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Agency Name:	National Science Foundation
Agency Tracking Number:	**2100488**
Organization:	
NSF Program:	ERC-Eng Research Centers
PI/PD:	Guo, X. Edward
Application Title:	NSF Engineering Research Center for Integrated Mechanobiology for Women's Health (IMWEL)

Review 1

Rating:

Very Good

Review:

Summary

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

The ERC pre-proposal seeks to understand material and mechanical properties in biological tissues focused on women's health. The researchers will develop convergent knowledge of mechanobiology at multiple scales using -omic technologies. Institutions include Columbia, Pitt, ECU, and UCI, although the bulk of the team is from Columbia (24/34, >70%). The idea focuses on the extreme material conditions in reproductive physiology, and notes that women's health research has been lacking. It's not clear that it is high-risk, but could have a high societal impact.

Strengths

Crosscutting studies of women's health issues would benefit from a coordinated and integrated research effort such as an ERC. All faculty are associated with a research area, testbed, and a non-research component to increase communication. WFD focused on various levels from K-12 Teachers to postdoctoral training; these are also used for DCI activities. Mentor training is a positive aspect of the proposed program. The IE engages

various initiatives and industry. However, it is not clear where or how the program will engage clinicians (outside of the research team) and potential patients, nor how these initiatives will be evaluated.

+Good details about how the research thrusts will use each other and the testbeds to gain new insights.
+The inclusion of bioinformatics is a plus, but it is not clear that the data needed is already available to mine and model.

Weaknesses
The benchmarks are not clearly defined. It is not clear how the SLC, Community Impact Advisory Board or Education Advisory Board will interface with the other components of the leadership. What are the inputs and outputs?
-Some of the connections between 'disease' states and the output from the testbeds are not clear. It is difficult to believe that one device, for example, can repair the uterus after all of the various disorders mentioned. This one size fits all strategy seems unlikely to change the outcome of women's health.
-How the information from the various councils and boards will inform the direction or research needs is not clear. What is the goal of having these boards? Some of the boards seem more operational than advisory, and this integration needs to be clarified, as the Infrastructure 'map' seems to imply internal advising

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths:
+Focus on women's health disparities
+Focus on women and intersectionality for EWD
+ RET program to engage younger students

Weaknesses:
- It would be useful to have a few points on how the RET will be integrated, particularly when focused on women's reproductive health (how young will the students be) and what the teachers will do. If they are developing modules for the classroom, how will standards be addressed across all of the various states, and how will it be evaluated?
-Overall, evaluation of the educational plan or EWD is not well discussed, and if outside evaluation will be performed

Please evaluate the strengths and
weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if
applicable

The potential for convergence in development of new systems is fairly high from the fundamental level, but a better understanding of the various clinical issues is likely necessary to move these new systems from bench to bedside.
The EWD is focused on women and intersectionality of race and sex at the trainee level. The training at REU level on women's health issues may also increase the interest of students in general to study these issues. However, it is not clear how the REU or RET programs will run with the numbers noted and 4 different institutions. The proposed DCI activities are joined with the EWD, and it is not clear how they will utilize evidence-based approaches except through precedence of programs to engage a diverse doctoral program at various institutions or because the institutions themselves have a high minoritized population. It would be necessary to evaluate the actual programs within the center for outreach and training. The proposal focuses on entrepreneurial training to expand partners and routes to commercialization. Industry engagement is mentioned, but where the partners will be from (which companies? Will those currently engaged in women's health or materials be partners or competitors?). The PI and the team are well qualified to lead the research and technology development.

Summary Statement

The ERC pre-proposal seeks to develop a research/testbed focused on the extremes that are components of reproductive physiology. The research areas are of interest and impact, however, it is not clear that all of the stakeholders are engaged. The testbeds have somewhat simplified outputs to address a wide array of problems, which may imply that the stakeholder engagement is even more necessary. The EWD and DCI are integrated and focused on women, but it is not clear how these programs will be evaluated or used to inform future EWD. Finally, the infrastructure of the leadership team is fairly typical of an ERC, but it is not clear how the feedback from the various councils will be integrated into the workflow of the center.

