

A MESSAGE TO TRANSLATIONAL RESEARCHERS

To the individual who devotes his life to science, nothing can give more happiness than increasing the number of discoveries, but his cup of joy is full when the results of his studies immediately find practical applications. — Louis Pasteur

Louis Pasteur captured the motivation of many of us who have dedicated our careers to improving the lives of patients in need. This desire is reflected in the rapid growth of the number of academic investigators engaged in translational research.

With an inherently different focus than traditional basic researchers, academic translational researchers must confront complex changes. Traditional funding models are evolving, reproducibility concerns are causing experimental standards to rise, and stronger interdisciplinary collaborations are becoming essential at earlier stages. These challenges must also be faced by a research community whose traditions can be difficult to change. Adaptation may not be easy.

In this State of Translational Research Survey Report, conducted in collaboration with the American Association for the Advancement of Science (AAAS)/Science Magazine, Sigma-Aldrich has collected the views of more than 600 self-described academic translational researchers. Together, we aim to better understand current practices, barriers to progress, and how to advance the field.

We hope everyone enjoys reading the report. We expect the results will provide a starting point for discussions about how translational researchers can best achieve our collective goal of improving human health.

Sincerely,

Amanda Halford

Vice President

Academic Research

Sigma-Aldrich Corporation

EXECUTIVE SUMMARY

The promise of translational research is tremendous. For this promise to be fully realized, academic researchers face new challenges that may require them to change many of the ways in which they think and act. The purpose of this survey is to discover if academics are ready and willing to take on these challenges. Do they have processes and cultural foundations in place to make them happen?

We found that among survey respondents the definitions of “translational research” and “translational researcher” are unclear. Without a clear definition of

who they are and what they do, academic translational researchers are unable to debate standards and build the peer networks and industry contacts necessary to fully engage and succeed in translational research.

Academic translational researchers have identified areas for improvement, but the majority do not act on them. There is a gap between attitudes and practices, and it is clear that the community is looking for the individuals, organizations, and networks to bridge that gap.

KEY FINDINGS:

- Although all survey respondents agreed that their research contributes to the development of laboratory discoveries into clinical applications, 28% of respondents did not identify their work as translational when asked to categorize their research. One-fifth (19%) of respondents indicated that basic research alone best described their work.
- Insufficient funding is considered the most significant barrier to progress in translational research; it was cited by 62% of the survey respondents, nearly double the percentage of respondents who cited lack of interdisciplinary training (33%) or an unclear path to creating successful commercial partnerships (33%).
- Only 22% of the survey respondents had their funding decrease in the last 12 months, while the majority of respondents have had either no change or an increase in funding. Sixty-three percent of respondents also agreed or strongly agreed with the statement: *“Translational research improves funding.”*
- Sixty percent of the survey respondents agreed or strongly agreed that considering patents and commercialization activities in tenure evaluations would encourage young researchers to pursue faculty positions in translational research.
- Sixty-two percent of the survey respondents agreed or strongly agreed that collaboration with an institution’s business school would benefit translational research groups. However, only 13% reported current collaborations with their business school.
- One in five (22%) survey respondents rarely or never consult with peers, whereas only one in three (33%) do so often or always.
- Seventy-three percent of the survey respondents agreed that industry feedback on their research in its initial stages would be helpful. However, only 27% regularly consulted with industry scientists for such commentary.
- Survey respondents were evenly split on the question of whether individuals working in translational research should be held to a higher standard of laboratory practice/experimental design than those working in basic research, with 45% indicating they should and 44% indicating they should not.
- To ensure that their research was perceived as reproducible, survey respondents were most willing to make changes inside their labs and less willing to seek outside help. Only three percent of respondents were unwilling to make any changes.
- One in six researchers (16%) repeat experiments less than three times before including the resultant data in a manuscript submission.

METHODS

AAAS/Science Magazine conducted an anonymous online survey of a random sample of researchers who subscribe to *Science Translational Medicine's* electronic table of contents (eToC) alerts and work at academic and non-profit research institutions. Individuals were qualified to participate in the survey if they answered "yes" to the question: ***"Does your research contribute to the development of laboratory discoveries into clinical applications?"***

During the six days that the survey was fielded, 608 qualified individuals completed the full survey. Those 608 surveys serve as the basis for this report. The market researchers at Harris D. McKinney and

