YALE JOURNAL OF BIOLOGY AND MEDICINE 94 (2021), pp.379-380.

YALE JOURNAL OF BIOLOGY AND MEDICINE
YJBM
CELEBRATING 90 YEARS 1928–2018

SPECIAL FEATURE: DISCUSSION

The Practice of Science as the Pursuit of Knowledge

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Choosing what scientific project to pursue is the most important decision that scientists at all levels continually face. Time devoted to a project can further desirable knowledge and advance a career or cost years in lost opportunity. Knowing what to consider before embarking on a specific scientific journey, as well as when to drop a project and change course, offers a way of practicing science that keeps us mindful of what is relevant at a given time and place while preserving our freedom to explore the most exciting findings. This article explores both the pressures that restrict this delicate decision-making process and the processes that scientists can apply to overcome those pressures. Above all else, as it turns out, we must still love the pursuit of knowledge for its own sake – and this love directly impacts our results.

I have always wanted to know more than what I was taught in a classroom. Starting in elementary school, the information communicated by teachers felt incomplete and compelled me to learn more. This meant visiting libraries, where I would read books and documents that had been succinctly presented in class. Because the teachers did not satisfy my curiosity, at the time, I thought that they were not doing a good job. In retrospect, I had excellent teachers because they triggered in me a desire to learn about particular topics and about how we know what we know.

All scientific projects start with a question. The question may take the form of a particular hypothesis that the project wishes to test. For example, one may want to solve the mechanism by which a particular molecule, such as a human hormone, triggers a response in specific tissues or to understand how an integral membrane protein mediates the movement of a specific solute across a membrane. Alternatively, a scientific project may be purely exploratory, entailing the collection of data that, when analyzed with the appropriate tools, are expected to provide a description of a particular phenomenon that, in turn, may generate new hypotheses. This is the case for studies that compare RNA, protein, or metabolite abundance in a cell prior to and after experiencing a stress condition or that survey the microbiota composition of different animal or plant tissues. *How do we choose a particular project from among the many that are possible?*

The most important consideration in choosing a project is how much the scientist cares about solving the question posed. We must truly want to know the answer to our question, rather than focus on its downstream effects, such as publishing a paper that reports the findings of the project (or uploading them into preprint servers), filing a patent for potential applications of the discovery, building a CV or resume, giving a talk, or

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Keywords: discussion, research project, practice of science, scientific literature

landing a job. Obtaining the answer often brings an immense satisfaction that energizes the scientist to continue on the scientific journey. As is often the case, finding an answer to a specific question raises further questions that could not have been imagined without the newly developed knowledge.

All this assumes that a scientist has absolute liberty to choose any project to pursue, which is not always the case and often depends on the stage of one's scientific career, availability of funding, and setting in which the project is being carried out. In the biomedical sciences, for example, graduate students and postdoctoral fellows at academic institutions or government laboratories tend to pursue projects that are of direct interest to the investigator heading the laboratory and that reflect its source of funding. However, this should not prevent junior scientists from identifying and following their own path within the realm of the host laboratory. I have had the immensely satisfying experience of mentoring trainees in my laboratory who – driven by intellectual curiosity – pursued research that was not part of the original plan and made amazing discoveries that opened up new areas of investigation.

Before even beginning to think about how a project will be carried out, find out whether an answer to the question that the project is designed to address is available from research reported by others. Even in the case of an affirmative answer, this does not necessarily mean that you must choose a different project. The current project may still be worth pursuing if the reported answer is wrong or incomplete. Junior members who actively explore knowledge from diverse sources can gain legitimacy (and potentially funding) by successfully carrying out a project because, frequently, an individual who has solved problems is more likely to solve a new problem than an individual who has yet to demonstrate this ability. Seniority and research funding also usually remove some of the constraints faced in choosing a project.

Once embarked on a scientific journey, how do we know when to change course? **It is essential to closely monitor the scientific literature.** The longer a scientist pursues a project or system, the more likely the scientist is to grow emotionally attached to it, which can make it difficult to leave the project or system behind. However, the question you posed may be solved and reported by others, and the chances of publishing the *same* findings dramatically decrease, at least in most respected journals.

Being well versed in the scientific literature at large is also critical because it allows scientists to make changes in the implementation of the project by adopting novel methodologies that allow for faster, more sensitive, and more accurate ways to carry out experiments. Moreover, we may change course by deviating from the original plan to investigate a more important topic as indicated by how the research findings fit with newly available knowledge. Over decades in the biological sciences, I have witnessed how the reluctance to change methodologies resulted in projects taking far longer than necessary, and how the refusal to deviate from a road map, say at a thesis proposal, prevented fellow scientists from pursuing the most impactful science, regardless of the journal in which it is published.

Certain projects have defined goals and objectives. For example, the development of a vaccine requires that it be safe, effective, and readily accessible to the target population. Even projects that pursue avenues solely for the sake of knowledge often give rise to unintended applications. For instance, investigation of the mechanisms by which bacteria resist the lethal effects of bacterial viruses resulted in the recombinant DNA and CRISPR/Cas technologies that have transformed research and generated a variety of products having an immense impact on human health. Thus, the desire to learn can itself result in valuable applications.

I love science, and it is this love that has most significantly sustained my career. I want to encourage a mindfulness that allows scientists to determine what is relevant at any given time and place, and to find the means to address it. The practice of science must at all times reflect a true pursuit of knowledge – with the freedom to choose the question one believes is most critical and the willingness to change course based on all obtained results.

Acknowledgments: I would like to thank Jennifer Aronson for the discussions, comments, and editing that resulted in this article.