CASE STUDY

Mentoring Interdisciplinary Research Teams for the Study of Sex and Gender Differences in Health and Disease

指导跨学科研究团队开展健康与疾病的两性和性别差异研究

Tutorización de equipos de investigación interdisciplinaria para el estudio de las diferencias de sexo y género en la salud y en la enfermedad

Virginia M. Miller, PhD, *United States*; Rebecca S. Bahn, MD, *United States*

INTRODUCTION

Initiatives to hasten the translation of basic science discoveries to clinical care have necessitated the development of new approaches to interdisciplinary collaboration and training of future investigators. This has been nowhere more important than in the study of sex differences with implications for extension into areas of gender medicine. Clearly, gaining better understanding of the role that sex and gender play in health and disease is essential to the implementation of truly individualized medicine. This case study will describe our experiences in developing the Mayo Clinic Building Interdisciplinary Research Programs in Women's Health (BIRCWH) program, an interdisciplinary research and training program in women's health and sex and gender differences. We identify both our successes and the barriers we have encountered in order that others who are developing similar programs might benefit from our experiences.

TERMINOLOGY

We have found it important that everyone involved in a program such as ours have a clear understanding of what is meant by the terms *sex* and *gender*, as these often are used incorrectly as synonyms. "Sex" refers to biology according to reproductive organs and chromosomal complement. "Gender" includes aspects of psychosocial context as a person's self-representation as male or female or how that person is responded to by social and cultural institutions.¹ Thus, gender includes a complex interaction among biology, society, and environment that needs to be considered in studies of factors contributing to health disparities and that is referred to as gender medicine. Most basic science studies of cells, tissues, and experimental animals that examine sex differences do so based on chromosomal complement unless specifically designed to evaluate social group interactions. In contrast, in human investigations, it is possible to assess both sex and gender differences depending upon the hypothesis being tested and the experimental design. Women's health was historically considered in the context of reproduction. Today, sex and gender differences are considered more broadly. This offers the potential to begin to understand why 54-year-old Mrs Jones has different health risks and presents with a particular disease differently than 54-year-old Mr Smith, who might be

diagnosed with the same condition. Two professional societies, the Organization for the Study of Sex Differences (OSSD, www.ossdweb.org) and the International Society of Gender Medicine (IGM, www.isogem.com), reflect the duality of each aspect of sex and gender differences research.

RESEARCH TEAMS AND MENTORS

In order for mentors to help scholars design appropriate experiments for specific research topics, they must not only understand the difference between sex and gender but also be aware of the important impact that the basic biological variable of sex has on interactions of genes with sex steroids and the environment in the relevant field. As obvious as this statement seems, it may not be easy to identify individual scientists and clinical investigators who could serve as mentors and are competent in these fundamental areas. Many may have established their own investigative careers in the era when most studies of disease mechanisms used either only male animals or cells or included animals in which the sex was unreported.^{2,3} Similarly, women have been underrepresented in clinical trials, and as a result, sex and gender are infrequently considered in the development of clinical guidelines.⁴ Thus, a first step in developing a mentoring program in women's health and sex and gender differences may be an educational effort directed toward potential mentors. A list of resources for such efforts is provided in the Table, and a checklist for developing research projects in areas of sex and gender research is provided in the Appendix.

When developing our interdisciplinary program, we found it important to invite key stakeholders in various areas of investigation and medical specialties that reach beyond our specific areas of expertise to join an executive advisory team. This collective group of thought leaders not only brings a true interdisciplinary nature to the program but also offers a stronger voice in approaching institutional leaders for resources needed to sustain or grow the program. These individuals meet with each scholar as a group at least twice yearly to review research progress and contribute interdisciplinary expertise. In addition, the group identifies areas for further career development and sets timelines for manuscript preparation and grant applications. Our executive team consists of investigators funded through peer-

Author Affiliations

Departments of Surgery and Physiology and Biomedical Engineering (Dr Miller) and Internal Medicine, Division of Endocrinology (Dr Bahn), Mayo Clinic, Rochester, Minnesota.

Correspondence

Virginia M. Miller, PhD
miller.virginia@mayo.edu

Citation

Global Adv Health Med. 2013;2(5):109-112. DOI: 10.7453/gahmj.2013.057

Key Words

Gender medicine, interdisciplinary, sex-based medicine, translational research

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest, and Dr Miller disclosed receipt of funding for the Building Interdisciplinary Research Careers in Women's Health award and Mayo Clinic Center for Translational Science Activities. Dr Bahn disclosed no potential conflicts of interest.

