

# Translational Research Portfolio for the NCI Translational Research Working Group

## Introduction and Summary

The National Cancer Institute (NCI) supports research that spans basic through clinical investigations. Specific research awards may predominantly address basic research, translational research, clinical research, or a combination. The NCI's fiscal year 2004 research portfolio was analyzed to understand the Institute's overall effort in translational research, to inform the deliberations of the NCI Translational Research Working Group (TRWG), and to serve as a pilot for future efforts at analyzing translational research. This document presents the methods used for identifying NCI's translational research awards and programs and the summarized results of the analysis.

## Key Findings

1. **The portfolio analysis identified awards valued at \$1.3 billion (relative to a total NCI research budget of \$4.4 billion in FY 2004<sup>1</sup>) that fit the inclusion criteria for “translational research”** (see subsequent discussion for specific criteria). As the criteria were applied expansively—including as “translational” all awards that had any translational component—the portfolio likely overestimates the value of NCI-sponsored translational research. A more detailed assessment of a sample of 65 R01 awards for the degree of their translational research relevance (see page 4 – Validity of Translational Research Funding Estimate) suggests that this estimate of overall funding for translational research may be high by 20-40%.
2. **Awards identified as “translational” are distributed throughout the Institute.** All NCI award-sponsoring Offices, Centers, and Divisions fund translational research, to varying degrees (Figures 1A, 1B, and 1C).
3. **Awards identified as “translational” are distributed across many different funding mechanisms to varying degrees** (Figures 2A, 2B, and 2C and Tables 1 and 2). Approximately the same dollar value of “translational” funds is awarded through program and cooperative award mechanisms and through individual research awards.
4. **The majority of “translational” funds are awarded to institutions with NCI-designated Cancer Centers** (Figures 3A and 3B). The percentage of NCI funding identified as “translational” at both institutions with NCI-designated Cancer Centers and those without them is similar (Figure 3C).

## Methodology

### Criteria for Including Awards as “Translational Research”

The scope of activity of the TRWG can be defined as “early translation” based on the continuum developed by the President's Cancer Panel.<sup>2</sup> With this and the interest in capturing the broadest possible landscape in mind, criteria were defined to identify awards to be included in the analysis. An award abstract that met at least one of the inclusion criteria for a single specific aim was considered “translational,” even if a significant portion of the proposed work did not meet the criteria. Generally, awards were identified as “translational research” based on the award abstract proposing to conduct research that would result in moving a discovery along the pathway to a defined clinical goal or product according to the bench-to bedside model, including using clinical research results to guide basic laboratory studies. If an award abstract did not meet any of the inclusion criteria, the award was not considered translational.

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<sup>1</sup> “Fact Book,” National Cancer Institute, 2004, Page B-2. <http://fmb.cancer.gov/financial/04Factbk.pdf>. Total NCI budget in FY 2004 was \$4.7 billion, from which the \$329 million for “Program Management and Support” was excluded.

<sup>2</sup> <http://deainfo.nci.nih.gov/advisory/pcp/pcp04-05rpt/ReportTrans.pdf>.

The following criteria were used to identify awards to be included in the portfolio:

- Studies of agents, including chemical, biological, immunologic, imaging, etc., at any stage from evaluating the agent in relevant model systems through Phase 2 clinical trials.
- Studies of markers and assays to measure the efficacy of an agent or interventional device, at any stage from development of an assay to testing for clinical utility in preclinical and clinical studies.
- Studies of interventional devices anywhere along the continuum from building a complete prototype device to testing a device in Phase 2 clinical trials in humans.
- Studies of biomarkers and assays for detection, diagnosis, prognosis, and prediction anywhere along the path from epidemiologic findings to a trial of the clinical utility of the marker in humans.
- Studies of imaging devices anywhere along the continuum from building a complete prototype device to testing the clinical utility of the device in humans.
- Endogenous (e.g., genetic and molecular) and exogenous (e.g., viral, dietary, and environmental) epidemiologic studies involving a sample population of at least 150 cases.
- Awards that include the creation or expansion of repositories of cohort data and/or specimen banks.
- Lifestyle, dietary, or behavioral studies that develop and validate or test an intervention for cancer control and/or prevention purposes (e.g., tobacco use cessation, changes to diet/exercise, and increased participation in cancer screening).
- “Bedside-to-bench” studies in which results from preclinical and clinical studies of agents and devices are used to enhance the capacities of the agents or devices, including the evaluation of basic mechanisms newly inspired by the preclinical or clinical studies.
- Awards for core facilities and shared resources involved in translational research.
- Awards that propose to conduct Phase 1 and/or Phase 2 clinical trials.
- Phase 3 clinical trial awards that include a correlative research component.

The following are examples of types of awards that were not considered “translational”—awards that fell only into these categories were excluded from the translational research portfolio:

- Discovery or mechanistic studies.
- Studies designed entirely to develop a model, whether biologic, population, statistical, or other type.
- Small-scale, hypothesis-generating epidemiology studies.
- Development of tools to enable basic or clinical research (e.g., computer software, nonclinical assays, and enhancements to proteomics/arrays).
- Late-phase clinical trials, with no indication of correlative components.
- Surveillance, survivorship, and outcomes research.
- Studies to develop components of new devices/assays but not to develop a complete prototype device or assay.
- Development of educational materials for care providers or general cancer educational materials—materials not directly intended to change a behavior to control or prevent cancer.
- Studies that reference long-term translational goals subsequent to the current grant funding period.
- Awards for which the abstract is ambiguous or unavailable.

