

**Evaluation of the
National Cancer Institute (NCI)
Specialized Programs of
Research Excellence (SPORE)**

Judith A. Hautala

Jamie M. Doyle

Oren Grad

Brian L. Zuckerman

November 2012

Executive Summary

Program Overview

The Specialized Programs of Research Excellence (SPORE) awards funded by the National Cancer Institute (NCI) are specialized center grants designed to support multi-project, interdisciplinary translational research involving both basic and applied scientists with the goal of developing diverse new approaches to the prevention, early detection, diagnosis and treatment of human cancers. Each SPORE award is focused on a specific organ site, such as breast or lung cancer, or a group of highly related cancers, such as gastrointestinal cancers and sarcomas. Seventeen organ sites or systems, (bladder, brain, breast, cervical, endometrial, gastrointestinal, head and neck, kidney, leukemia, lung, lymphoma, myeloma, ovarian, pancreatic, prostate, sarcoma, and skin cancers) are represented in the current portfolio of 62 SPORE awards.

All SPORE grants include at least four translational research projects that should be designed to include a clinical trial, a human observational study or experiments using human specimens (all defined as a “human endpoint”). SPORE grants also support Developmental Research awards for funding pilot projects as well as Career Development awards that support junior faculty and established investigators in expanding their careers into translational research. Other key features of SPORE awards (also referred to in this report as “SPOREs”) include support of specialized core services (e.g., biospecimen acquisition and storage, pathology, and biostatistics) and the flexibility to terminate projects that are either not progressing well or have been completed ahead of schedule and replace them with new projects (the “flexibility option”). Finally, SPORE-supported investigators are explicitly expected to participate in collaborations with other SPORE and non-SPORE research groups to facilitate the progress of translational research.

Focus of Evaluation

The IDA Science and Technology Policy Institute (STPI) was tasked by the NCI to conduct an evaluation of the SPORE program guided by 11 NCI-developed study questions. One of these is an overarching question concerning the impact of SPORE research on oncology, while the other 10 questions are specific to particular aspects of the SPORE program.

1. What specific concepts or scientific findings that arose from SPORE research have had an impact on the practice of oncology?

2. How well have the SPOREs been meeting the translational research goal of reaching a human endpoint within the five-year funding period?
3. How well have basic and applied scientists worked together on the design and implementation of individual research projects?
4. How well have SPOREs collaborated with other SPOREs in their own organ site or across organ sites; with NCI networks, such as Cancer Centers and Cooperative Groups; with other government and non-government biomedical research mechanisms; or with industry to move important findings along the translational research pathway with the ultimate goal of having an impact on medical practice?
5. How well have SPOREs used the flexibility option to change research direction to have an immediate impact on improving cancer prevention, detection, diagnosis, and/or treatment?
6. How well have the SPOREs fostered translational research careers?
7. How well have the SPOREs used the Developmental Research Program for pilot studies?
8. How well have the Specialized Resource Cores supported the research projects?
9. Did the Biospecimen Core provide materials for investigators outside the SPORE?
10. How many clinical trials/studies were initiated and completed within the SPOREs?
11. What are the significant publications from the SPOREs since 2004?

STPI's task was not to answer these questions as they were posed but rather to collect information and conduct analyses that could be used by NCI and its extramural advisors to make a reasoned judgment as to "how well" the SPOREs performed in each of these areas.

As the project evolved, STPI researchers recommended, and NCI SPORE leadership concurred, that two additional analyses, not directly linked to these 11 study questions, should be performed. The first was to draw conclusions concerning the role of the SPORE program in advancing cancer-related translational research based on data collected in the course of the study. The second was to analyze SPORE research projects in terms of their ultimate translational objective and the types of translational activities proposed. This information provided essential context for understanding both the effectiveness of SPOREs in advancing translational research and interpreting certain of the other study findings.