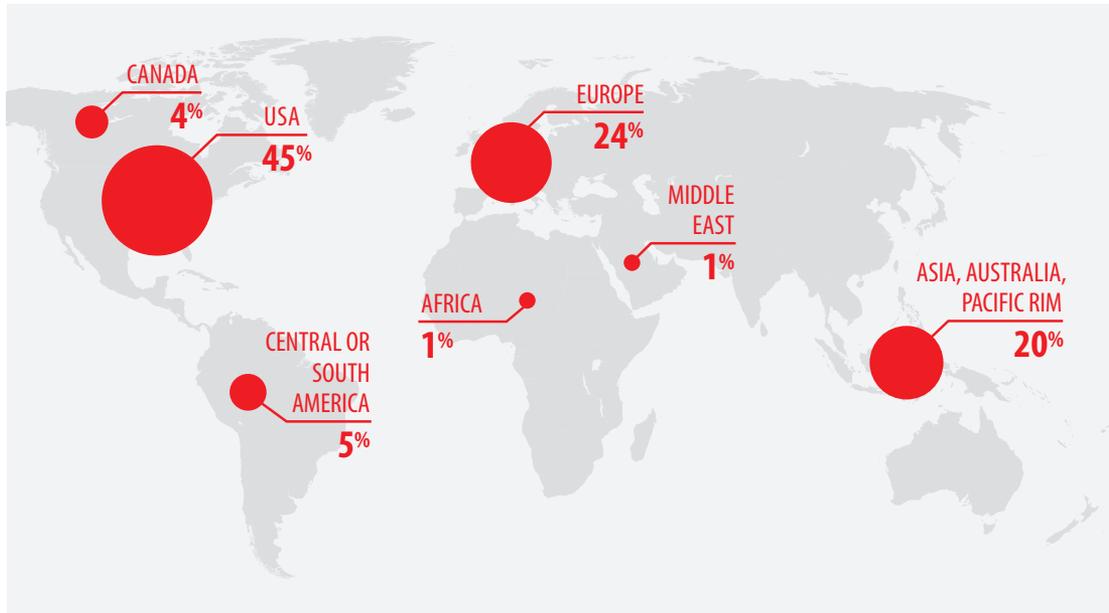
AAAS/Science Magazine tabulated and interpreted the data. The margin of error for the full set of data is less than $\pm 4.0\%$ at the 95% confidence level.

Respondents were solicited by an e-mail blast sent by AAAS/Science Magazine on Thursday July 11, 2013 to a randomly selected group of 20,000 individuals, as previously described, who both subscribe to *Science Translational Medicine's* eToCs and identify as employed by an academic or non-profit research institution. A prize drawing for an Apple iPad® 2* was offered as an incentive to participate in the survey.

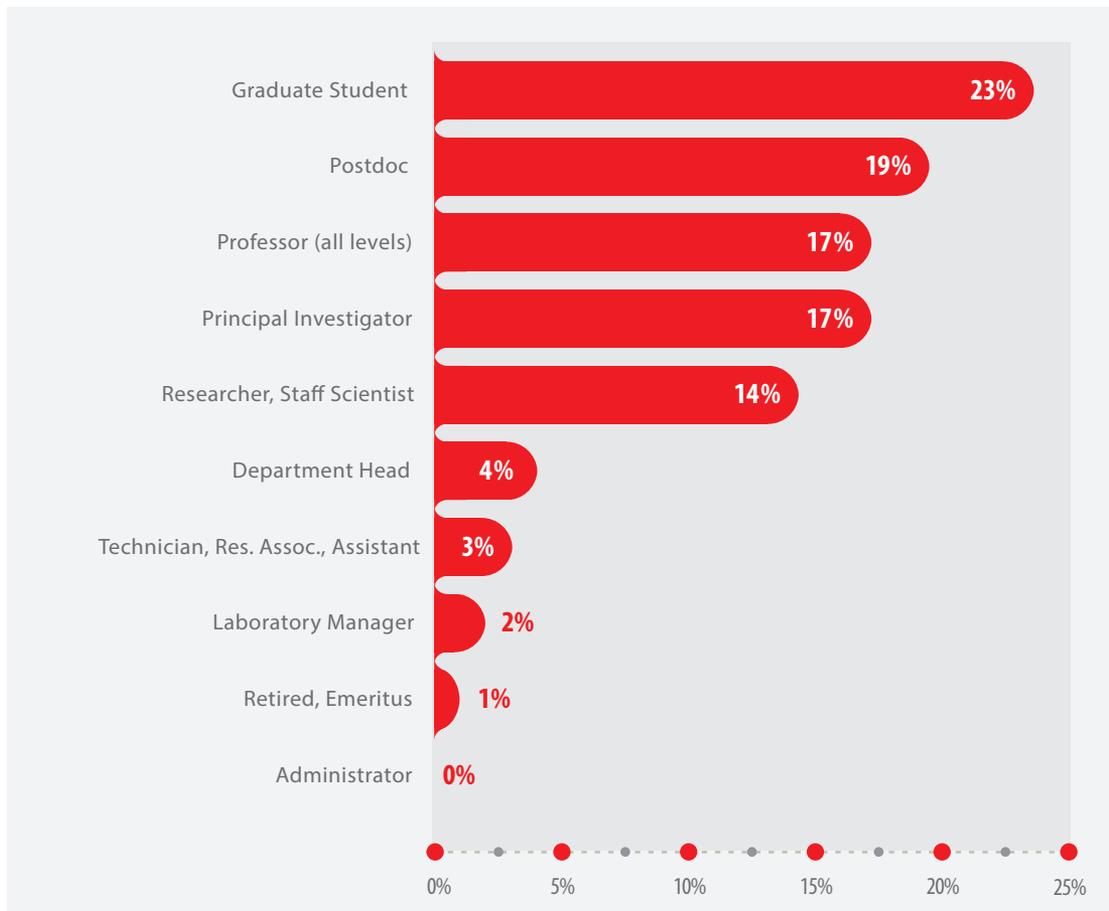
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RESPONDENT DEMOGRAPHICS

Location



Job Title



RESULTS AND CONCLUSIONS

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1: AM I A TRANSLATIONAL RESEARCHER?

Q: Indicate the area that best describes your research. (Check all that apply.)