Table Professional Resources**Textbooks**

- Legato MJ. Principles of gender-specific medicine. 2nd ed. Amsterdam: Elsevier; 2011.
- Oertelt-Prigione S, Regitz-Zagrosek V. Sex and gender aspects in clinical medicine. New York: Springer; 2011.
- Schenk-Gustafsson K, DeCola PR, Pfaff SW, Plsetsky DS. Handbook of clinical gender medicine. Basel, Switzerland: Karger Publishers; 2012.
- Regitz-Zagrosek V, editor. Sex and gender differences in pharmacology. New York/Heidelberg: Springer-Verlag; 2012.
- Mattison DR, editor. Clinical pharmacology during pregnancy. Amsterdam: Elsevier; 2013.

Web-based Continuing Medicine Education Courses

- NIH ORWH Sex and Gender Differences in Health and Behavior. <http://sexandgendercourse.od.nih.gov>
- NIH ORWH The Basic Science and the Biological Basis for Sex and Gender Differences. <http://sexandgendercourse.od.nih.gov>
- TTUHSC Laura W. Bush Institute for Women's Health. Y Does X Make A Difference?. www.laurabushinstitute.org
- Women's Health Info Site: Sex and Gender Resource for Clinicians and Trainees. <http://wheducom.blogspot.com>
- National Association of Women's Health Medical Educators Faculty Guide. http://drexelmed.edu/portals/0/NAWHME_Guide.pdf
- Resource listing of various educational modalities to use in integration efforts. <http://www.drexelmed.edu/HomeOtherPrograms/WomensHealthEducationProgram/Resources.aspx>

Web-based Research and Educational Resources

- Sex and Gender Women's Health Collaborative. www.sgwhc.org
- Stanford University's Gendered Innovations. <http://genderedinnovations.stanford.edu>
- Canadian Institute of Gender Health. What a Difference Sex and Gender Make. <http://www.cihr-irsc.gc.ca/e/44082.html>

Articles Outlining Experimental Design Methodology

- Becker JB, Arnold AP, Berkley KJ, et al. Strategies and methods for research on sex differences in brain and behavior. *Endocrinology*. 2005;146(4):1650-73.
- Greenspan JD, Craft RM, LeResche L, et al. Studying sex and gender differences in pain and analgesia: a consensus report. *Pain*. 2007;132:S26-45.
- Miller VM, Kaplan JR, Schork NJ, et al. Strategies and methods to study sex differences in cardiovascular structure and function: a guide for basic scientists. *Biol Sex Differ*. 2011;2:14. doi:10.1186/2042-6410-2-14.

Journals

- Biology of Sex Differences. <http://www.bsd-journal.com>
- Journal of Women's Health. <http://www.liebertpub.com>
- Women's Health Issues. <http://www.whijournal.com>

Abbreviations: ORWH, Office of Research on Women's Health; TTUHSC, Texas Tech University Health Sciences Center.

reviewed extramural agencies (ie, National Institutes of Health [NIH]) and includes individuals with laboratory-based programs and/or clinically based programs in physiology, epidemiology, endocrinology, nephrology, gynecology, and general surgery.

One approach to interdisciplinary research and training programs is a linear paradigm. This approach centers on basic and clinical investigators working in parallel to identify a research question or problem, generate and test hypotheses, and publish results. As such, each investigator tends to seek collaborations with the other only at the end of the process (Figure). We con-

tend that a more productive approach is for individuals from diverse backgrounds and disciplines to identify problems together in the early stages of inquiry. They would then work simultaneously to generate hypotheses and develop collaborative approaches to testing these hypotheses. Separate but conceptually related investigations may evolve using both experimental models (cells, tissues, and animals) and human clinical studies. However, in academic settings, the presence of silos of expertise and physical separation of laboratory and clinical environments do not facilitate such interactions. This may present challenges to both mentors and scholars who attempt to form such collaborative groups.

MENTORING AND MENTORING EVALUATION

We have found that identifying the expectations of both scholar and mentor early in the relationship guides articulation and alignment of those expectations.⁵⁻⁷ Research mentoring and career mentoring are not necessarily mutually exclusive but may involve different emphasis and strengths on the part of a mentor. Therefore, articulating expectations early in the relationship eliminates any ambiguity and may identify needs and expectations that could be met by another mentor. Thus, one strength of an interdisciplinary mentorship team is that a spectrum of expertise is available to the scholar within a defined timeframe.