## Data Collection

The analysis was based on all awards active in Fiscal Year 2004 as contained in the Cancer Research Portfolio database system.<sup>3</sup>

Analyzing research projects requires either using data from an established coding system or evaluating research project abstracts to classify the projects. Translational research is not captured in any of the codes applied to grants, such as Special Interest Category (SIC) or NIH Clinical Aspect (NIHCA) codes; therefore, individual project abstracts were evaluated to identify the translational grants. Projects were filtered to limit the analysis to the subset of the portfolio most likely to include translational research projects. A set of funding mechanisms and initiative programs was entirely included in the analysis due to the focused translational nature of the programs (e.g., Specialized Programs of Research Excellence [SPORes], Small Business Innovation Research [SBIR]/Small Business Technology Transfer [STTRs], and Rapid Access to Intervention Development [RAID]). For other funding mechanisms, the NIHCA<sup>4</sup> code was used to filter the projects to analyze only those with 25%–100% clinical aspect. Other funding mechanisms were entirely excluded due to either the unavailability of abstracts (e.g., contract awards such as the N01 mechanism) or their emphasis of non-research goals (e.g., training and education awards such as T32 and R25).

The following award categories were included without review of abstracts or specific application of the inclusion criteria due to (1) the lack of detail in project abstracts and the perception that these are translational and (2) the inclusion of Phase 1 and 2 clinical trials as translational research:

- All Clinical and Comprehensive P30 Cancer Centers (but no Basic Cancer Centers)
- All K12 mechanism clinical oncology research career development awards
- All projects of the RAID and Drug Development Group (DDG) programs, sponsored by the NCI's Developmental Therapeutics Program
- All projects of the Rapid Access to Preventive Intervention Development (RAPID) program, sponsored by the NCI's Division of Cancer Prevention

In the following award categories, abstracts were reviewed for translational components according to the inclusion and exclusion criteria:

- All awards funded through the following initiatives: Specialized Programs of Research Excellence (SPORes), Early Detection Research Network (EDRN), Mouse Models of Human Cancers Consortium (MMHCC), Network for Translational Research: Optical Imaging (NTROI), In Vivo Cancer Molecular Imaging Centers (ICMICs), and Integrative Cancer Biology (ICB)
- All Phase 1 and Phase 2 SBIR and STTR awards (mechanisms R41, R42, R43, and R44)
- All intramural research awards (Center for Cancer Research [CCR] and "Parent" Division of Cancer Epidemiology and Genetics [DCEG])
- R24 and U24 Core facility awards

In the following award categories, only awards with 25%–100% NIHCA codes were reviewed for translational components according to the inclusion and exclusion criteria:

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<sup>3</sup> The Cancer Research Portfolio (CRP) is a public website with information on cancer research and funding opportunities gathered from the NIH-wide Information for Management, Planning, Analysis, and Coordination (IMPAC II). The CRP is managed through the NCI Office of Science Planning and Assessment.

<sup>4</sup> NIHCA codes are quartile-based measures, assigned by NCI's Research Analysis and Evaluation Branch (RAEB), of the relevance of projects to the NIH definition of clinical research. NIH defines human *clinical research* as follows: (1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, or (d) development of new technologies. (2) Epidemiologic and behavioral studies. (3) Outcomes research and health services research.

- K01, K05, K07, K08, K22, K23, and K24 career development awards
- P01, P20, R01, R03, R21, R33, R37, U01, U19, U54, and U56 awards

Awards coded as translational were stratified using sponsoring division, the common scientific outline (CSO) codes, and the institutions where the research grants are held to identify patterns of translational research projects. For example, research institutions were aggregated into 3 categories based on the available institutional data. All translational intramural awards were collected in one category, and the translational extramural awards were divided into 2 categories—those where the research grants were held at clinical and comprehensive NCI-designated Cancer Centers and those where the grants were held at other institutions (including basic Cancer Centers).

### Assessment of Inclusion Criteria—P01/R01 Analysis

To gain insight into the validity of the classification system for P01 and R01 awards, two analyses were undertaken. First, NCI program directors identified awards in two groups: translational and not translational. They identified a total of 7 P01 awards as translational and 11 P01 awards as not translational. For each of these awards, the classification assigned by the program directors was compared with the classification of these same awards in the original portfolio analysis based on review of the abstracts. In this exercise, 6 of the 7 P01 awards identified as translational by the program directors had also been coded as translational during the original portfolio analysis. Moreover, 9 of the 11 P01 awards identified as not translational by the program directors had also been coded as not translational during the original portfolio analysis.

Second, a set of 36 R01 awards active in FY 2004 were identified by TRWG members as translational awards. The classification of these awards based on abstract review during the original portfolio analysis was as follows:

- 30 awards had been classified as translational
- 2 awards had been classified as not translational
- 4 awards were not included in the abstract review because they had a 0% NIHCA code

These results indicate that the inclusion criteria were reasonably accurate in identifying awards that would be considered translational by NCI program directors and TRWG members

### Validity of Translational Research Funding Estimate

To gain insight into the accuracy of the translational research funding estimate (see Table 1), 100 randomly selected awards from the list of R01 awards classified as translational in the original portfolio analysis were evaluated for the extent to which they were truly translational based on specific aims. Of the 100 awards, 65 were determined to have abstracts that clearly identified specific aims. Each of these 65 award abstracts was reviewed a second time to assess the extent of translational research relevance and assigned a translational score according to the percent of the specific aims that were considered translational. Of the 65 awards reviewed, 40 received translational scores of 76%–100%, 8 received scores of 51%–75%, 13 received scores of 26%–50%, and 2 received scores of 1%–25%. The remaining 2 projects previously identified as translational based on the original abstract review were considered to have no translational components in this second review. Applying these translational scores to calculate a weighted average of translational character for this set of awards suggests that the overall estimate of funds attributable to translational activity may be overstated by approximately 20-40%.

## **Findings: Translational Research Awards by Award Category**

Table 1 summarizes by mechanism the awards coded as “translational.” The mechanisms are also grouped by award category. The second column identifies the number of active awards identified as “translational” according to the criteria discussed earlier. The third column identifies the total number of active awards in that mechanism in FY 2004. The fourth column is the result of dividing column 2 by column 3, to show the percentage of awards in that mechanism identified as translational. The fifth column shows an estimate of the total funding in FY 2004 for the awards coded as translational.