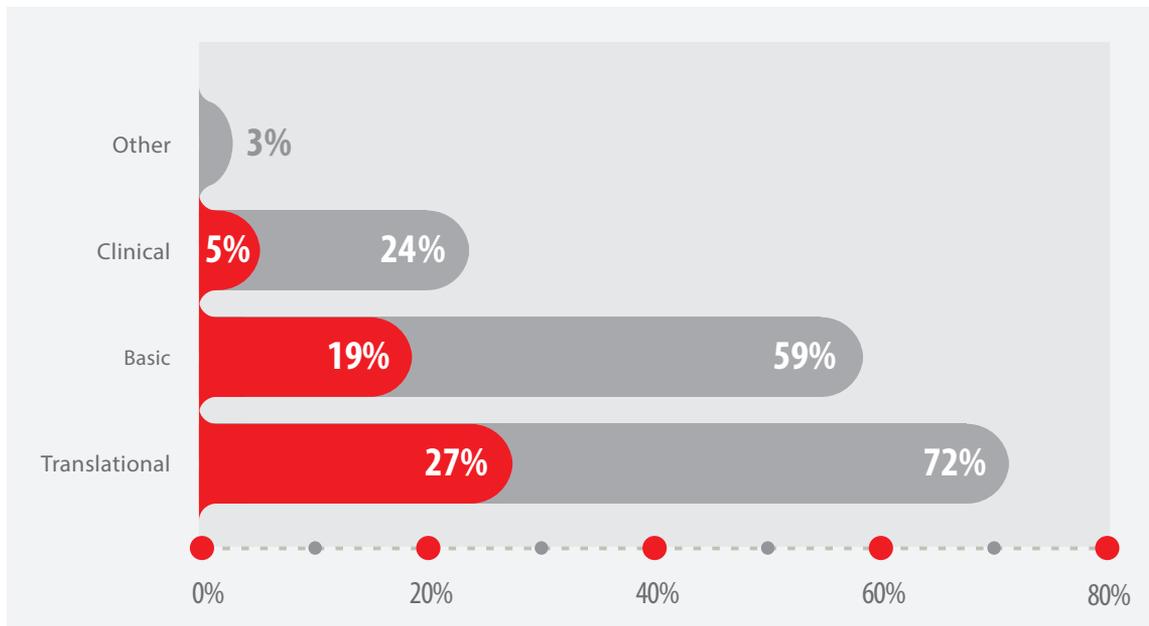


Figure 1. Self-identified research areas

Gray bars indicate the total response for each type of area. Red bars indicate the number of unique responses for that area only.

One in five (19%) researchers surveyed classified their work as basic research exclusively (Figure 1), despite the fact that all respondents currently subscribe to *Science Translational Medicine* eToCs and qualified to complete the survey by answering “yes” to the question: **“Does your research contribute to the development of laboratory discoveries into clinical applications?”**

An agreement in the community about what constitutes translational research is necessary to debate standards and build effective networks within the community. This is particularly important not only for researchers, but also for

organizations designing programs to benefit translational researchers. The lack of clarity on who is conducting translational research leaves the community in a gray area when it comes to debating and implementing standards and practices to move ideas from lab to clinic.

We believe it is useful to the readers of this survey to keep in mind this translational research identity crisis insight while interpreting results.

2: TRANSLATIONAL RESEARCH – BARRIERS TO PROGRESS

Q: As a translational researcher, what are the most significant barriers to progress? (Check up to three.)