Review 2

Rating:

Good

Review:

Summary

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

Strengths: The proposal uses a holistic approach to examine and understand the highly complex female reproductive systems, focusing on biomechanics and mechanobiology. The proposal includes multiple length scale characterization and modeling, and connects chemical and biological cues with cellular and structural changes.

The PIs and the team appears to be highly qualified.

Weaknesses: The “engineered systems” on the 3-Plane Strategic Planning Chart are “diseases,” and the output are insights, thus making a clear translation path less clear.

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths: The team has an excellent plan for Engineering Workforce Development as well as Diversity and Culture of Inclusion.

Weaknesses: IMWELL should consider partnership opportunities with industry, government agencies, and other entities to develop a plan for translation of discoveries to market.

Please evaluate the strengths and
weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if
applicable

Summary Statement

IMWELL (Integrated Mechanobiology for Woman’s Health) aims to advance fundamental, sex-specific biomechanics and mechanobiology knowledge. Knowledge gained has the potential to support healthy reproduction, childbirth, and aging.

Review 3

Rating:

Very Good

Review:

Summary

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

Strengths
(1) Scientifically, this proposal addresses an important knowledge gap – mechanobiological investigation of tissues at childbirth and in pregnancy. This aspect impacts several important health issues of women undergoing childbirth.
(2) Some of the studies build on efforts by co-PI Meyers on biomechanics studies in hormone-mediated growth and remodeling of cervical tissue as well as soft tissue mechanics work by M. Oyen (she is not listed as co-PI on cover page but written in the proposal as co-PI.
Weakness

(1) Some leadership issues are noted. Oyen is listed as co-PI in the proposal but not on NSF proposal cover page. Her CV is also not provided. Maiti leads the important area of multiscale but is not listed as coPI
(2) Theoretical multiscale modeling section is completely devoid of any description of the multiscale- is it ab initio to finite element? Is it hierarchical multiscale? PIs plan some imaging to be related to overall mechanics—this cannot be called multiscale or even modeling.
(3) The tissue and organ mechanobiology is also weak. A vague description of organ level mechanics is presented.

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths
(1) PIs address the outreach and education gaps in understanding physiology unique to women
(2) Several very innovative programs are presented: Women Innovators in Entrepreneurship & STEM Careers, Career Placement addressing pipeline issues for female undergraduate, graduate, and postdoctoral scholars, support women trainees, also address issues pertaining to women of color, recruit postdoctoral candidates from minority serving institutions, in addition to efforts in RET.
(3) Leverage off the UCIs NSF ADVANCE
(4) Creative K-12 activities are also presented as their Inside Engineering program.
(5) Overall a grassroots study in biomechanics with sex differences is presented.
Weakness
(1) Reviewer is concerned about the ‘required all women’ programs planned might cause loss of respect for researchers on their campuses since it appears to exclude male students. It is suggested that PIs plan this focus on women health with a more inclusive recruitment. Is the focus on lack of science on women’s health or lack of women scientists. The demarcation is blurred and it appears that perhaps the two may be related but need to be scientifically addressed explicitly.

Please evaluate the strengths and
weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if
applicable

The proposed ERC pre-proposal represents excellent efforts in diversity, women's physiology related data, STEM education.
A strong team of researchers presented but it appears the strongest and most relevant members are not co-PIs. For instance the proposal would be better served by including Oyen and Maiti as co-PIs or PIs. The organizational structure needs to be reworked.

Summary Statement

The focus of this proposal is to improve on knowledge base regarding female-specific physiology and the dramatic structural changes exhibited by tissues during pregnancy and childbirth. This Center aims to develop mechanobiology database at molecular, cellular, and tissue scales, using BigData and BioInformatics technology thrusts, with Multiscale models to develop, systems-level understanding of physiologies specific to pregnancy and childbirth in women. It is the reviewers opinion that it is farfetched to say that it is "women’s health” at this point since there are many issues in women’s health that are not directly related to childbirth. The proposal is a collaboration between Columbia, U Pitt and UC Irvine. It is not clear what PIs mean by two minority focused institutions.. Overall a great efforts. Some details are missing on the thrust areas. The computational (multiscale modeling) is very weak aspect of the proposal.