Early in the development of the BIRCWH program, we realized that we could leverage the Mayo Clinic Center for Translational Science Activities (CTSA) to greatly strengthen and expand the offerings available to our scholars. The Mayo Clinic CTSA is funded by the NIH's Clinical and Translational Science Award program. This initiative is led by the NIH's National Center for Advancing Translational Sciences (NCATS) that supports the participation of approximately 60 academic medical institutions across the country. Our BIRCWH scholars have been integrated into many of the educational activities and program evaluation systems developed by the Mayo Clinic CTSA for their early career clinicians and scientists. In particular, we ask that our scholars as well as their mentors complete an annual questionnaire similar to the one that the CTSA uses to evaluate the effectiveness of interdisciplinary mentoring relationships formed in the course of their career development programs. The questions asked in this survey are based on a mentoring effectiveness scale developed at the Johns Hopkins University School of Nursing.⁸ In addition, when a scholar exits the BIRCWH program, we ask both parties to assess the effectiveness of the mentoring relationship both independently and together. We also arrange for the scholar to be interviewed regarding his or her overall experiences in the program by an institutional educational expert and unbiased third party who gives feedback to both the mentor and the executive team. A factor analysis of these evaluations conducted by the Mayo Clinic CTSA identified three elements that were most important to a successful mentoring relationship: (1) the mentor's sup-

Figure Framework of traditional method to develop interdisciplinary collaboration (A) and an alternative approach (B) that allows continuous interaction and feedback beginning at the inception of the project. The latter approach may facilitate translational discoveries and provide scholars in women's health and sex and gender-based medicine a more integrated approach to experimental design.

portiveness of the scholar; (2) the amount of contact time the mentor devoted to the scholar; and (3) the ability of the mentor and mentoring team to provide access to interdisciplinary collaboration. Though electronic communications can be used to remove physical and local barriers, the benefit of face-to-face meetings, discussions, and close mentoring cannot be underestimated. Knowing the importance of these factors early on in the process will help direct agreement between the mentor and scholar. Quantitative tools have been developed and used prospectively to both guide and monitor the effectiveness and productivity of the mentoring relationship. Both the Mayo CTSA and the BIRCWH program use mentoring agreements between scholar and mentor that are based on materials developed by the American Association of Medical Colleges that are available online ("Compact Between Postdoctoral Appointees and Their Mentors," <https://www.aamc.org/initiatives/postdoccompact/>).

Initiating, designing, and assessing the scholar-mentor research relationship can be framed as a multi-part process. The first component is a mentoring agreement that is signed by both mentor and scholar after they have agreed to work together but prior to actually beginning the research. This agreement serves to initiate discussion between the scholar and mentor concerning their respective roles and mutual goals for the relationship. This document also serves to articulate the commitments that each member makes to the other in areas including mutual respect, time commitments, and ethi-

cal conduct of research. A potential barrier for mentoring clinical investigators is time constraints due to the clinical responsibilities. For interdisciplinary relationships between clinical scholars and basic science mentors, flexibility on the part of the basic scientist regarding meeting schedules often is helpful. The initial mentorship agreement opens this discussion to clearly articulate these expectations.

Shortly after the research has begun, a second, more specific agreement is developed that focuses on details that will vary depending upon the scholar's stage in career development and that are specific with respect to the scholar-mentor relationship. The goals and expectations should align with each other's goals as well as the overarching goal of the program. At the individual level, the goals can be specific as to research milestones including protocol development and approval, presentations, manuscripts, and grant submissions. Issues regarding resources and research expenditures should be addressed at this meeting, and interactions with other members of the research team, other mentors, or co-investigators, including the nature and frequency of meetings, should be established. Other areas that may be addressed include courses that should be completed or academic skills that may need to be developed, as well as how this plan will be accomplished. The agreement also facilitates the open discussion of interpersonal factors that may affect the quality of the relationship. These may include gender or race/ethnicity differences, personality types, time management styles, or the articulation of the other competing responsibilities that either scholar or mentor carries.

The mentoring agreement is revisited once a year by scholar and mentor to identify successful elements in the relationship, career development goals that have been accomplished, and expectations that may not have been met. This also may be a time to identify obligations regarding time committed to research by clinical fellows, and sometimes a mentor must intervene with a scholar's clinical chairperson to ensure that his or her funded research time is solely devoted to that activity. This is also an ideal opportunity to consider whether broadening the mentoring team would benefit the research or strengthen the mentoring environment. The executive group with their interdisciplinary view is often able to suggest individuals who could lend wider perspective or special expertise to the mentoring team. Keep in mind that informal mentoring with peers also adds to the scholar's development.