“Awards for core facilities and shared resources involved in translational research” was one of the inclusion criteria employed. That criterion identified a set of award mechanisms that fund research infrastructure, including the Cancer Centers (P30 mechanism) and R24 and U24 awards. As these infrastructure awards may be used for purposes spanning basic, translational, and clinical research, they were separated from those mechanisms intended to fund translational research projects. These infrastructure awards are summarized in Table 2. It was also noted that many of the collaborative research mechanisms (e.g., P01, and P50) also fund core facilities as one facet of the overall award. Therefore, these core facilities were evaluated for the degree to which they supported translational research and the results are included in Table 2.

**Table 1. Awards Identified as Translational by Project-Funding Mechanisms**

Award Category	Awards Coded as Translational	Total Active Awards <sup>a</sup>	% of Active Awards Coded as Translational	Estimated Funds in FY04 for Translational Awards (\$M)
<b>Program and Cooperative Awards</b>				
P01	107	207	51.7	215.0
P20	8	34	23.5	3.0
SPORE (P50)	58	58	100.0	131.7
ICMIC (P50)	7	7	100.0	15.8
EDRN (U01/U24)	28	28	100.0	21.8
MMHCC (U01)	10	23	43.5	8.1
Other U01	122	209	58.4	98.6
U19	5	18	27.8	3.7
NTROI (U54)	3	3	100.0	3.8
Other U54	10	19	52.6	13.0
U56	4	40	10.0	1.6
DDG projects	18	18	100.0	11.1
RAID projects	45	45	100.0	16.3
RAPID projects	19	19	100.0	3.1
<b>Career Development</b>				
K01	14	116	12.1	1.9
K05	1	19	5.3	0.1
K07	37	93	39.8	4.8
K08	21	139	15.1	2.5
K12	21	21	100.0	8.8
K22	13	42	31.0	1.4
K23	55	64	85.9	6.8
K24	25	34	73.5	2.2
<b>Individual Research</b>				
R01	1,161	4,450	26.1	447.0
R03	150	320	46.9	8.1
R21	288	599	48.1	43.8
R33	62	121	51.2	24.2
R37	11	74	14.9	6.6
<b>Small Business</b>				
R41 (STTR Phase 1)	28	42	66.7	4.7
R42 (STTR Phase 2)	12	19	63.2	3.8
R43 (SBIR Phase 1)	87	246	35.4	13.3
R44 (SBIR Phase 2)	102	176	58.0	39.4
<b>Intramural</b>				
Z01	257	630	40.8	164.4
<i>Total:</i>	2,789	7,933	35.2	1,330.4

<sup>a</sup> Total Awards identified as being active in fiscal year 2004 from the Cancer Research Portfolio (intramural awards and initiative programs like ICMIC), the Developmental Therapeutics Program (DDG and RAID), the Division of Cancer Prevention (RAPID) and the Research Analysis and Evaluation Branch (all other mechanisms).

**Table 2 – Awards Identified as Translational by Infrastructure-Funding Mechanisms**

Award Category	Awards Coded as Translational	Total Active Awards	% of Active Awards Coded as Translational	Estimated Funds in FY04 for Translational Awards (\$M)
<b>Infrastructure<sup>a</sup></b>				
P30 Cancer Centers	54	61	88.5	212.5
R24	8	43	18.6	1.5
U24 (excluding EDRN)	8	14	57.1	6.0
<i>Total:</i>	70	118	61.0	220.0
<b>Extramural Core Facilities</b>				
Core Facilities supported through SPORC, P30, and P01 awards <sup>b</sup>	1,165	1,364	85.4	N/A

<sup>a</sup> It should be recognized that some individual awards of “project-funding” mechanisms are in fact used to fund infrastructure (e.g., 14 Z01 and 2 U54 awards were identified that were solely for infrastructural purposes) and some Cancer Center funds are used to support projects.

<sup>b</sup> The Extramural Core Facilities section shows numbers for the core facilities identified at SPORCs, comprehensive and clinical P30s, and translational P01s (Awards Coded as Translational) and at all SPORCs; basic, comprehensive, and clinical P30s; and translational and non-translational P01s (Total Awards Reviewed). The number of core facilities is not directly related to the estimated FY2004 funding of the Infrastructure award category, which does not include funds for SPORCs and P01s.



## Future Considerations for Translational Research Analysis

### Recommended Improvements in Award Coding System to Facilitate More Accurate Analysis of Translational Research Portfolio

At the time the portfolio analysis exercise was prepared, it revealed that there is no existing coding system that captures translational research; the TRWG therefore developed an *ad hoc* system to support its deliberations. The *ad hoc* system was labor-intensive to apply and resulted in a set of findings that some TRWG members found to be counterintuitive (especially the overall size of the enterprise and the substantial amount of translational research conducted under individual investigator awards). Managing translational research more effectively in the future requires a more logistically straightforward and precisely defined method for coding awards as translational research. To that end, the following recommendations are made.