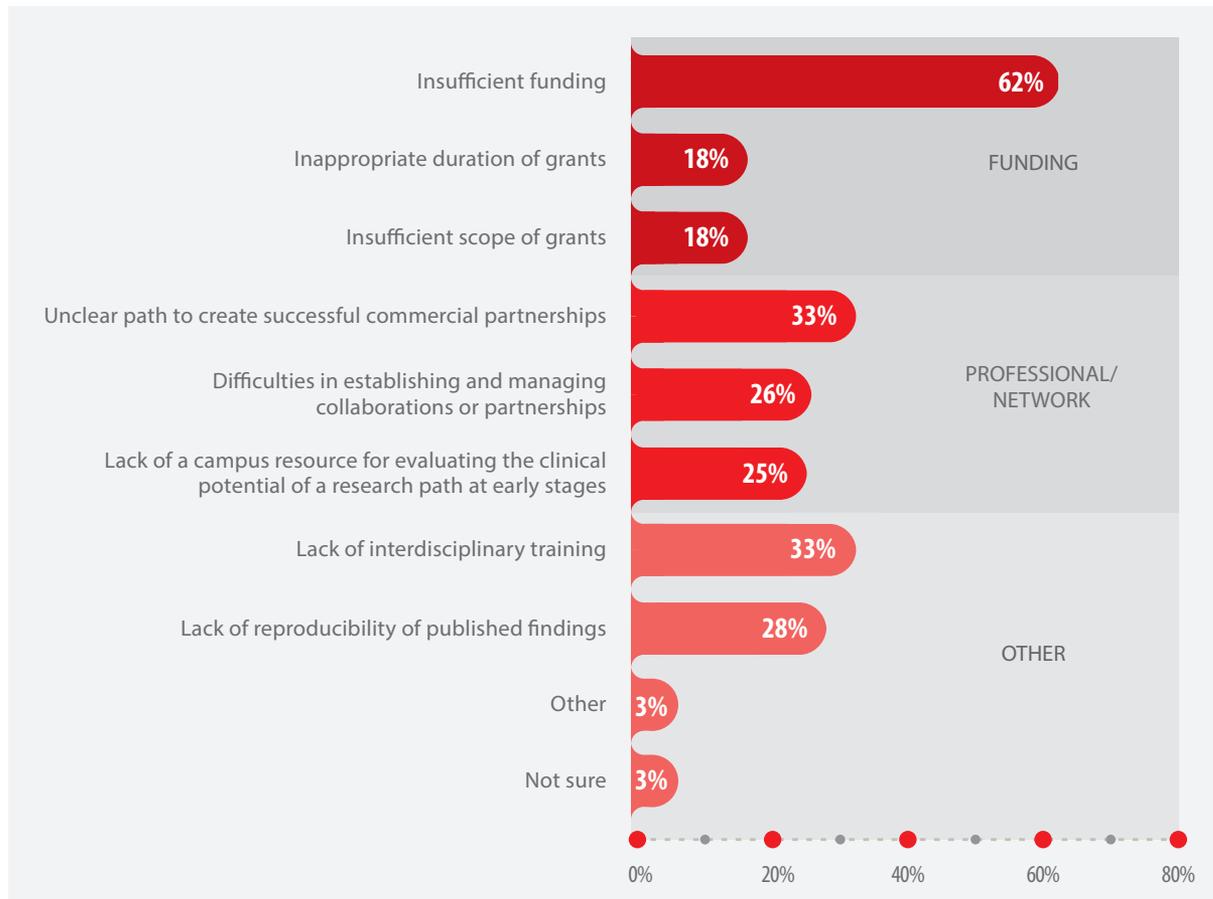


Figure 2. Perceived significant barriers to translational research progress

"Other" barriers included responses such as: government regulations, difficulty publishing in well-respected journals, lack of access to large numbers of clinical samples, and a lack of respect from NIH study sections and the scientific community for theoretical perspectives that are still in their adolescent stages.

Change can be particularly difficult for organizations, such as academic institutions, which operate on long-standing traditions and habits. However, translational research is fundamentally different than traditional basic research and strict adherence to what has worked in the past may hinder progress for translational researchers.

Respondents cited insufficient funding as the top barrier to progress, pointing to a need for alternative sources of funding. With waning government grants and a higher cost of research due to demand for increased quality and reproducibility, outside factors are aligned to push a cultural shift in how early stage funding may be obtained.

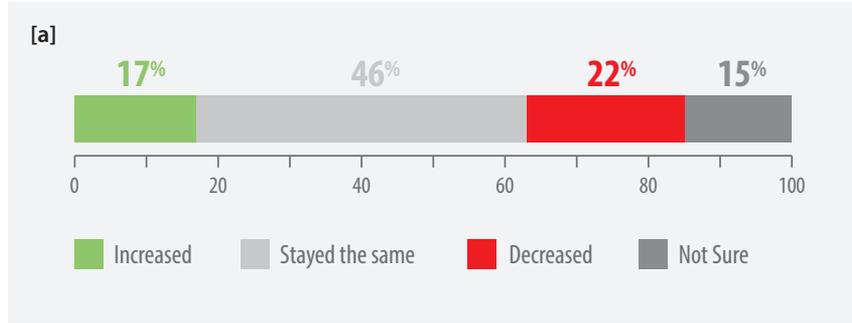
On the individual level, scientists may need to be more agile in the way they seek funding. This also presents new challenges as the demands for NIH grants and long-term pharmaceutical company interests are not the same.

Professional issues (difficulties in managing partnerships, lack of clear pathways to successful partnerships, lack of campus resources) are also perceived as significant barriers and collectively indicate the need for change. What researchers are begging for is a shift in the status quo.

Academic culture, which by its nature is slow to change, has been indirectly identified here as the most significant barrier to progress.

3: TRANSLATIONAL RESEARCH – CURRENT FUNDING SITUATION

Q: How has your funding for translational research changed in the last 12 months?



Q: Involvement in translational research improves my funding situation. Indicate your level of agreement.

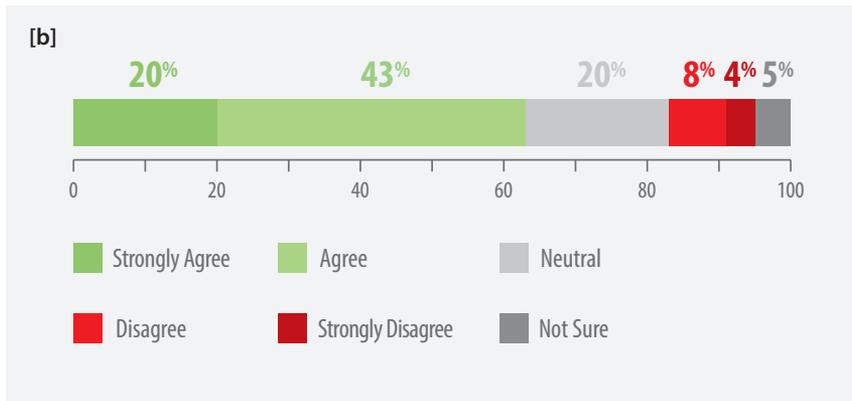


Figure 3. Translational research funding

The NIH and other funding organizations have acknowledged the “valley of death” between academic ideas and clinical applications, and they have invested heavily in programs and grants to enable academics to close this gap. As potential recipients of these investments, the majority (63%) of

respondents hold an optimistic view that they are more likely to be funded than their peers in other fields. However, despite this optimism, the majority of survey respondents have not seen an increase in actual funding. Only a small minority (22%) of respondents experienced a decrease in funding.