The BIRCWH program is still in its infancy, having been funded only since mid-2010. To date, we have "graduated" three scholars and have entered seven into the program, six of whom are female. We are particularly proud of the fact that our scholars represent many different disciplines, including psychology, physiology, orthopedics, obstetrics/gynecology, nephrology, and biomedical statistics/informatics. In addition, each of our scholars has identified multiple mentors from an equally varied range of disciplines. The measures of success for each of our scholars are based upon both the attainment of the

Appendix Checklist to Guide Development of Research Proposals in Aspects of Sex and Gender Differences^a**Hypothesis Development**

- If the research involves humans as research objects, has the relevance of sex and gender to the research topic been analyzed?
- If the research does not directly involve humans, have studies using cells, tissues, or animals provided insight into sex and gender differences relevant to the question to be addressed?
- Have you reviewed literature and other sources relating to sex and gender differences in the research field?

Proposal Phase

- Does the methodology ensure that (possible) sex and gender differences will be investigated and that sex- or gender-differentiated data will be collected and analyzed throughout the research cycle and made part of the final publication?
- Does the proposal explicitly and comprehensively explain how sex and gender issues will be handled (eg, in a specific work package)?
- Have possible differentiated outcomes and impacts of the research on women and men been considered?

Research Phase

- Are questionnaires, surveys, focus groups, etc, designed to unravel potentially relevant sex and/or gender differences in your data?
- Are the groups involved in the project (eg, samples, testing groups) sex and/or gender balanced?
- Are data analyzed according to the sex variable? Are other relevant variables analyzed with respect to sex?

Dissemination Phase

- Do analyses present statistics, tables, figures, and descriptions that focus on the relevant sex and gender differences that were discovered in the course of the project?
- Are institutions, departments, and journals that focus on sex and gender included among the target groups for dissemination, along with mainstream research magazines?
- Have you considered a specific publication or event on sex and gender-related findings?

^aAdapted from Toolkit: Gender in EU-funded research. http://www.yellowwindow.be/genderinresearch/downloads/YW2009_GenderToolKit_Module1.pdf. Accessed July 29, 2013.

scholar's personal goals relative to the program and objective outcome measures identified by the executive group. These measures include the scholar's successful completion of the graduate school coursework undertaken, number of presentations at national and international meetings, number of peer-reviewed publications, successful application for extramural funding, and placement in advanced academic positions.

BUILDING AN INTERDISCIPLINARY RESEARCH PROGRAM

Striving for excellence in an interdisciplinary research program begins with engaging individuals who share common goals and a willingness to seek out others with mutual interests. Attending seminars and conferences outside of one's discipline and consulting with review panels or other experienced individuals or groups broadens perspective, facilitates networking, and allows for the integration of diverse views. Unrecognized sex and gender bias among institutional leadership may slow development of the program and may ultimately derail its successful implementation. Because leaders in education and administration, potential mentors, and other stakeholders may require some education into the nature of sex and gender research, we have found that building a mature interdisciplinary program may take years and requires persistence. Finally, do not underestimate the benefits gained from documenting and celebrating success of the scholar and program. This provides the needed data to assure institutional leaders of the value that the program brings to the institution and to the program's *esprit de corps*.

SUMMARY

The success of next-generation researchers depends upon the commitment of both scholars and mentors to work toward attainment of mutual goals. The process is slow because it relies on building trusted relationships and may require the formation of nontraditional scientific partnerships. However, engaging talented scholars early in their careers and providing excellent mentorship and resources prepares them to develop new avenues of interdisciplinary research that will form the basis of their independent scientific careers. The development of a successful interdisciplinary research and training program in women's health and sex and gender differences ensures a solid infrastructure within which both new scholars and seasoned investigators can thrive and expand scientific knowledge in these areas.

REFERENCES

1. Wizemann TM, Pardue ML. Exploring the biological contributions to human health: does sex matter? Wizemann TM, Pardue ML, editors. Washington, DC: Institute of Medicine; 2001: 288.
2. Taylor KE, Vallejo-Giraldo C, Schaible NS, Zakeri R, Miller VM. Reporting of sex as a variable in cardiovascular studies using cultured cells. *Biol Sex Differ*. 2011 Nov 7;2:11.
3. Zucker I, Beery AK. Males still dominate animal studies. *Nature*. 2010;465(7299):690.
4. Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update: a guideline from the American Heart Association. *Circulation*. 2011;123(11):1243-62.
5. Abedin Z, Biskup E, Silet K, et al. Deriving competencies for mentors of clinical and translational scholars. *Clin Transl Sci*. 2012;5(3):273-80.
6. Fleming M, Burnham E, Huskins W. Mentoring translational science investigators. *JAMA*. 2012;308(19):1981-2.
7. Huskins WC, Silet K, Weber-Main AM, et al. Identifying and aligning expectations in a mentoring relationship. *Clin Transl Sci*. 2011;4(6):439-47.
8. Berk RA, Berg J, Mortimer R, Walton-Moss B, Yeo TP. Measuring the effectiveness of faculty mentoring relationships. *Academ Med*. 2005;80(1):66-71.