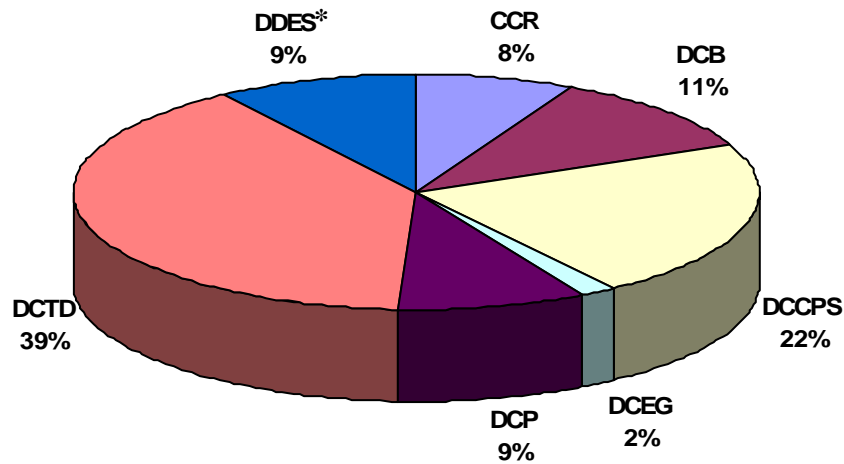
1. ***New coding methods need to be developed to identify, classify, and categorize “translational research.”*** As shown in Figure 4, awards identified as “translational” are distributed across NCI’s CSO codes. Figures 5A and 5B show that awards identified as “translational” are distributed across NIHCA codes as well. Moreover, analysis of the R01 awards designated as translational by TRWG members suggests that the 0% NIHCA code also contains some translational projects. Figure 5B suggests that NIHCA codes are a partially effective filter, however, as the likelihood of being identified as “translational” increased from the NIHCA 25% quartile to the 75% quartile.<sup>5</sup> The difficulty in using standard coding mechanisms in classifying research as “translational” or “not translational” suggests that new mechanisms need to be developed to identify, classify, and categorize “translational research.” It will be important to code several specific aspects of translational research (e.g., study population by organ, stage of cancer development; intended clinical goal(s)—risk assessment device, intervention agent, intervention device, immunologic intervention, lifestyle modification; and mechanistic pathway under investigation) in a consistent manner.
2. ***Precise definitions of translational research and subcomponents of translational research and specific examples of both translational and nontranslational awards will be required as part of developing any new coding process.*** Operationalizing the TRWG’s inclusion criteria for translational research proved difficult even when individual award abstracts were reviewed. However, the exercises performed to assess the inclusion criteria suggest that review of abstracts, though laborious, resulted in judgments consistent with those of scientists closely associated with the individual projects.
3. ***A database needs to be created that completely and accurately collects the current status of core facilities and infrastructure, captures their total dollar value or number, and allocates their usage to basic, translational, and clinical research.*** Core facilities and infrastructure are funded through many mechanisms. The dollar amounts for P30, R24, and U24 awards can be captured, but these awards are not 100% infrastructure. It is also possible to determine the number of P30, P50, and P01 cores but not the dollars associated with them. Moreover any cores associated with R01, U-series mechanisms, etc. are not captured at any level. For the reasons discussed earlier, it also proved difficult to classify core facilities and infrastructure as either “translational” or “not translational.”
4. ***A database needs to be created that completely and accurately tracks and codes the individual components and projects of multi-project mechanisms (e.g., P01, EDRN, SPORE, and P30 awards).***

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<sup>5</sup> Figure 5C, however, shows that only 1% of NCI awards active in FY 2004 were classified as being in the 75% NIHCA quartile.

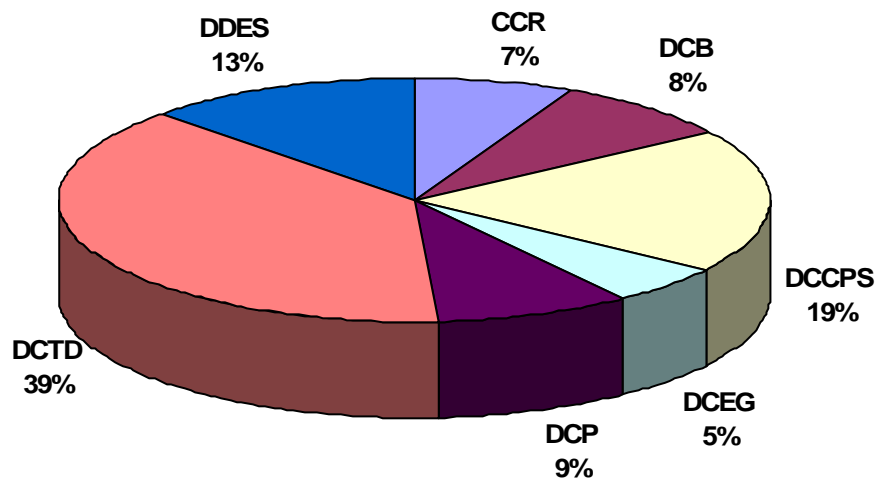


## Appendix Figures: Cross-Tabulations of NCI Translational Research Portfolio

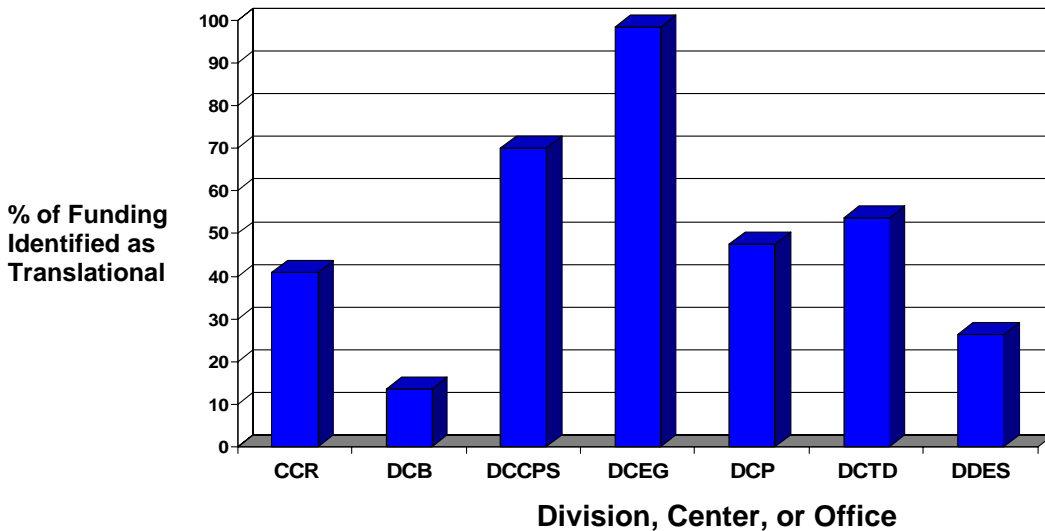


**Figure 1A. Percentage of the total 2,789 project-funding awards identified as translational in FY 2004 supported by each NCI Division, Center and Office.**

