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First international workshops on Provocative Questions (PQ) in cancer research, October–November 2014, New Delhi, Bengaluru, and Thiruvananthapuram, India



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ABSTRACT

In 2011, the National Cancer Institute (NCI, USA) introduced the Provocative Questions (PQ) Initiative, a new approach allowing active researchers to define major unsolved or neglected problems in oncology unaddressed by existing funding. Last year, the U.S. NCI teamed up with the Indian Department of Biotechnology (DBT) to pilot the PQ approach in three cities in India. Workshop outcomes included the generation of fundable “PQs” (perplexing questions understudied by the international scientific community), as well as the identification of several non-PQ projects and research-related issues of importance to DBT and other Indian funding groups. The workshops clearly indicated the need to expand beyond crafting “PQs” when considering the best areas for research funding in international settings. Nonetheless, the first set of PQ workshops provided a forum to discuss key issues regarding cancer research in India, including the paucity of cancer research funding, and the lack of relevant human resource training and technology sharing platforms. Continued open debate between researchers, funders and policymakers will be essential to effectively strengthen the cancer research portfolio in India.

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1. Introduction

How best to allocate funds across a research portfolio is a key question for medical research funders. Within this context, funders often develop initiatives to stimulate research in specific understudied areas. In 2011, the National Cancer Institute (NCI, USA) proposed the Provocative Questions (PQ) Initiative, an innovative approach to define major unsolved or neglected problems in oncol-

ogy that were unaddressed by existing funding, but still deserving of special attention. A key feature of the PQ Initiative is that questions are proposed not by the NCI or its leadership, but rather by active scientists within the continuum of cancer research, including prevention, risk, cancer biology, detection, diagnosis, prognosis, therapy, outcome, and clinical effectiveness [1]. Given that the PQ Initiative was conceived in the context of NCI's already large, established program for funding across the cancer research continuum, its purpose was not to replace existing research funding, but rather to highlight areas of need and to stimulate inquiry in areas that receive less focus.

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The concept of holding an International PQ workshop was first conceived in January 2014 during discussions held between Dr. Harold Varmus (Former Director, NCI) and Dr. K. VijayRaghavan (Secretary, Department of Biotechnology, Government of India). Here, we summarize key outcomes from the first international PQ Workshops.

1.1. NCI Provocative Questions (PQ) initiative in the U.S.

In the U.S., most Provocative Questions have been generated through a set of moderated one-day workshops comprising a small group of leading scientists invited from the cancer research community. While some workshops have been open to participants with a wide range of research expertise, others have covered specific areas, such as aging and senescence, clinical practice, combination therapies, and small cohorts in epidemiology. Participants submit their most interesting question for discussion and consideration in advance, and the proposed questions are used to generate an agenda for the day's discussion. At the meeting, participants propose, refine, and prioritize research questions that address particularly compelling and understudied problems in cancer research. Augmenting the workshop process is a public website open to all researchers for submission of questions and comments (<https://provocativequestions.nci.nih.gov>).

Once a year, NCI staff review all PQs generated from the workshops and the website. The final set of questions is selected by expert judgment following an analysis of existing published literature and the funded portfolio of several major government funding bodies including the National Institutes of Health (NIH), the National Science Foundation, the Department of Energy, and the Defense Technical Information Center. The final PQs are funded through requests for applications (RFAs) issued using two mechanisms: the Research Project Grant (R01) and the Exploratory/Development Research Grant (R21). A recent analysis of PQ applicants in the U.S. indicates that U.S. PQ grants have attracted substantially more new investigators and applicants with medical degrees than the general NCI applicant pool [2]. Since the program's inception in 2011, four separate RFA's have been issued, under which 47 unique Provocative Questions have been opened for grant applications. In the years 2011 through 2013, 1822 applications were reviewed, 188 new grants approved, and \$74 million awarded in first year funding.

1.2. International NCI Provocative Questions (PQ) initiative

In January 2014, Dr. Harold Varmus (NCI) visited India to define opportunities for collaboration in cancer research and prevention with leading Indian institutions. During discussions with Dr. K. VijayRaghavan, Secretary of the Department of Biotechnology (a major funder of cancer research in India), the idea emerged of co-hosting an International PQ Workshop in India. Given differences in the cancer research portfolios, grant funding mechanisms, and funds available for research in the two countries, it was immediately evident that the workshop format would have to be modified to suit Indian needs, and that the process would continue to evolve after the first set of workshops. An organizing committee was comprised consisting of key individuals from NCI and DBT, and led by Dr. Edward Harlow, special advisor to the NCI Director.

To clarify the goals for the workshops, the organizing committee considered the following questions:

- Should the scope of topics be basic or applied, and should questions be restricted to those relevant to India, or should any questions relevant to cancer be considered?
- What were the expectations for PQ meetings in India, and what would the Indian partner agency (DBT) do with PQs identified through the process?
- Would DBT set aside funds and use RFAs to fund research in response to the questions developed (similar to the NCI), or would the questions be used in other ways?
- Would the PQ meetings be held with Indian scientists only or would U.S. and other international scientists also be invited?
- Should a wide range of experts be invited to the workshop, or were there particular topics that DBT wished to focus on for specific workshops?
- Do we invite questions that seek to better understand the cancer research needs in the Indian context even though they may not be 'provocative' in nature?

The committee decided that the main goal of the meeting would be to generate scientific discussion followed by the identification of a number of key fundable questions. All questions relevant to cancer would be considered, whether basic or applied, and whether particularly relevant to India or not. The final set of questions from the workshop would be funneled into both the usual NCI PQ process for generation of RFAs open to all investigators internationally, and would also be considered separately for funding in India. Given that various funding bodies exist in India, including the DBT, the Department of Science and Technology (DST), the Indian Council of Medical Research (ICMR), and the Department of Atomic Energy (DAE), and that these institutions fund different aspects of research in cancer, the specifics of funding in India would be decided after the questions were generated. The committee felt that the inclusion of both international and Indian scientists would be an important feature of the workshop. Three independent workshops would be held in different Indian cities, and each of these would be hosted by a leading research institution in that city: the National Institute of Immunology (NII) in New Delhi; the National Center for Biological Sciences (NCBS, Tata Institute of Fundamental Research) and the Stem Cell Institute inStem in Bengaluru; and the Rajiv Gandhi Center for Biotechnology (RGCB) in Thiruvananthapuram. Although the organizing committee considered specialized workshops focused on particular research disciplines in different cities, it was decided that researchers across the spectrum would be invited to each. Each workshop would be limited to a maximum of 25 participants (15 from India and 10 from other countries across the globe) to allow small group discussion and deeper consideration of each question. The workshops were jointly funded by the NCI and DBT.

During the development of the pilot PQ workshops in India, the organizing committee made a series of modifications to the usual U.S. format, summarized below.

1. Website. In order to facilitate participation from a wide range of Indian scientists and experts, the organizing committee felt strongly that the website should play a larger role in the Indian PQ Initiative than it has in the U.S. As a result, a special section for posting Indian PQs was added to the NCI PQ website. The link to the website was disseminated widely to Indian cancer investigators through the DBT, and researchers were invited to post questions on the website. Two months prior to the workshops, experts from NCI and India reviewed website-generated PQ's, and a small number of researchers who posed interesting Provocative Questions were invited to participate in person at the workshops.
2. Observers. Given the keen interest in participating in the workshops, and the limited number of available spots, each PQ workshop allowed a small number of observers who did not participate in the main discussions, but were invited to submit one question in writing at the time of the workshop. In addition, after

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