Rigor and reproducibility in shared resources: ABRF Committee on Core Rigor and Reproducibility survey update

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INTRODUCTION

Biomedical research is a process of exploring the unknown, deconstructing the complexity of life processes and the pathogenesis of disease, and applying new discoveries to improve and advance the life of humans, animals and society. As scientists, we build on existing knowledge, taking incremental steps toward understanding with the occasional leap forward provided by a major discovery or paradigm shift. Science advances through the publication of novel results and independent replication studies upon which others in the field build new hypotheses to better elucidate biological processes. Reproducible research practices include rigorously controlled and documented experiments using validated reagents. These practices are integral to the scientific method and they enable reliable and actionable research results. However, the art and practice of science is affected by challenges that go beyond the inherent complexity of the biology being explored.

Journal editors also recognize the need to improve reliability and efficiency of scientific research. Recently, *Nature Human Behavior* published a manifesto for reproducible science (Munafo, MR et al., *Nature Human Behavior*, 1:1-9, 2017). The authors discuss why measures to optimize elements central to the scientific process such as methods, reporting and dissemination, reproducibility, evaluation and incentives are essential to improve the transparency, reproducibility and efficiency of scientific research. Granting agencies make significant investments in core facilities to provide cutting-edge technologies and expert consultation to scientific investigators (Chang, M and FB Grieder, *J Biomol Tech*, 27:2-3, 2016). As a result, cores play an essential role in supporting scientific investigators and their efforts to improve the transparency and reproducibility of their research.

Within this broader national conversation of research quality, it is important to emphasize the critical role that shared research resources can play in achieving efficient use of research funds and broadening access to advanced skills, expertise and technologies. Shared *scientific research resources generate the majority of research data at many institutions* so their role in maintaining needed expertise and generating quality data is considerable. Recognizing this, federal granting agencies have already made significant investments in shared resource cores via a variety of direct and indirect mechanisms, with the goal of providing cutting-edge technologies and expert consultation to individual scientific investigators (Chang, M and FB Grieder, *J Biomol Tech*, 27:2-3, 2016). Therefore, the scientific shared resource community must continue to take the lead in promoting and supporting rigorous, transparent, and reproducible (R&R) research, as well as in providing critical mentoring and technical training.

The CCoRRe conducted a survey to assess how shared resource facilities are currently assisting investigators with their need to demonstrate transparency and rigor in their research. In addition, the survey captured information from the shared resource personnel related to the challenges they face, and the resources they need to support scientific transparency, rigor and reproducibility (R & R).

MATERIALS AND METHODS

Survey Overview. The CCoRRe committee developed an 18-question on-line survey and shared it using SurveyMonkey©. The survey was announced on the ABRF listservs and blogs and was open from February to April 2017. All survey participants remained anonymized.

Data Analysis . The survey contained both multiple choice and open-ended text questions. Results from the multiple-choice questions were calculated by counting the number of responses for each element for a given question. The open-ended text questions were evaluated by first conducting an inductive content analysis of text to categorize the responses. At least two committee members then independently coded text units using these categories. After the independent coding, the committee members discussed any discrepancies and reviewed differences to determine if consensus could be reached. Results reflect the average counts of responses in each category.

A manuscript that provides a more comprehensive presentation of the survey results presented in this poster has been accepted by *The Journal of Biomolecular Techniques.*

RESULTS & DISCUSSION

Survey Demographics

- 243 respondents
- Respondents from 21 countries, 79% from the United States
- 53% ABRF Members
- 69% were core facility directors that work in an academic setting (72%)
- Broad range of technologies were represented by the respondents (Figure 1)

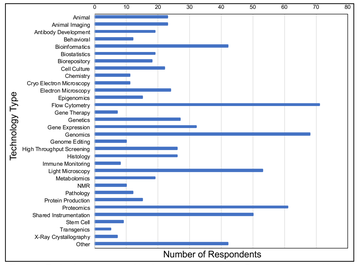

Figure 1. Technologies supported by the survey respondents. Respondents were able to select more than one technology type.