4: NEW TENURE REQUIREMENTS FOR FACULTY

Q: Considering patents and commercialization activities in tenure evaluations would encourage young researchers to pursue faculty positions in translational research. Indicate your level of agreement with this statement.

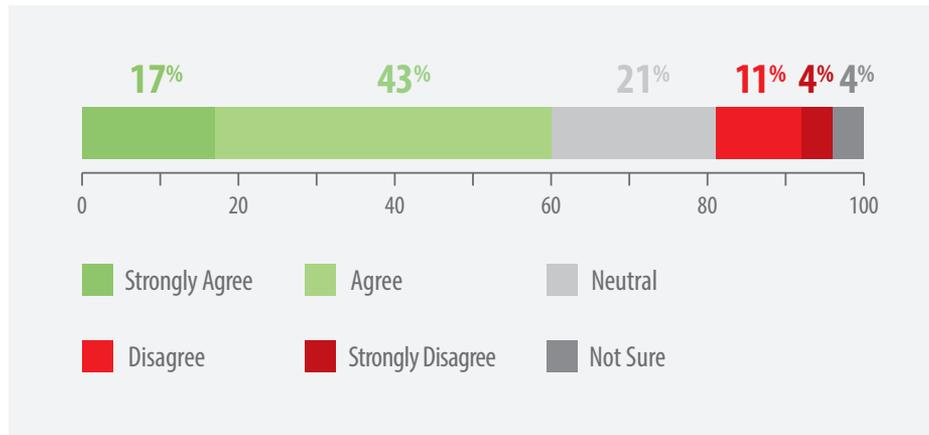


Figure 4. Revisions to tenure requirements

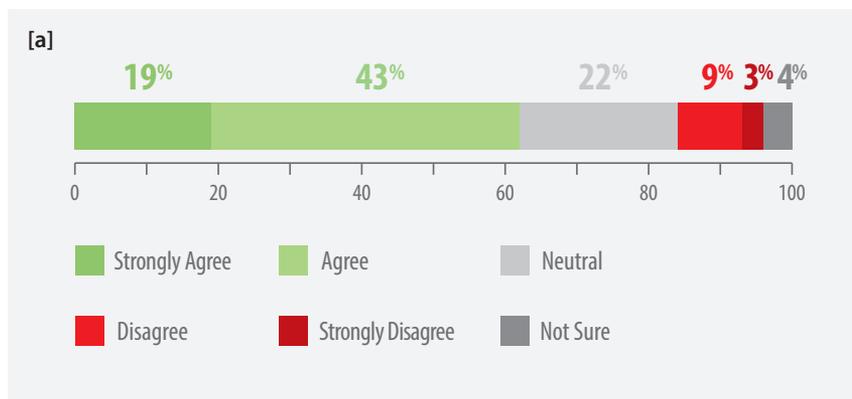
Translational research does not offer publishing opportunities in the same quantity that basic research does. In order to ensure careers align with expected hallmarks of success, it may be desirable to include other outputs of productivity, in particular those related to intellectual property, in tenure evaluations.

Currently, patents and commercialization activities are not considered in tenure evaluations for new faculty

at most research institutions. However, reforming this practice may be beneficial for the long-term growth of this field, as 60% of respondents agreed or strongly agreed that considering patents and commercialization activities in tenure evaluations would encourage young researchers to pursue faculty positions in translational research (Figure 4).

5: BUSINESS SCHOOL COLLABORATIONS

Q: Collaboration with an institution's business school would benefit translational research groups. Indicate your level of agreement with this statement.



Q: Does your research group currently collaborate with your institution's business school?

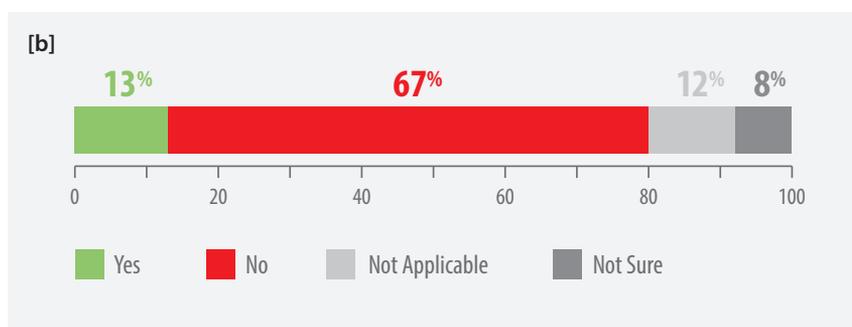


Figure 5. Business school collaboration attitudes (a) and practices (b)

Translational research and commercialization often go hand in hand, but the business implications and expedient commercial path may be difficult for bench scientists to adequately address by themselves. Although some universities offer courses for scientists, the business world is still an unfamiliar domain.

Translational scientists are getting into the commercial mindset, specifically in terms of building partnerships with their institution's business schools, as 62% agree or strongly agree that collaboration with their business school would benefit their research group (Figure 5a). However, only 13% of respondents actually collaborate with their business schools (Figure 5b). This lack of collaboration is due not to the lack of business

school presence, as only 12% of respondents did not have business schools at their institutions (Figure 5b). Rather, there appears to be a lack of certainty about how to get started or when a relationship would be appropriate to develop.

