

Peer Review Notes Jan 2014

How Peer Reviewed Science Powers U.S Science and Health



“As we look to improve how NIH reviews grant applications, we shouldn’t forget that peer review works very well most of the time,” said CSR Director Dr. Richard Nakamura. “Scientific and health breakthroughs are heralded in the press almost every day. And you often can trace them back—directly or indirectly—to one or more NIH peer review groups that found great promise in an application.”

“There are powerful stories that need to be told,” he said. “They illustrate why support for peer-reviewed science is so important to

our future.” CSR is starting to do this by sharing stories like the one below.

The Blossoming of Regeneration Research

Dr. Alejandro Sánchez Alvarado didn’t have high expectations in 1997 when he submitted his first NIH application for independent research at the Carnegie Institution of Washington.

“I was trying to develop a model system that -- if not forgotten -- was at least the laughing stock of the scientific establishment,” said Dr. Sánchez Alvarado. He wanted to study regeneration in the flatworm (planaria). About the only individuals studying flatworms at the time were kids who watched them regenerate themselves from tissue bits in biology class.

“Most of the regeneration research in the U.S. at that time was being done in vertebrates and, for the most part, it was phenomenological,” he said. What made his application extraordinary was that he proposed to “develop tools to perturb and manipulate the process molecularly and genetically.”



“I had no evidence I could do this,” he explained. “I just had a list of experiments that needed to be done and a series of tools that needed to be developed . . . I hoped the little preliminary data I had could convince the review panel there was some really interesting biology to be discovered.”

“It was a bold application for a new investigator,” said Dr. Judith Greenberg, who was his Program Officer at the time. “And this was not the work he had done as a postdoc.” Dr. Greenberg is now

Acting Deputy Director at the National Institute of General Medical Sciences (NIGMS) and Director of its Division of Genetics and Developmental Biology.

Getting a “Bad” Score

His application was reviewed in October 1997, and six months later he anxiously tore open the NIH scoring letter.

“It was such a low score I thought I had flunked out,” said Dr. Sánchez Alvarado. “Before I got the comments, I called Dr. Greenberg for some advice on how to improve my score. After some paper rustling, she said, ‘I’m not at liberty to tell you anything now, but I can tell you -- in my experience at NIH – almost no one with this score has ever been denied funding.’”

“I got it totally backwards!” he laughed. No one had told him how the NIH scoring system worked.

Getting the Review Right

When the summary statement arrived, it stated: “This is an ambitious but exciting application . . . if successful, it promises to teach us much about the mechanism of regeneration . . . A great deal rests on the applicant developing transgenesis with planarians, but there is much confidence in Dr. Sanchez’s ability and this is further corroborated by the thoughtful and well documented strategy in the proposal which is backed up with alternative methodologies. Despite the risk involved, this was considered to be a most promising application”

“The reviewers got it right,” said Dr. Greenberg. “They overlooked the risk—or maybe embraced it—and they recognized the potential.”

“With this grant, he developed most of the tools needed,” she said “and he has reinvigorated the field of regeneration research and launched the careers of a lot of researchers.” He also has served as an NIGMS Council member and received an NIH MERIT Award. He currently is a Howard Hughes Medical Institute Investigator at the Stowers Institute for Medical Research in Kansas City, Missouri.

Advancing Basic Research

Because planaria and vertebrates share an incredible number of genes, the characterization of gene functions in planarians promises to advance studies of human stem-cell function, regeneration and wound healing. How this

could unfold is still a scientific mystery.

"It is really early to know what will come of this," said Dr. Sánchez Alvarado. "The linear plot of a good narrative would be that we might be able to identify a series of molecular cascades or cellular events that may be coaxed to promote or induce regeneration in organs or organisms that are not very good at it."

"Of course, science is never linear," he noted. "Still, in my heart of hearts, I think that to really understand and address many of the problems that afflict us, we need to look beyond the present emphasis to produce practical outcomes, which in my opinion is artificially restricting our way of interrogating life to unacceptably narrow confines and unsatisfactory depths."

Could NIH Fund this Kind of Application Today?

"I know it is tough these days," said Sánchez Alvarado. "But I think there is always room for good science and a need for new paradigms of investigations." He tells his students they need to "have a thick skin and deep-seated belief that what they are doing is important and it will matter down the road."

As a reviewer and former NIGMS council member, he understands the challenges reviewers face today when budgets are tight and there are so many really good applications to consider. "The granularity of resolution is not there for an individual reviewer to distinguish an A+++ from an A++ application, and both of these projects may be really, really important," he said.

He encourages reviewers to "fight for two or three applications they think are truly meritorious. Keeping an eye on the long-term is the best way to navigate this storm."

Know a Great Story Where Peer Reviewers Identified Research that Had a Big Impact? Let us know.