Respondent Awareness of R & R

The survey first asked the respondents to indicate whether they were aware of NIH policies/guidelines on R & R.

Nearly 75% indicated they were at least somewhat aware (Figure 2).

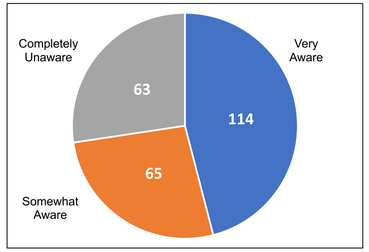

Figure 2. Survey respondents self-assessments of their knowledge and awareness of the current NIH guidelines on Rigor and Reproducibility.

The survey then asked whether they have been asked to provide documentation of the rigor and reproducibility practices used by their facility

~70% of respondents indicated that they have not received requests from their clients to provide documentation (Figure 3).

Given the apparent disconnect between awareness of the NIH R & R guidelines and the requests to have cores provide this information for grants or publications ***suggests that many do not see cores as playing a major role in the R & R solution.***

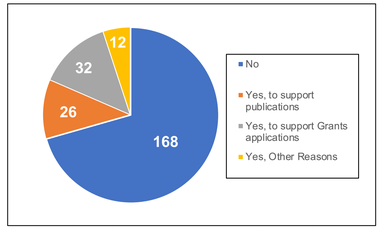

Figure 3. Lack of requests for rigor and reproducibility documentation by users of shared resources. Response to the multiple choice question: Has your core's rigor and reproducibility practice statement has been requested?

Challenges that Impact Compliance and Implementation of R & R in Cores

The survey asked respondents to indicate factor(s) that they feel are currently contributing to the lack of compliance with good Rigor and Reproducibility practices (Table 1).

- 213 individuals (88%) provided over separate 400 responses
- **Several common factors contributing to lack of rigorous and reproducible research** and non-compliance with Federal guidelines were cited, including **lack of training, mentorship, expertise or oversight.**

Some notable responses to this question include:

- A respondent wrote that there is not enough training of individuals doing the research: "*Lack of proper training, full understanding of technology, proper controls. I think every graduate student should have to take a "How to do Research Course." We spend a lot of time teaching our users how to "do science" before we even get to training them how to do flow.*"
- A respondent implied that research laboratories are not providing adequate mentoring to new personnel: "*Chiefly a lack of trained senior personnel in research labs, post-docs and senior graduate students, who simply are not available to mentor younger students and train them properly in the use of controls. The PI's don't always have the time to keep on top of the work of junior personnel and probably assume that experiments were carried out in a well-controlled manner.*"
- A respondent noted that the scientific community needs to reevaluate how success should be evaluated: "*The measure of success in the scientific community is incorrect. There is too much emphasis on the number of papers a researcher publishes and not enough on the quality of the papers. As a result, fly-by-night journals pop-up and report less-than-trustworthy data that cannot often be reproduced. We should be policing ourselves much better than we are.*"

The survey then asked what the challenges are in implementing R & R in a core setting (Table 2).

- 216 individuals (89%) provided over separate 400 responses
- **The major challenges noted were that cores are limited to the quality of samples provided followed by level of training of the individuals preparing them, poor experimental design and use of SOPs**

Some notable responses to this question include:

- A respondent noted issues associated with sample quality or quantity: "*I don't prepare the samples: people bring me samples to work with. I have no control over how the samples are prepared, or what controls are prepared, which means generating reproducible results really falls on the investigator who I'm working with.*"
- The following comment: "*…researchers who want to "go ahead anyway" despite all our concerns about poor samples*", represents a challenge factor noted by a number of respondents.
- One respondent commented that "*The greatest challenge is getting researchers to seek out our assistance from the beginning. Seeking out our guidance before they design their experiments and collect data will improve rigor and reproducibility.*"
- One responder wrote: *"We have exponentially increased educational offerings to try to overcome our biggest issues (sample quality, proper controls, best practices, etc.) but while this works for researchers in the lab it doesn't always translate up to the PIs and we see a general aversion to some of our recommendations due to cost restrictions."*