This presents an opportunity for business schools to teach scientists about the potential of and the steps needed to commercialize their research and vice versa. If people with this knowledge are not currently part of the business school, then the future opportunity lies with more science minded individuals, i.e., those with at least an undergraduate major in science, to pursue MBAs and create these types of valuable positions within institutions.

6: NETWORKING WITH PEERS

Q: How often do you seek counsel from academic scientists in other disciplines about how to conduct your studies to support downstream development?

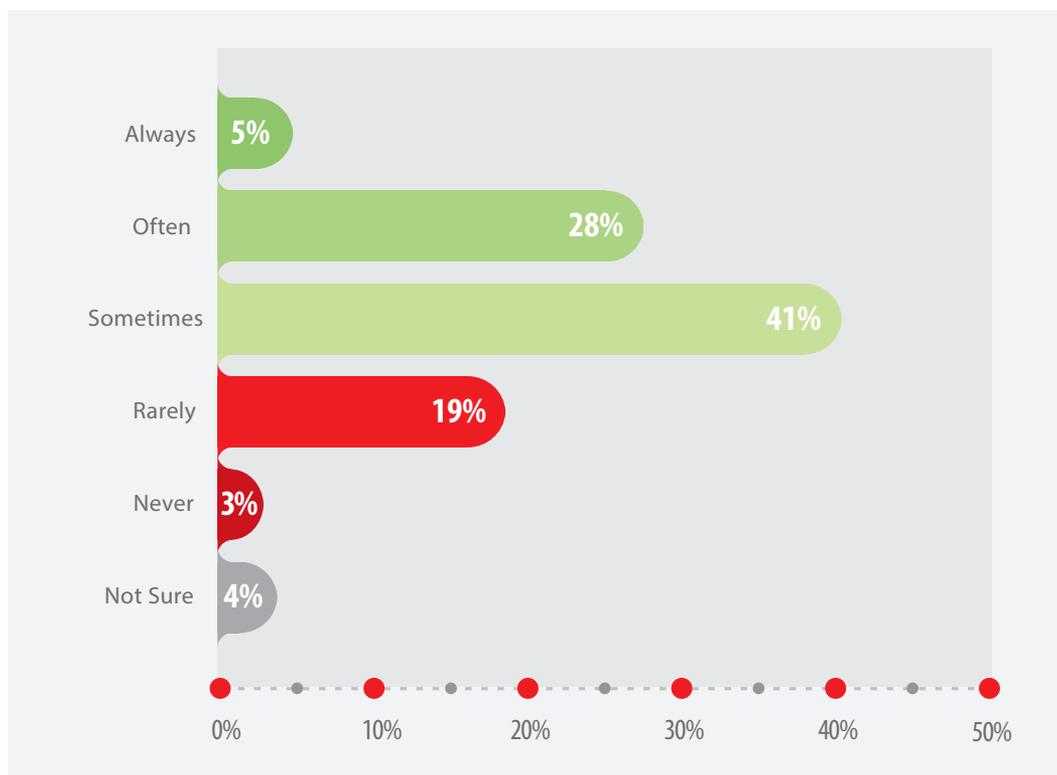


Figure 6. Interdisciplinary dialog

The chemistry–biology gap, i.e., the cultural difference between chemists and biologists that often frustrates communication, is well known to most interdisciplinary researchers. For translational researchers, this gap is wider and more perilous, because translational research requires interdisciplinary dialog.

Only one-third (33%) of respondents often or always consult with their peers on research matters. Nearly one-quarter (22%) of respondents rarely or never consult with their peers (Figure 6).

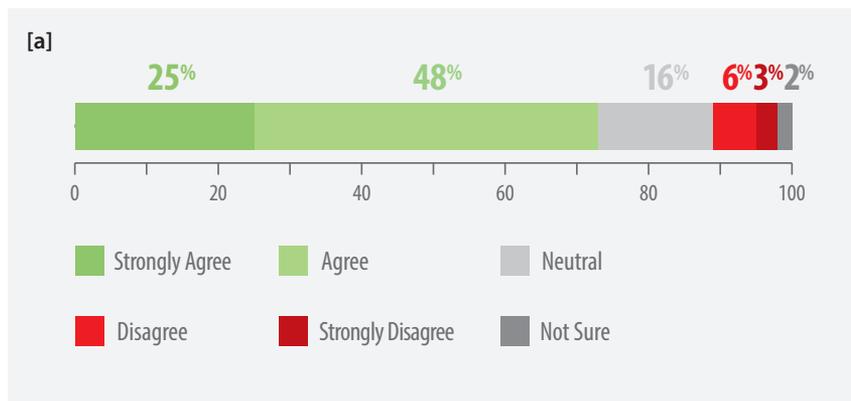
Academic culture can be slow to change. Traditional schools of thought that divide science into strict and separate fields such as biology and chemistry are still prevalent. It is not uncommon in academic research to value one's own field as superior to others, thus devaluing outsider commentary.

Although interdisciplinary collaboration is touted as valuable, channels to collaborate may not exist, potentially due to reasons such as internal resistance or geographical distance, i.e., departments are housed in different research buildings. Furthermore, with the pressure to “publish-or-perish,” researchers may not be sharing their findings for fear of their colleagues publishing before they do.

Open access and social media tools may encourage translational researchers to share their work, provided that they view sharing as an opportunity to be cited and acknowledged.

