ASBMB today

A monthly publication of
The American Society for
Biochemistry and Molecular Biology



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president's message

# The Yamamoto Plan

BY SUZANNE PFEFFER

Last month I wrote about the importance of explaining the significance of our research at every opportunity: in papers, in talks and in research proposals. Keith Yamamoto, executive vice dean of the University of California San Francisco School of Medicine, has played an incredibly important, behind-the-scenes role in steering the evaluation of U.S. science toward impact. He also has crafted a valuable scheme to help job and grant applicants be most successful; I call this the Yamamoto Plan and share it with you here.

First, a few words about Keith. One of my first wishes as a first-year graduate student was to rotate in the Yamamoto lab. My wish came true in the winter of 1978, and I remember coming in to lab on Saturday mornings only to find Keith sitting quietly in his office reviewing Journal of Biological Chemistry manuscripts. At that time, his office had a glorious view of the Golden Gate Bridge, so it was a pretty nice place for him to work. He won't remember this, but Keith personally taught me how to culture mammalian cells, and during my rotation, he reminded me that devising new methodologies is just as important as scientific findings because new techniques often can enable new discoveries.

In 1994, Harold Varmus, then director of the National Institutes of Health, asked Yamamoto if he would work with the Division of Research Grants (now the Center for Scientific Review) to enhance the NIH peer review process. Since that time, Yamamoto has served as chairman of the Advisory Committee to the CSR and as a member of the NIH director's Peer Review Oversight Group, the CSR Panel on Scientific Boundaries for Review, and the Advisory Committee to the NIH Director. He also co-chairs both the Working Group to Enhance NIH Peer Review and the Review Committee for the Transformational R01 Award.

Each of these committees has discussed the importance of distinguishing between science that just provides more information and thus moves the field horizontally, and transformational science that has the potential to move an entire field forward vertically. Now, during an era in which scientists can do so much more but must operate with tightly constrained resources, we need to select the questions that will provide the most important answers. I have said this before: Every cell has 10,000 proteins; we need to focus on the classes of protein functions that are most relevant to understanding fundamental biochemistry, biology and the molecular basis of disease. Over the past 15 years, Yamamoto has steered this important idea through the halls of NIH, culminating in several new mechanisms for support of especially bold ideas as well as new guidelines for the review of grant applications that stress overall impact over detailed approach. No country has enough research dollars to fund all possible science, and our limited dollars need to be directed toward the areas of greatest significance to the entire scientific community.

Yamamoto also has devised a plan to help UCSF junior faculty craft their first research grants. His approach can be useful to graduate students and postdoctoral fellows in conceiving research proposals for their theses,

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courses and fellowships. Industrial colleagues also may find value in this very wise plan. At UCSF (and also in my Stanford biochemistry department), grant-writing faculty members select a small number of colleagues to serve as an advisory committee. Several months before a deadline, the grant-writing faculty member drafts a single Specific Aims page highlighting the question to be addressed, why it is important and three to five sets of experiments that will advance our understanding. The role of the advisory committee is to help their colleague ensure that the research question, and the specific aims to approach it, will truly move that field forward vertically. Is the question impactful in concept and/or practice and clearly articulated? Are the experiments, even if bold and untested, technically feasible, and do they employ the most advanced approaches? Would a collaborator add conceptual or technical breadth to the potential outcome? Face-to-face conversations with the full committee uncover uncertainties and ambiguities, resolve differences of opinion, and often stimulate improvements. Then, and only then, does the scientist write the research proposal.

A major advantage of the Yamamoto Plan is that quality advice and mentorship can be obtained at an early stage, long before hours are wasted writing up what might not be the best approach. In contrast, scientists commonly seek feedback regarding a completed grant application just a few days before a deadline. At that point, it is way too late to send someone back to the starting block to recraft a proposal that is off the mark. Once you write an entire grant application, mental cement can set in.

The Yamamoto Plan provides, as he says, "honest feed-forward instead of less-than-honest feedback," saving time and effort for both applicant and mentors: Most scientists happily will read a one-page Specific Aims description carefully and provide forthright impressions.

Job candidates and prospective postdoctoral fellows take note: This plan can be used to hone your CV and research description before you apply for a job. An advisory committee also can prepare you for interviews; don't be shy in asking for help.

I recently reviewed what struck me as an unusual grant application from a successful and fairly well-known scientist. What was unusual was the fact that this applicant listed ten other well-known scientists as unpaid "key collaborators." The applicant could have carried out all the science described in his own lab, but including a list of collaborators left this reviewer with the impression that this long list of scientists really cared about the outcome of the proposal under review and would do all they could to support the project and guarantee its success. I recently have come to appreciate the importance and value of scientific collaboration and will write about that in greater detail in a future column. But I add it here as a reminder to younger scientists: Collaborations permit us to accomplish more with limited resources. Collaborations bring additional expertise and methodologies to our work. Our industrial colleagues understand the value of team science. Never be shy in asking for help to move your science forward, be it help with a set of experiments or help crafting a proposal.

And wholehearted thanks to Keith Yamamoto for helping all of us stay focused on impact. XXX