Analysis Methodology

The SPORE program constitutes a diverse portfolio of awards, with some extending back to 1992 and several new Type 1 awards being funded in the last four to five years. However, for both data consistency and a manageable project scope, it was necessary to define a representative subset of awards and restrict certain aspects of the analysis to activities occurring in the most recently completed five-year award cycle for those awards. STPI researchers and NCI SPORE leadership therefore decided that the evaluation would focus on the 55 SPORE awards that were active at some point subsequent to 2004¹ and had completed at least one five-year award cycle by 2011. Although most of the data collection was limited to these specified five-year award cycles, there were certain aspects of the evaluation (e.g., the impact on oncology) which, for robustness, required data over the lifetime of the awards.

Two primary data sources were used. The first was application documents for the selected five-year award period for each award, including the competitive application, a full set of Type 5 progress reports, and a final report/subsequent competitive application. These documents were analyzed to capture information on: (1) the ultimate translational objective and intended translational activities of each research project; (2) clinical trials; (3) non-clinical trial research activities (human observational studies, biospecimen utilization and laboratory/animal model research); (4) collaborations; (5) use of the flexibility option; and (6) core services.

The second major data source was a series of individual discussions with SPORE Principal Investigators (PIs). Several major topics were included in the discussions: (1) SPORE concepts or findings that have had an impact on the practice of oncology; (2) clinical trials associated with SPORE research projects; (3) collaborations; (4) value of the flexibility option; (5) value of the Career Development and Developmental Research Programs; (6) use of core services and their integration with those of the host Cancer Center; and (7) provision of biospecimen samples to non-SPORE investigators.

Major Conclusions (Chapter 1)

When the SPORE program was launched in 1992, it was the first NCI program specifically designed to fund early translational research (i.e., projects aimed at moving promising discoveries in a coordinated fashion from the lab, clinic, or population into early phase human testing) and it remains today the only NCI program focused on all steps in this early translational research continuum. Based on information gathered in the course of the evaluation, STPI researchers reached five major conclusions about the role of the SPORE program in advancing cancer-related translational research.

¹ The year 2004 was chosen because that was the year the SPORE program was first open to all organ sites.

Clear Focus on Early Translation

The first conclusion is that SPORE projects are in practice and not just in theory focused on critical steps in early translation. Only 4% of the 273 projects originally proposed by the 55 SPORE awards were primarily mechanism-of-action or tool-development studies, while all other projects had a defined intervention or biomarker test development objective. Moreover, for the intervention-focused projects, over 80% proposed late-stage development activities, either early phase clinical trials or development of a specific intervention in anticipation of clinical testing. In contrast, only 27% of the biomarker projects proposed development of a clinical grade assay or prospective human testing; these projects were much more heavily weighted toward biomarker identification and confirmation activities. This focus on the earlier steps in translation is perhaps not surprising given that development of cancer biomarker tests for clinical use is a much more recent advance than intervention development. In addition, diagnostic or screening assay development and testing is much less familiar to academic investigators than is intervention development and testing. This may result in an earlier hand-off of biomarker projects to commercial partners for later stage development.

Award-Related Constraints to SPORE Translational Progress

The second conclusion is that, despite this clear focus on translating discoveries from “bench to bedside,” the SPORE program imposes certain constraints on the ability of SPORE projects to meet their translational goals. The primary constraint is financial as the typical funding of a SPORE research project (\$200K to \$400K per year total cost) is often not sufficient to conduct even a small phase I or phase II trial. If the experimental product must also be manufactured for clinical use, the shortfall is even greater. As a result, SPORE investigators generally must obtain non-SPORE funding for these activities. This puts a constraint on the projects that can be pursued and can often cause delays. Moreover, even if funding can be obtained, five years is a short time for moving from a discovery to human testing if investigators must perform all the required identification, confirmation, validation, quality control, and safety evaluation steps. This may favor projects already well advanced in development and restrict pursuit of innovative, high risk ideas if the investigators cannot use a subsequent award cycle to conduct human testing.