7: NETWORKING WITH INDUSTRY

Q: It would be helpful for industry scientists to provide commentary about the direction of my research at an early stage, based on their knowledge of compound toxicity, clinical needs, and commercialization issues. Indicate your level of agreement with this statement.



Q: Do you regularly consult industry scientists for commentary on your research at an early stage based on their knowledge of compound toxicity, clinical needs, and commercialization issues?

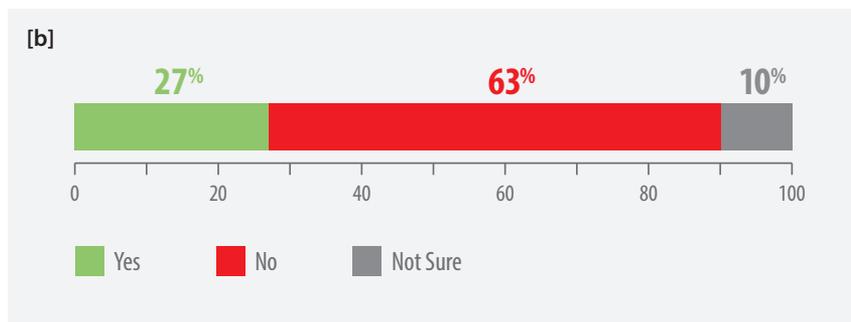


Figure 7. Academic scientists' attitudes (a) and practices (b) towards industry relationships

Therapeutic and device development are complicated, time-consuming processes. It is important for researchers to know in advance the weak points of their discoveries that may hinder the journey to the clinic. Industry scientists are useful resources for these types of insights, and 73% of respondents agree or strongly agree that it is helpful for industry scientists to provide commentary on their research at early stages (Figure 7a). However, despite the fact that respondents think this would be helpful, most do not consult industry scientists (Figure 7b).

There is again incongruence between what researchers believe are helpful and current practices.

It should, however, be a priority to work out the mechanism for early dialogs in order to protect both academic and industry interests, while also ensuring academic translational research can benefit from critical knowledge that leads to patient benefit. Fear of loss of intellectual property may be one reason why the majority of translational researchers are not currently consulting with industry, although they think it would be helpful.

8: ARE OUR RESEARCH STANDARDS TOO LOW?

Q: Do you believe it is necessary for individuals working in translational research to be held to a higher standard of laboratory practice/experimental design than those working in basic research? Why?

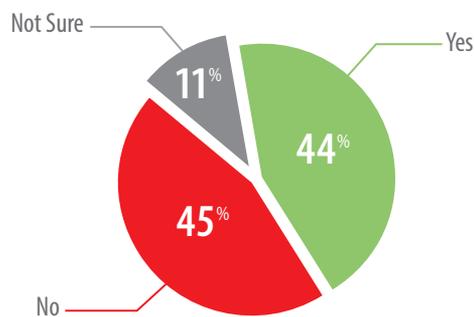


Figure 8. Translational research standards

Reproducibility and quality issues have been widely cited as barriers to drug development.^{1,2} Because of the direct human health implications of their work, should translational researchers be held to a higher standard of research?

Respondents were split evenly on this topic (Figure 8) and for different reasons (see verbatim responses on the following page). Interestingly, some respondents answered “no” because they believed that all research must be held to a high standard. Preconceived notions of existing standards, however, could be a hindrance to all researchers; they have been led to believe that current practices are reliable, but recent industry reviews indicate that academic translational research has serious reproducibility issues.

Representative Verbatim Responses:

Yes:

“A big topic...Clinical/human expectations are high and should be so for ethical reasons. Bench research can be allowed the flexibility of making errors and pursuing avenues that turn out to be fruitless.”

“Translational research in any field of science imparts tremendous effect on clinical practice. Therefore, it is very important for translational research scientists to practice high lab/experimental design standards. While I believe that the answer to this question should be ‘no’, I still feel that for translational science to be accepted, more rigorous investigations need to be performed in comparison to basic science.”

No:

“All should abide by the same high level of conduct in the scientific method, not just the translational scientists. If the basic discoveries are not valid, the translational effort is a waste of time.”

“All experiments have to have high standards. Translational or not...”

Not Sure:

“How do you categorize translational research? At what stage can you differentiate?”

“It depends on the subject of the research.”

Translational research is structurally different from basic research. Translational research has direct, immediate ramifications for patients, and translational researchers are more likely to have a pharmaceutical partner that bases funding on the validity of the research. A basic research grant from the NIH, for example, is not paid out on the basis of reproducibility (although this is starting to happen), thus no standard is directly enforced. If all grant payouts were based on reproducibility of results, would research standards increase across the board?

On the other hand, it is important to think about the following: At what point do high standards take away academic freedom? What is the responsibility of industry when it comes to translational research? At what point in the workflow should regulation begin and expectations rise?

Debate will be necessary to address this delicate issue. Clear guidelines or expectations about the quality of academic/non-profit translational research should be established. These may not need to be higher than those for basic researchers, but written guidelines will help translational researchers in the pre-clinical stage prepare their discoveries for licensing by pharmaceutical companies and fulfill career and moral goals of helping patients in need.

When establishing academic translational research standards there must still be some room left for exploration. It is important to remember that scientific experimentation is often an exercise in failure and at its core, a learning experience. New standards and regulations cannot be so extreme that researchers must limit the scope of their work to what is safest and most commercially viable.

¹ C.G. Begley, L.M. Ellis, *Nature* **483**, 531 (2012).