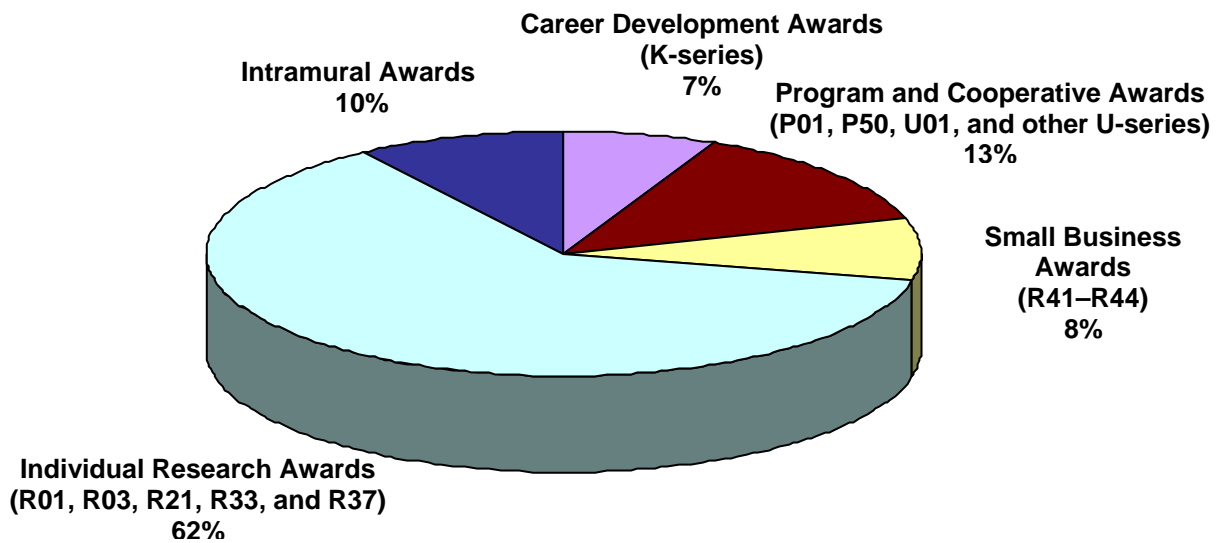
\* Office of the Deputy Director for Extramural Science (DDES) includes the Office of Centers, Training and Resources (Cancer Centers and SPOREs), the Office of Cancer Complementary and Alternative Medicine, and the Office of Grant Program Coordination.



**Figure 1B. Percentage of the total \$1.33 billion in funding identified as translational in FY 2004 supported by each NCI Division, Center and Office.**



**Figure 1C. Percentage of total FY 2004 funding in each NCI Division, Center, and Office that was identified as translational.<sup>6</sup>**

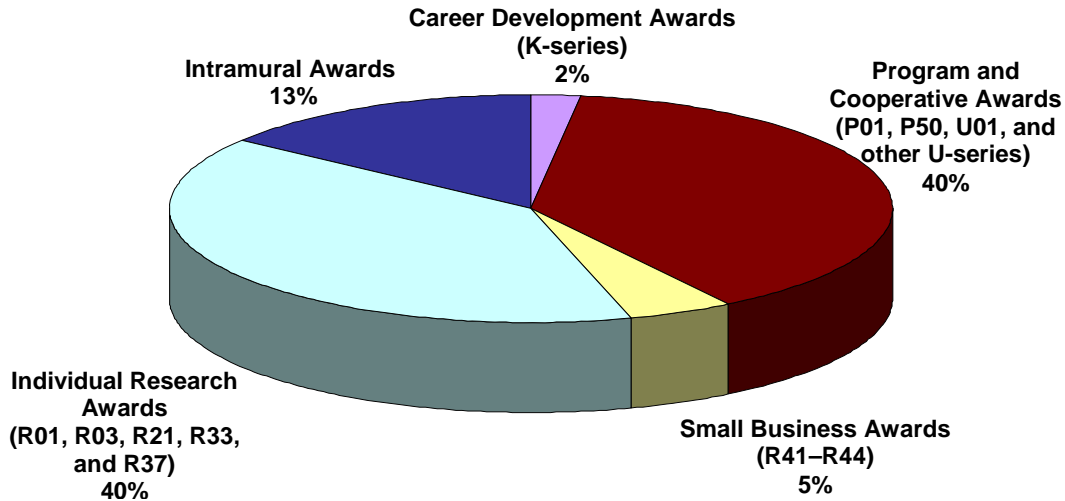


**Figure 2A. Percentage of the 2,705<sup>7</sup> awards identified as translational in FY 2004 that are funded through the major funding mechanisms.**

Included: Career Development Awards (K-awards), Program and Cooperative Awards (P01, P20, P50, U01, U19, U54, and U56), Small Business Awards (R41–R44), Individual Research Awards (R01, R03, R21, R33, and R37), and Intramural Awards. Not Included: RAID, RAPID, DDG, and U24 EDNR awards.

