How can we stimulate translational research in cancer genomics beyond bench to bedside?

To the Editor: A huge expansion in cancer “omics” research—including germline and somatic mutation analysis, gene expression, epigenomics, and proteomics—is promising a new era of personalized cancer care and prevention.¹ Nevertheless, to maximize the health benefits from genomic discoveries, translational research is needed to move basic science discoveries—not only from the bench to the bedside but also to clinical and public health practice.² Several advisory and working groups have been cautioning about the chasm between basic science discoveries and translation to population health benefits.³ Khoury *et al.*² proposed four phases of translational research in genomic medicine. T1 research (bench to bedside) develops candidate health application (e.g., test or therapies). T2 research evaluates candidate applications and leads to evidence-based recommendations and guidelines. T3 research assesses how to implement and integrate an evidence-based recommendation into practice. T4 research assesses health outcomes and population impact. The authors also found that less than 2% of published genomics research between 2001 and 2006 was post-bench to bedside (T2 and beyond). We recently applied this framework to a portfolio analysis of National Cancer Institute (NCI) fiscal year 2007 (FY2007) extramurally funded research

in cancer genomics.⁴ We found that of the 1,019 funded grants, there was little funded and conducted research in the later phases of translation (T2 and beyond); only 18 grants (1.8%) were funded in this area.

In order to evaluate the current status of translational research in cancer genomics, we updated our analysis of the NCI cancer genomics grant portfolio for FY2010. One key goal for this updated evaluation was to assess the impact of the American Recovery and Reinvestment Act of 2009 (ARRA) “stimulus” funds, which included a special request-for-application (RFA) announcement for Research and Research Infrastructure “Grand Opportunities” grants program to conduct comparative-effectiveness research in genomic and personalized medicine.⁵

Of the 2,137 research grants funded in FY2010 that fit our inclusion criteria, 1,989 (93.1%) were regular non-ARRA-funded research grants, and 148 (6.9%) were ARRA-funded. Examples of types of studies in each translation research phase are shown in [Table 1](#). Only 36 (1.7%) of the grants we reviewed were classified as T2 or beyond: 14 were T2, 21 were T3, and 1 grant was classified as T4. This distribution is similar to the finding from the FY2007 portfolio analysis.

However, when we stratified our analysis by type of projects, we found that among the regular non-ARRA grant pool ($n = 1,989$), only 28 (1.4%) of the grants were T2 or beyond: 10 were T2, 17 were T3, and 1 was T4. On the other hand, among ARRA-funded projects ($n = 148$), 8 (5.4%) of the grants were classified as T2 or beyond: 4 were T2 and 4 were T3. Seven of the eight ARRA grants were T2 or beyond projects that were

Table 1 The continuum of translational research in cancer genetics: types of research and examples from the portfolio analysis

Translation research phase	Notation	Examples of types of research	Example from portfolio analysis
T0	Gene and other discoveries	GWASs, candidate gene studies	A GWAS of prostate cancer in African Americans
T1	Discovery to candidate health application	Phase I and II clinical trials; observational studies to characterize genes and gene–environment interaction; pharmacogenomics	Prospective validation of genomic signatures of chemosensitivity in non–small cell lung cancer
T2	Health application to evidence-based practice guidelines	Phase III clinical trials; observational studies; evidence synthesis and guidelines development	Clinical utility of genetic markers associated with early-onset prostate cancer Programs in clinical effectiveness of cancer pharmacogenomics
T3	Practice guidelines to health practice	Dissemination research; implementation research; diffusion research; phase IV clinical trials	Sociocultural factors and BRCA genetic counseling for diverse Latinas Building a genome-enabled electronic medical record
T4	Practice to population health impact	Outcomes research; population monitoring of morbidity, mortality, benefits, and risks	Lung cancer model: risk, progression, and intervention

GWAS, genome-wide association study.

funded through the Research and Research Infrastructure “Grand Opportunities” grants program.

As a result of the ARRA, in 2009, we saw stability in translational research funding beyond the bedside in our FY2010 search. However, when evaluating the NCI’s general grant portfolio for FY2010, we found that only 1.4% of cancer “omics” grants were T2 and beyond. This is a slight decrease from the 1.8% in the FY2007 grant portfolio. Because there is no new stimulus funding for this type of research on the horizon, we are concerned about the sustainability of cancer genomics translational research beyond bench to bedside.

The NCI has a strong record of funding basic science work in cancer genomics discoveries and early translation (bench to bedside) of these discoveries. This is not matched by funding to assess the value added of genomic discoveries in practice and measuring their health impact. Although our analysis highlights the continued lack of funding for translational research (beyond bench to bedside) in cancer genomics, the barriers to this type of research are unclear. Are investigators not submitting post-bedside applications to NCI? Is the National Institutes of Health review process not supportive of these types of applications? No matter what the cause, NCI will continue to find solutions to overcome the barriers to funding post-bedside research. Targeted funding announcements (such as the Clinical Sequencing Exploratory Research funding announcement released by the National Human Genome Research Institute⁶) may be one way to spark this type of research. The post-bedside translational research gap will need to be filled in order to fulfill the promise of gene discoveries for cancer care and prevention in the 21st century.

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