² F. Prinz, T. Schlange, K. Asadullah, *Nature Reviews Drug Discovery*, **10**, 712 (2011).

9: ON REPRODUCIBILITY

Q: Which of the following actions would you be willing to take to ensure that your research is perceived as reproducible? (Check all that apply.)



Figure 9. Willingness to ensure reproducibility

With increasing concern over reproducibility and budgets squandered on unverifiable science, the NIH may soon require researchers to validate the results and protocols in grant applications. This requirement would force many applicants to amend the fundamentals of their research process, from the way data are recorded to the types of reagents that are used.

The question remains as to what can be done to improve reproducibility. This spring *Nature* released a reproducibility checklist that must accompany manuscript submissions, but lab practices beyond the contents of this checklist may also need to be addressed. Ninety-seven percent of respondents were willing to take some type of action to ensure reproducibility, above and beyond what they are currently doing. Still, less than half of respondents think that translational researchers should be held to a higher standard (Figure 8). From the combination of these

data, it is apparent that translational researchers view the reproducibility of translational studies and the quality of their own work as separate.

Changes in laboratory methods appealed to the majority of respondents, suggesting that researchers are aware that these changes would help to ensure reproducibility. Those “method” changes are ones that can be made inside the lab without having to hire more staff or obtain outside input. Changes that required researchers to purchase materials or seek outside input received fewer responses.

Ninety-seven percent of respondents are willing to take some kind of action, thus strongly suggesting that the translational research community is open to change. Campaigns and initiatives to address reproducibility concerns are recommended.

10: EXPERIMENT REPEATS

Q: In your current lab, what is the minimum number of times an experiment is conducted before including the resultant data in a manuscript submission?

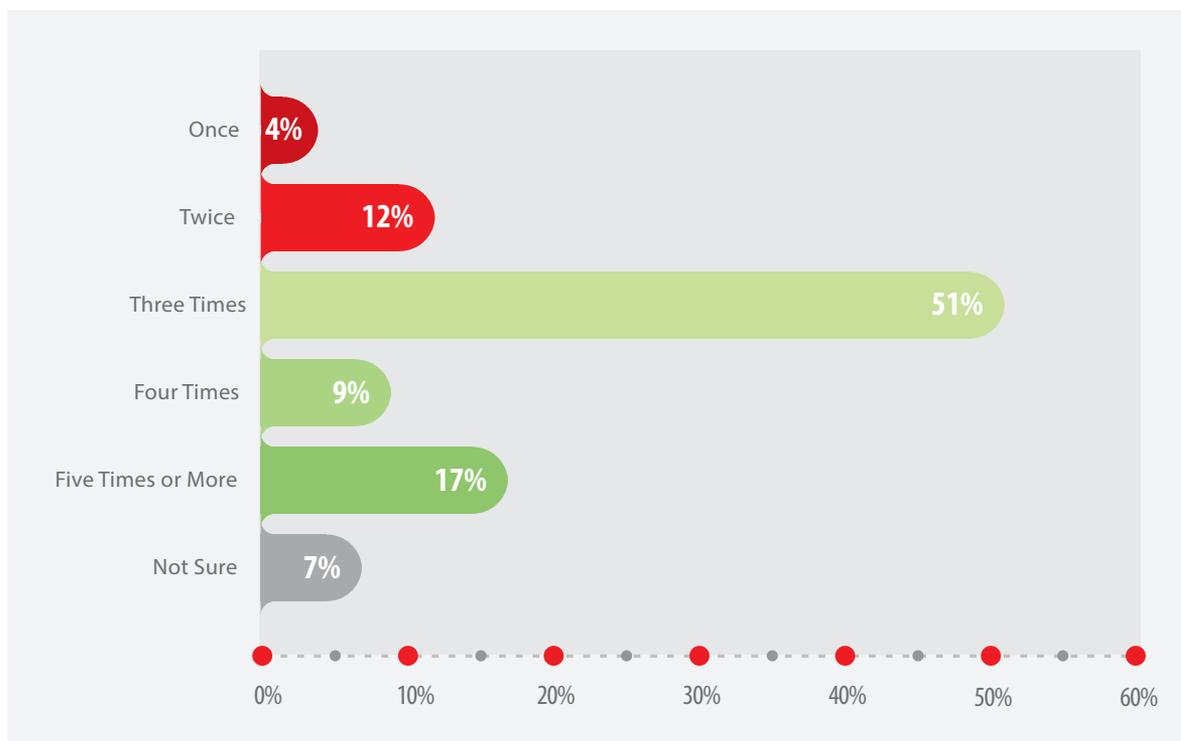


Figure 10. Minimum number of experimental repeats

Criticism about the current standards for pre-clinical research has called into question the reproducibility of published research findings. We remember from basic chemistry lab courses that we need to repeat our experiments three times to verify results. But do translational researchers adhere to this in practice?

The good news is that 77% of respondents are repeating their experiments at least three times (Figure 10).

However, it is concerning that approximately one in six (16%) researchers repeat experiments fewer than three

times before including the data in a manuscript (Figure 10). This has implications for the quality of data we see in manuscripts. How do we know if that research group has repeated their experiments sufficiently? Should we be taking the time to reproduce a published finding before we build upon it? Whose responsibility is it to make sure researchers repeat experiments three or more times? What types of experiments are repeated fewer than three times? Are there cases in which fewer or more than three repeats is necessary?

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