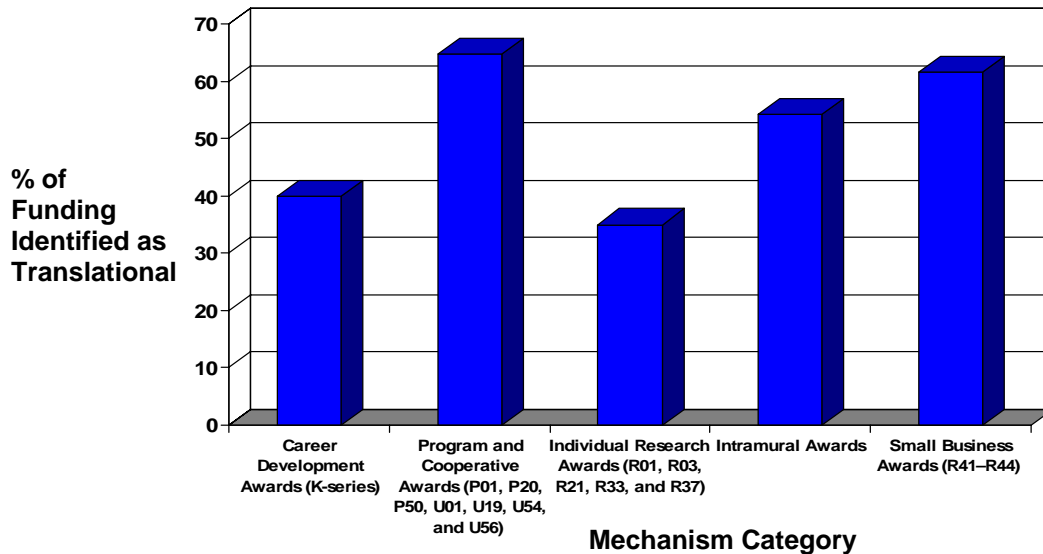
<sup>6</sup> Most awards with NIHCA codes of 0% were excluded from the review; however, the percentages shown in the figure are based on the total number of active awards in FY 2004 for each Division, Center, or Office. Therefore, the percentages represent minimal percentage values. The extent that projects with NIHCA quartile of 0% are translational was beyond the scope of this analysis.

<sup>7</sup> The number of awards is different from the total number of awards identified as translational (2,789) due to exclusion of 82 RAID, RAPID, and DDG projects active in FY 2004 that were primarily funded through contracts and not through the major funding mechanism categories and 2 EDNR U24 infrastructure-based awards that also did not match the major funding mechanism categories.



**Figure 2B. Percentage of the \$1.30 billion in funding identified as translational in FY 2004 that are supported through the major funding mechanisms.**

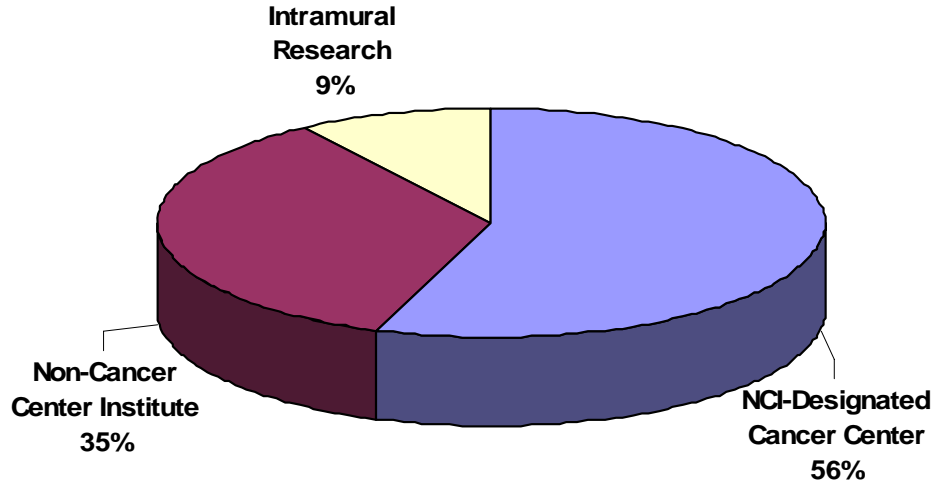
Included: Career Development Awards (K-awards), Program and Cooperative Awards (P01, P20, P50, U01, U19, U54, and U56), Small Business Awards (R41-R44), Individual Research Awards (R01, R03, R21, R33, and R37), and Intramural Awards. Not Included: RAID, RAPID, DDG, and U24 EDRN awards.



**Figure 2C. Percentage of total FY 2004 funding within each award mechanism that was identified as translational.<sup>8</sup>**

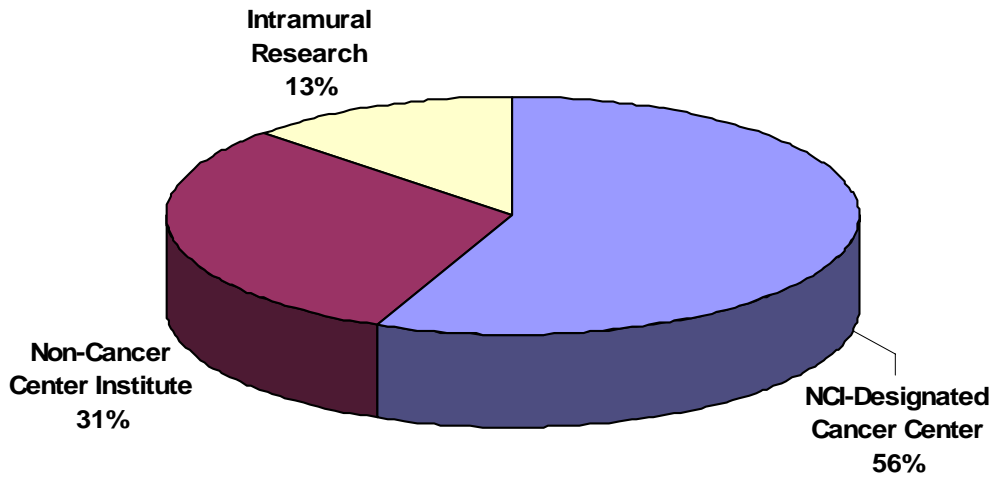
Included: Career Development Awards (K-awards), Program and Cooperative Awards (P01, P20, P50, U01, U19, U54, and U56), Small Business Awards (R41-R44), Individual Research Awards (R01, R03, R21, R33, and R37), and Intramural Awards. Not Included: RAID, RAPID, DDG, and U24 EDRN awards.

<sup>8</sup> A majority of individual research awards were not reviewed because they had the NIHCA quartile of 0% while a majority of awards in the other mechanism categories were reviewed. The percentages in this figure may be considered minimal percentages, as in Figure 2A (see footnote 6).