Review 4

Rating:

Excellent

Review:

Summary

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to intellectual merit.

Strengths:
+ The idea for a Center to focus mechanics and mechanobiology research and development on women’s health is high-reward. There is a paucity in mechanical studies on diseases disproportionately affecting women. An NSF Center would raise awareness of the disparity in healthcare and research in this subject and provide a focal point for research and training, creating a pipeline of new researchers for this important topic.

+ The team of renowned experts in the mechanics of women's health understand the state-of-the-art and have laid out a plan for gauging progress including creation of customized imaging, in vitro modeling, and computational modeling platforms.
+ The convergence of the fields of mechanics and women's health is necessary to tackle the big challenges in the field. The use of –omic technologies for mechanobiology at molecular, cellular, and tissue scales and analysis using "Big Data" methods and multiscale computational models will be facilitated by having a large, dedicated Center.
+ The 4.3.2. THEORETICAL MULTISCALE MODELING and 4.3.3. TISSUE & ORGAN MECHANOBIOLOGY thrusts are established strengths of this group and have a high chance of success and future impact.

Weaknesses:

- The proposed analysis methods or focus on women's health are not particularly high-risk, except possibly that the funding for such studies is not at the level it should be (and thus those trained in the area may find funding difficult to secure).
- The big data/bioinformatics thrust is not closely connected to the mechanics/mechanobiology focus of the center. The predictive models for preterm birth and preeclampsia do not (clearly) rely on unique mechanics data, rather they are based on existing biomarker data and genome-wide genetic profiling.
- In the 4.3.1. EXPERIMENTAL MOLECULAR, CELLULAR & TISSUE MECHANICS thrust, the molecular and cellular aspects are not described.

In the context of the five review elements, please
evaluate the strengths and weaknesses of the proposal with respect to broader impacts.

Strengths:

+ The unified focus on women's health has a potential for broad impacts into delivering engineering systems to support healthy reproduction, childbirth, and aging – addressing the significant disparities in medical products and systems addressing women's needs.
+ The proposed programs will advance the career goals of researchers, particularly women and underrepresented minorities, providing a diverse cadre of future leaders of and workforce for this emerging field. The workforce development is a particular strength of this center; it is well laid out in terms of future women innovators, optimizing racial diversity, and career support. The overall plans for diversity and culture of inclusion are strong with existing and planned resources.
+ The efforts towards training engineers how to communicate research and results with a wide range of communities is a strength. This is especially important for potentially uncomfortable subjects that are inherent in reproductive health.

Weaknesses:

- The leadership may be strengthened by having a women's health researcher as the PI, although the current PI is clearly more than capable of leading the center.
- Not a weakness, but a question: will the annual conference focused on women's health needs and innovations be open to all, or only Center participants?

Please evaluate the strengths and
weaknesses of the proposal with respect to any additional solicitation-specific review criteria, if
applicable

+ IMWEL's 3-Plane Diagram clearly demonstrates the high-level needs (e.g., pelvic floor disorders), necessary technology base to address the needs, and the underlying knowledge base required to develop the enabling technologies. Barriers are clearly identified in each of the "planes".
+ Having dedicated Community Impact Advisory and Education Advisory Boards will give a strong voice to for patient advocates and provide important guidance for the center leadership.
- It would be helpful to expound upon how the SLC would be empowered to guide the activities of the center (and if they have a budget for their activities)

Summary Statement

The convergence inherent in the Integrated Mechanobiology for Women's Health ERC would lead to a new level of understanding of the extreme material properties and distinct mechanobiology of female-specific biological tissues and cells. This knowledge will be leveraged into technology platforms which will be applied to the creation of new devices, imaging/computational systems, and products for detecting, predicting, and improving women's health, a field in which there are current significant disparities in innovations and medical products. The leadership team is diverse and has solid plans for administering the Center with a focus on creating a supportive and inclusive culture and on communicating their (potentially uncomfortable) findings to the public.