Table 1. Factors contributing to lack of compliance with R&R guidelines

Category	Number of Responses[a]
Lack of training, mentorship, technical expertise or oversight	79
Time pressures	67
Inadequate standardization of protocols, guidelines, and data analysis	54
Poor experimental design, including sufficient replicates, sample size, and adequate controls	45
Experimental cost	40
Inappropriate experimental and analytical tools	36
Irresponsible research conduct	31
Incomplete documentation of experiments and data management	27
Inadequate peer review	13
Responses that could not be assigned to a category[b]	32

[a]Average number of responses from 3 scorers.
[b]A category was not created unless five similar responses were obtained. Examples of unassigned responses include: "*It's the Wild West, and we like it that way?, Is it really inadequate?, The increasing drive to commercialize research*, and *No rules.*"

Table 2. Major challenges to rigor observed in shared resources

Category	Number of Responses[a]
Poor sample quality from users/sample variability/limited biological material	51
Lack of well-trained principle investigators and lab members/Poor oversight	45
Poor experimental design: Lack of sufficient replicates/inadequate sample size/lack of adequate controls	43
Inadequate standardization of protocols or guidelines, and data analysis	43
Cost and time	39
Failure to leverage the core's expertise/following the core's advice/no consulting beforehand	23
Inadequate documentation of experiments/data management	19
Instruments: maintenance, upgrades, changes	15
Responses that could not be assigned to a category[b]	11

[a]Average number of responses from 3 scorers
[b]A category was not created unless five similar responses were obtained

CONCLUSIONS

In this survey, the CCoRRe explored the perception of research core personnel as it relates to research rigor and reproducibility in light of new expectations introduced by the NIH.

- This survey identified strategies and solutions for addressing these barriers.
- The survey illustrated that scientists and core service providers need:
  - Additional support (training, time, resources, personnel and guidelines) to implement and efficiently sustain best practices.
  - The support of their institutions and users, to ensure that there is a firm understanding of, and commitment to, the factors that support sound science and reproducible research outcomes.
- Core science inherently supports transparency and scientific reproducibility, in part by protecting against cognitive bias in research design and statistical analysis. Core personnel maintain considerable expertise that is important for the quality of their work and for sharing with research scientists in their important role as research mentors. Core personnel ensure continuous improvement through professional and educational development and through their systematic approach to research methods.
- **Therefore, it is critical that core facilities lead the pursuit of research accountability and reliability.**

FUTURE DIRECTIONS

- The goals of the NIH and other research stakeholders are more likely to be achieved when core facilities and research scientists work together to identify and minimize risk to research data, thereby improving research quality, rigor and reproducibility.
- The shared goals of research stakeholders, core facility personnel and users, and professional scientific societies such as the ABRF should continue to provide opportunities to improve research outcomes across the complex research enterprise.

Seven Steps to Rigorous and Reproducible Experiments in Biomolecular Research

1. If using a core facility, **consult** with the core staff in the planning stage. Consult with a statistician if you need help developing a Power Analysis.
2. Design your experiment with **sufficient controls** (rigor) **and replicates** (reproducibility).
3. Assure that ALL of your reagents (antibodies, cell lines, mice) are **fully validated**.
4. Have a clear and **detailed protocol** (SOP) and data analysis plan. Document any deviation from the protocol.
5. Assure that the staff or students performing the experiment are **well trained** and understand each step and the importance of performing them precisely (rigor again).
6. Use only **well-maintained instrumentation**, preferably maintained and operated in a core facility with expert staff (see #1 above).
7. **Document all steps**, reagents, equipment and data analysis methods used in the experiment. Assure that the both the documentation and the data itself are properly stored in a safe data management repository.

- ***From the ABRF Committee on Core Rigor and Reproducibility (CCoRRe), 2019.***