Success in Reaching a Human Endpoint

The third conclusion is that, despite these constraints, SPORE research projects have been successful in reaching a “human endpoint” as defined by the SPORE Guidelines (i.e., performance of a clinical trial or human observational study or use of human specimens). Based on the SPORE clinical trial data discussed in Chapter 4 of this report and the information on observational studies and use of biospecimens discussed in

Chapter 5, 93% of the 273 research projects originally proposed by the 55 SPORE awards reached a “human endpoint” during the five-year funding period. The 20 projects that did not reach such an endpoint² were distributed over 16 different awards, although 1 award had 3 such projects and 3 additional awards had 2 each. It is of interest that of these 20 projects, 6 were terminated under the flexibility option, 3 of which were in the award with 3 original projects that did not reach a human endpoint and one each in 2 of the awards with 2 “non-human endpoint” original projects. This demonstrates that achievement of a human endpoint by SPORE research projects is potentially higher than 93% and that the flexibility option is exercised when projects are not progressing.

Distinct “Niches” for SPORE Translational Research

The fourth conclusion is that the SPORE program occupies three distinct niches in translational research. One important niche is the ability of SPOREs to pursue translational research objectives perceived by industry (or foundations) as too complex or risky to justify early investment. SPORE projects engage basic and applied researchers in a team-based environment where ideas, research results, and potential new research directions are constantly shared to encourage thinking “outside the box” in attacking a complex or risky problem. This pursuit of innovative ideas and approaches is facilitated by the pilot projects funded through the Career Development and Developmental Research Programs that allow proof of concept testing of novel ideas that might not have sufficient preliminary data to be successful in standard peer review.

The second niche is in creating a community of investigators pursuing diverse approaches for a disease. Involvement with a SPORE entices basic scientists to think about applying their research results to a specific disease and provides an avenue for moving discoveries into the clinic while, for clinicians, a SPORE provides the opportunity to participate in the clinical application of recent scientific advances and the testing of novel interventions and biomarkers. The Career Development and Developmental Research Programs again play a role by integrating new investigators into the network of translational research in a disease area.

The third niche is the pursuit of collaborative projects with industry whereby an industry drug or drug candidate is taken forward by a SPORE for an initial or a new indication, often in combination with other approved or unapproved drugs. These projects exploit the synergistic capabilities of SPOREs and industry — SPOREs provide investigator expertise, research tools, biospecimen acquisition/analysis and access to

² This number includes two projects for which comprehensive clinical trial information was not available from the PI discussions but no clinical trials, human observational studies, or use of biospecimens were identified from the analysis of applications and progress reports.

patients while industry provides much needed supplemental funding as well as access to drugs and drug development capabilities.

SPORE Roles in Translational Research Capacity Development

The fifth conclusion is that SPOREs make a substantial contribution to building an early translational research capacity both within their host institutions and in specific disease areas. For host institutions, a SPORE award provides a translational core infrastructure around a specific disease including specialized tissue repositories, laboratory equipment and technical/statistical expertise. The award also often serves as a “center of gravity”, raising the profile and legitimacy of translational research at the institution. Within disease areas, SPORE-SPORE collaborations create a national community of translational research investigators which is particularly important for large, epidemiologic studies, the collecting and sharing of biospecimens, clinical trial design and accrual of patients.

Major Advances (Chapter 2)

In order to address the overarching study question (i.e., What specific concepts or scientific findings that arose from SPORE research have had an impact on the practice of oncology?), STPI researchers specified three categories of major advances: advances accepted into clinical practice; advances in late-phase human testing; and advances with broad clinical potential. Identification of SPORE-supported advances falling into these three categories involved a two-step process.

First, during their individual discussions with STPI researchers, SPORE PIs were asked to identify advances in each of these categories that were derived from research conducted in their SPORE and to describe the role SPORE research played in achieving each advance. STPI researchers then conducted an independent analysis of each advance to expand upon and verify the information provided by the PIs. This included a review of National Comprehensive Cancer Network (NCCN) Guidelines, searches on clinicaltrials.gov, analysis of papers obtained from MEDLINE searches, and accessing information from industry, government, and not-for-profit organization websites. In order to conclude that the major advance was attributable to the SPORE, some level of corroborating evidence was obtained that the concepts and scientific findings leading to the advance were either completely SPORE-derived or, in situations where multiple groups contributed, SPORE-conducted research and researchers played a substantial, active role.

