recognized limitations of a higher order of magnitude than previously seen in the field, owing to the nature of the technology. Uncertainties in genetic testing are nothing new, however, and we certainly have the foresight and fortitude to develop tools to deal with these issues. Therefore, we must continue to move forward and work together to use this powerful and promising technology to the best of its ability to benefit medicine.

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Tackling Neglected Areas of Oncology with Provocative Questions

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In an era of low funding rates and tightening budgetary constraints, researchers are inevitably nudged toward taking a conservative approach and thus focus on safe research questions to which answers are likely to be found. This approach not only risks limiting the scope of conducted research, but also discourages thinking outside of the box and tackling highly ambitious and not immediately obvious questions, or questions that have proven exceptionally difficult to address. Yet answering these types of questions may have very important ramifications for both clinical medicine and the advancement of scientific knowledge.

To combat these issues, the US National Cancer Institute (NCI) developed the Provocative Questions initiative, an innovative new program aimed at promoting research in neglected and unsolved areas of oncology (1). Through workshops held at NIH and other locations across the US, the NCI solicited perplexing questions in cancer research that need to be addressed, but would usually be hard pressed to receive substantial attention. The scope of this process was expanded through the NCI’s Provocative Questions website (2), where scientists from around the world could propose their own intriguing questions, comment on existing questions, and learn more about the Provocative Questions initiative.

The importance of the 24 most appealing questions, as well as the likelihood and the potential implications of answering them, are described in detail at the Provocative Questions website (2). Examples of these questions include:

1. Given the recent successes in cancer immunotherapy, can biomarkers or signatures be identified that can serve as predictors or surrogates of therapeutic efficacy?
2. How does the lifespan of an organism affect the molecular mechanisms of cancer development, and can we use our deepening knowledge of aging to enhance prevention or treatment of cancer?
3. What environmental factors change the risk of various cancers when people move from one geographic region to another?
4. Given the appearance of resistance in response to cell-killing therapies, can we extend survival by using approaches that keep tumors static?

The NCI provisionally set aside $15 million from the 2012 budget to fund the most powerful ideas for answering any of the 24 provocative questions in cancer research. The request for applications received a strong response, with each question catching the interest of several scientists. Although this response is perhaps not surprising in the current funding climate, it does imply that many re-
Searchers are keen to tackle neglected areas of cancer research given an appropriate funding opportunity. As a result, the NCI plans to add additional provocative questions to the current list through website suggestions and further workshops. In addition, they plan to issue requests for applications annually for at least the next 2 years, with the possibility of expanding the program in the future. Although it will likely take several years before satisfying answers to these questions are uncovered, the NCI Provocative Questions initiative has provided an avenue to begin tackling neglected areas of oncology.

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