**Figure 3A. Percentage of the 2,707<sup>9</sup> project-funding awards identified as translational in FY 2004 made to major categories of institution.**

Included: Research awards to institutions designated as comprehensive or clinical Cancer Centers, research awards to institutions not designated as comprehensive or clinical NCI Cancer Centers, and NCI intramural awards.  
 Not included: RAID, RAPID, and DDG awards.



**Figure 3B. Percentage of the \$1.30 billion in funding identified as translational in FY2004 awarded to major categories of institution.**

Included: Research awards to institutions designated as comprehensive or clinical Cancer Centers, research awards to institutions not designated as comprehensive or clinical NCI Cancer Centers, and NCI intramural awards.  
 Not included: RAID, RAPID, and DDG awards.

<sup>9</sup> The number of awards is different from the total number of awards identified as translational (2,789) due to exclusion of the 82 RAID, RAPID, and DDG projects.

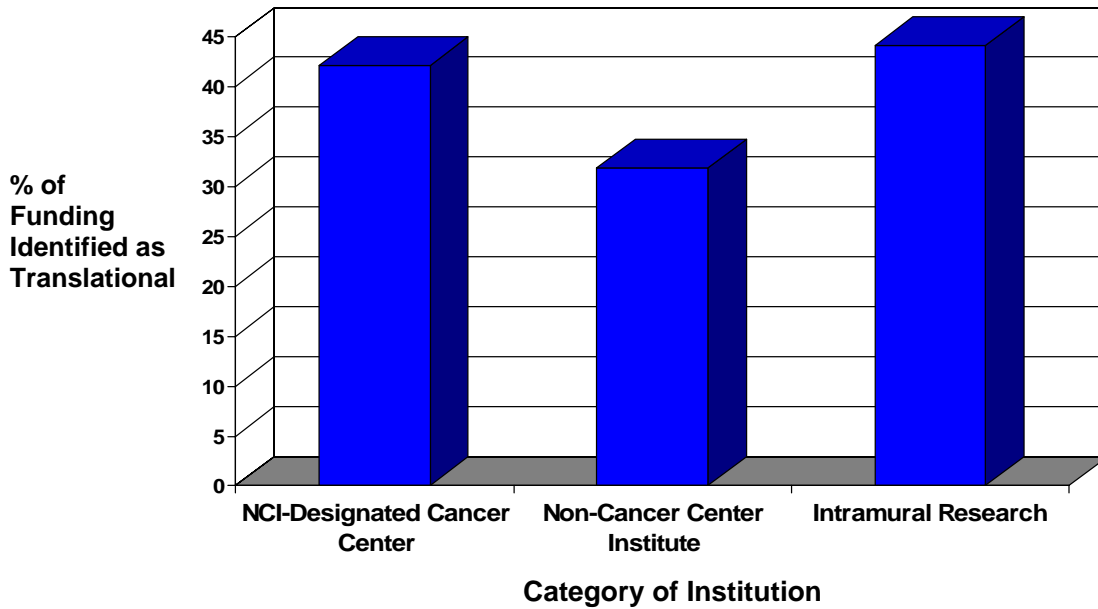


Figure 3C. Percentage of total FY 2004 funding at major categories of institutions that was identified as translational

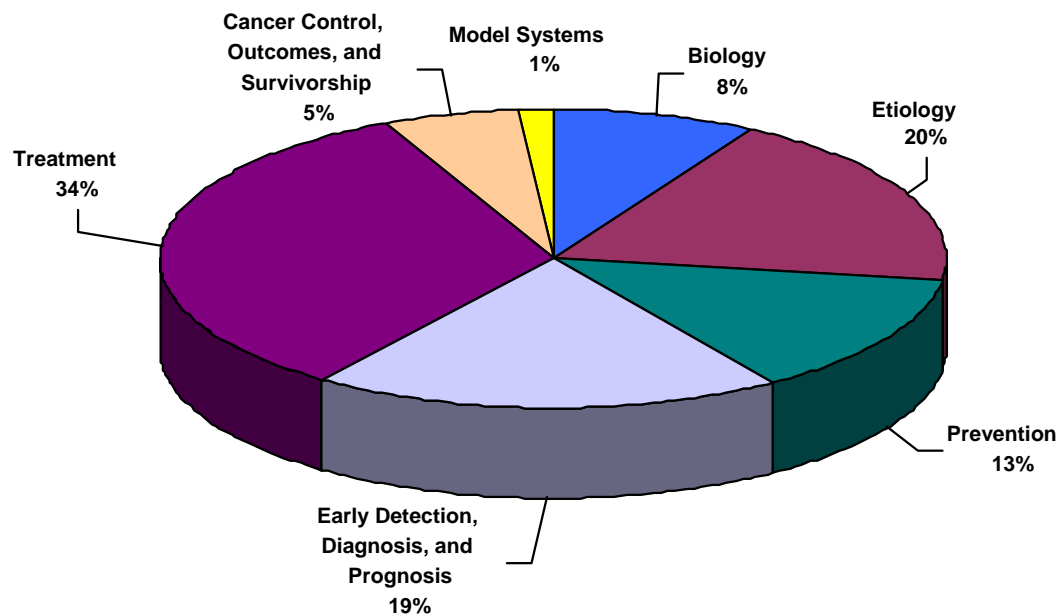
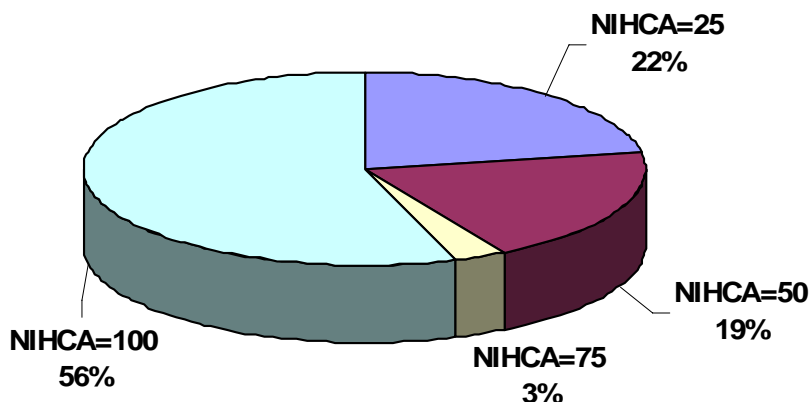


