mentorship, peer networking, and sponsorship to create new opportunities for faculty to catch up from the opportunities lost during the pandemic.^{19,20} There is a greater need to train senior mentors and principal investigators to effectively promote gender, racial, and other forms of diversity in science and medicine through the integration of SABV and gender into their scientific exploration and those of their mentees as well to gain mentoring skills specific to supporting and growing a diverse workforce.^{21–23}

Although many private foundations, such as the American Heart Association and the Alzheimer's Association, provide grants to investigators at academic institutions, to our knowledge, this is the first published report of a partnership that established a pilot grant program on a specific, mutually high-interest research area. In addition, the NIH has been committed to supporting foundations and professional societies' support of researchers, as demonstrated in the R25 mechanism from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). We demonstrated the additive impact of an academic–private foundation partnership where the additional funding significantly augmented the breadth and impact of training and pilot awards at our Institution.

We identified several growth opportunities to address in the future iterations of our CEC programming. First, we did not initially conceptualize the seed grant program as a mentored award, and most awardees reported having primary mentors. However, awardees also noted that their proposals were deemed "high risk" by mentors and collaborators who were less familiar with sex and gender analysis methods and may have been concerned about fundability and sustainability of future work. These concerns continue to be a barrier to advance sex and gender methods and analyses, and our program is designing more supports based on feedback, including regular outreach for troubleshooting, aims and grant review, and a SCORE writing accountability group to provide peer support. Second, most of our funded projects focused on either sex or gender considerations and lacked exploration into their intersection, as well as intersections with race, age, social vulnerability, and reproductive status.^{24,25} Given the importance and complexity of designing and conducting studies that consider intersectionality at multiple levels, including heterogeneity of effect, we are designing a series of workshops to build skills and open discussions about best practices.

We acknowledge limitations of our findings. First, our findings are limited to one Institution's experience with an academic–foundation partnership to support a seed grant program and may not be generalizable outside of this local content. It was our goal to describe our model that could be useful for other programs who can adapt it to their own partnerships, goals, and content areas. Second, despite the additional support for pilot grants, our program was small (12 awards over 3 years) limiting our ability to compare the awardee demographics and career trajectories with other

Awardee	Accomplishments	How CEC helped/can help				
Year 1—Seed grant rec Asst Prof 4 years at current rank	ipients (2019–2020) 3 new grants (funded) 5 publications (1 first author)	"Interactions with senior scientists; Feedback on research findings; Opportunity for junior researchers from different disciplines to communicate and form collaborations."				
Asst Prof 2 years at current rank	 new grant (in process) publication new interdisciplinary collaborations poster presentation 	"Every R01 I had submitted has had one common critique: that I am not studying sex and gender differences. Interacting with SCORE, I have realized how important it is to study both the sexes to validate my hypotheses." "I am new to sex-based researchconnections with any expert will help us tremendously "				
Asst Prof 2 years at current rank	 new grant submission (in process) publications 	"Lots of help already!!"				
Vear 2 Seed grant rec	2 new external collaborations					
Asst Prof	1 new grant (funded); 1 new	"Provides critical preliminary data to support my R03 and then				
6 years at current rank	grant (submitted)	R01 applications."				
	 Publication new internal interdisciplinary collaborations new external interdisciplinary collaboration 	helpful to distill a storywhere I need assistance is thinking about how to tease out the sex differences we are seeing. As I go up to promotion, I need more speaking opportunities nationally."				
		university. Seminars useful for considering how to include sex in animal experiments."				
Asst Prof	1 new grant submission	"Pilot grant is allowing me to obtain pilot data for NIH and				
I year at current rank	(in process) 4 publications	"Would like more networking, more frequent check-ins to				
	3 posters 1 invitation to be speaker re: sex and gender	monitor progress and help identify barriers."- "Due to the COVID-19 pandemic, we experienced significant delays in experiments due to resources constantly on back- order and only available in limited quantities at the time)."				
Asst Prof 4 years at current rank	2 new internal interdisciplinary collaborations1 invitation to be speaker re: sex and gender1 new grant submission in	 "With this pilot grant I established new collaborations, and we almost have enough preliminary data that we can submit for NIH grant proposals together." "I would like more mentoring in grant writing and tips on how to be successful in incorporating sex differences research 				
Asst Scientist	process	into my grants."				
1 year at current rank	 3 new internal collaborations 1 new external/international collaboration (Ethiopia) 	experiencing during pregnancy in Ethiopialed to a collaboration with the Gender Department at the Ethiopian Ministry of Health pilot grant has helped me learn immensely about the contracts, finance, and operations side of grants."				
		researchers to form future collaborations for grant writing."				
Year 3—Seed grant rec	cipients (2021–2022)	"A compal of data for multipation and for subsequent grant				
current rank	2 publications 1 oral abstract presentation 3 new internal collaborations	submissions."				
Asst Prof—5 years at current rank	1 new internal collaboration	"Flash talks [at annual symposium] are a great way to help promote our work. In-person meetings/events would be the most useful. It's hard to follow up on virtual introductions but a chat over a coffee can be really productive."				
		"It's hard to follow up on virtual introductions but a chat over a				
Asst Prof 2 years at current rank	2 new internal collaborations 1 new external collaboration	coffee can be really productive." "Funding helped me grow professionally to manage this project."				
2 jours at ouriont fails	i new external condociation	"I have had multiple COVID-related challenges."				

TABLE 2.	SUMMARY O	of Findings	OF EVALUATION	OF JOHNS	HOPKINS	Specialized	CENTERS	OF RE	SEARCH
Excellence Seed Grant Recipients									

CEC, Career Enhancement Core; NIH, National Institutes of Health; SCORE, Specialized Centers of Research Excellence.

longstanding seed grant programs. Third, our conclusions are potentially biased because we do not have a comparison group to compare career trajectories and experiences of people who applied but were not selected for funding or a matched control group of awardees from another pilot grant program. Fourth, the academic–foundation relationship between the Gender Medicine Foundation and Johns Hopkins was unique because Dr. Legato's legacy and mission was already grounded in academic medicine.

For this reason, it is not clear if the best practices from this partnership would apply to other academic–foundation partnerships, but we are hopeful that with more reporting on this topic, we could find commonalities.

Conclusions

In summary, we described the SADII SCORE CEC, which represented a collaboration and matching funds with a private foundation committed to supporting careers and research of faculty conducting research related to sex and gender. We provided data about the 12 awardees who have been productive despite challenges of the COVID-19 pandemic.

Authors' Contributions

W.L.B., L.M., M.L., and S.L.K. conceived of the idea; W.L.B. and L.M. designed the evaluation tool and carried out data analyses and validated the results; W.L.B. carried out the writing; J.L.P., M.L.S., and P.S. created the tables and figure; W.L.B., S.L.K., and M.L. acquired the funding for the project. All authors reviewed and approved the final version of the article.

Author Disclosure Statement

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Supplementary Material

Supplementary Data S1

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