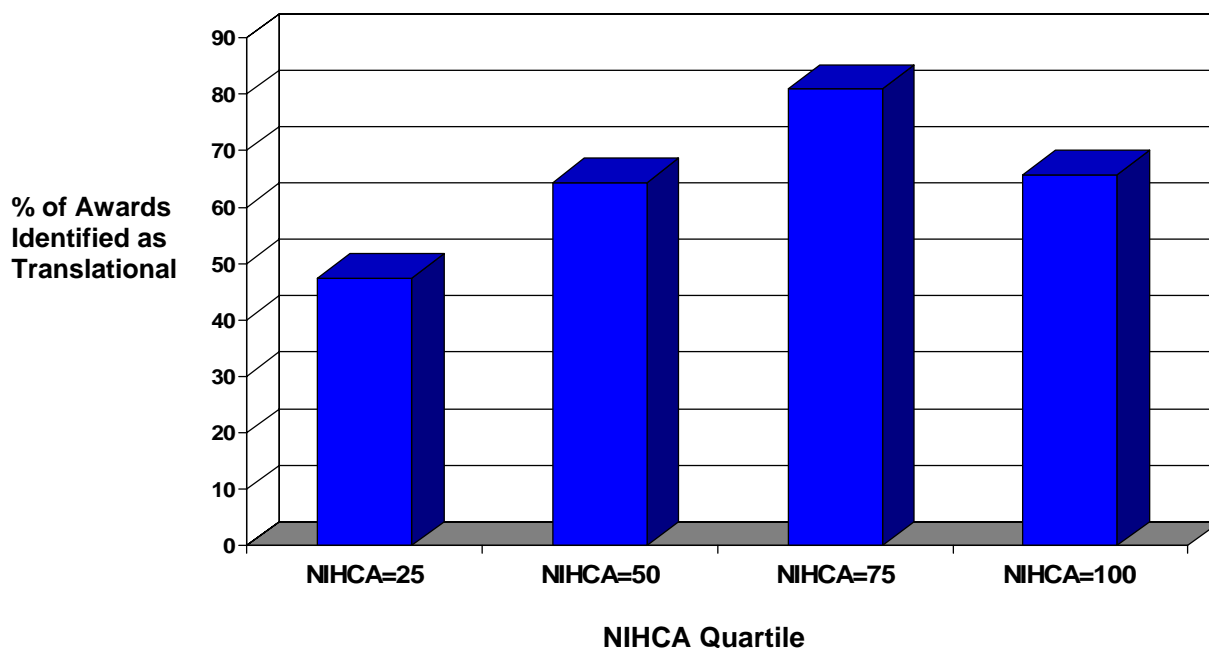
Figure 4. Percentage of the total 2,789 project-funding awards identified as translational in FY2004 cross-tabulated by the 7 major CSO categories.<sup>10</sup>

<sup>10</sup> Awards assigned to 2 or more CSO categories are counted toward all assigned categories.



**Figure 5A. NIHCA quartile of the 2,296 project-funding awards active in FY 2004 that had a 25%–100% NIHCA code and were identified as translational.<sup>11</sup>**

Included: All active extramural awards with NIHCA quartile assignments of 25%–100% identified as translational. Not included: Awards and projects not assigned NIHCA codes; including intramural awards (CCR and DCEG), RAID, RAPID, and DDG projects; and awards with 0% NIHCA quartile.

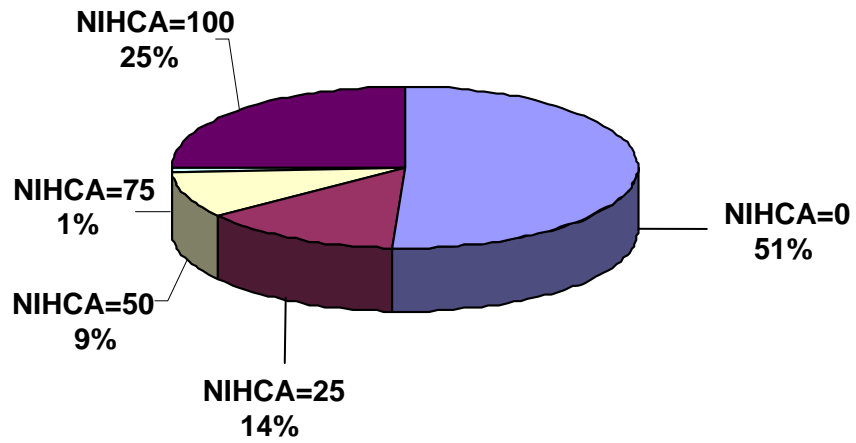


**Figure 5B. Percentage of awards in each NIHCA quartile identified as translational.<sup>12</sup>**

Included: All active extramural awards with NIHCA quartile assignments of 25%–100% identified as translational. Not included: Awards and projects not assigned NIHCA codes; including intramural awards (CCR and DCEG), RAID, RAPID, and DDG projects; and awards with 0% NIHCA quartile.

<sup>11</sup> Projects with NIHCA quartile of 0% were not included because only 8% of these awards were reviewed to identify translational research projects and the set of projects reviewed is not a representative sampling of the 0% NIHCA awards. Examining all such projects was beyond the scope of the portfolio analysis.

<sup>12</sup> See note 11.



**Figure 5C. Percentage of all active FY 2004 extramural project-funding awards by NIHCA quartile.**

Not included: Awards and projects not assigned NIHCA codes; including intramural awards (CCR and DCEG), RAID, RAPID, and DDG projects.