Through this process, 79 major advances were identified, including 24 accepted into clinical practice, 36 in late-phase human testing, and 19 with broad clinical potential. From these, NCI SPORE leadership selected the advances listed here as being the most significant. For those advances, STPI researchers conducted additional analyses to

elucidate more thoroughly the influence of the SPORE. Case studies describing these 14 advances and the role of SPORE research in their development are presented in Chapter 2.

Advances Accepted into Clinical Practice

1. Enzalutamide (MDV3100) for Late-Stage Prostate Cancer
2. Novel Agents and Regimens for Multiple Myeloma
3. Contemporary Partin Tables/Kattan Nomograms — Tools for Management of Prostate Cancer
4. Diagnostic Test for EML4-ALK Translocation in Non-Small Cell Lung Cancer (NSCLC) Patients
5. Predictive Assay for Lung Cancer Response to Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitors
6. Chromosomal 1p/19q Deletion as an Oligodendroglioma Prognostic/Predictive Marker
7. BRAF Mutation Detection and Prognostic Value in Papillary Thyroid Cancer
8. Screening and Monitoring in Endometrial Cancer and Hereditary Non-Polyposis Colorectal Cancer (HNPCC)/Lynch Syndrome

Advances in Late-Phase Human Testing

1. Difluoromethylornithine (DFMO) and Sulindac for Prevention of Colorectal Cancer
2. Heat Shock Protein Peptide Complex (HSPPC) 96 Vaccine for Brain Cancer
3. Rindopepimut (CDX-110) Vaccine for EGFR Variant III (EGFRvIII)-Expressing Glioblastomas
4. Transmembrane Protease, Serine 2 (TMPRSS2) Gene Fusions as Prostate Cancer Detection and Risk Markers

Advances with Broad Clinical Potential

1. Sensitivity and Resistance to EGFR Tyrosine Kinase Inhibitors in Lung Cancer
2. Risk Factors and Disease Subtypes in Breast Cancer

SPORE Research Project Characterization (Chapter 3)

As previously noted, although it was not a specific study question, STPI researchers and NCI SPORE leadership agreed that it would be valuable to characterize SPORE research projects in terms of both their ultimate translational objectives and the types of translational activities proposed. Therefore, the initial specific aims of the 273 research projects proposed by the 55 SPORE awards for the five-year award cycles analyzed were characterized in terms of both the long-term goal of the proposed research (i.e., the ultimate translational objective) and the activities to be undertaken during the award period (i.e., the intended translational activities).

For analysis of *ultimate translational objectives*, projects were classified into seven categories:³

1. Therapeutic intervention
2. Preventive intervention
3. Risk biomarker
4. Disease biomarker (detection, diagnosis, prognosis)
5. Stratification biomarker
6. Tool development only
7. Mechanism of action only

Of the 273 projects, 140 (51%) had only an intervention objective while 101 (37%) had only a biomarker objective. The remaining projects either had both intervention and biomarker objectives (8%) or had no specific objective other than the conduct of mechanism-of-action or tool-development studies (4%). Among the intervention projects, the majority (84%) were focused on therapeutics. The biomarker projects were more diverse with 65% focused on disease markers, 31% on risk markers, and 22% on patient stratification markers.

For analysis of *intended translational activities*, the proposed research was classified into 11 categories:

1. Develop/refine a research tool
2. Mechanism of action: carcinogenesis/disease progression
3. Mechanism of action: therapeutic or preventive effect
4. Mechanism of action: drug resistance

³ With the exception of the “tool development only” and “mechanism of action only” categories, the classification was non-exclusive and projects could be classified in more than one category.

5. Identify intervention targets or biomarkers
6. Confirm intervention targets or biomarkers
7. Develop/refine modality⁴
8. Safety/efficacy testing: SPORE-developed modality
9. Safety/efficacy testing: externally developed modality
10. Human biomarker study: prospective cohort or nested case control early validation study
11. Human biomarker study: observational study to confirm correlation with disease risk/progression

Of the 273 projects, fewer than 10% involved only mechanism-of-action or tool-development activities. For ease of interpretation, analysis of intended translational activities for the remaining projects was performed separately for intervention projects and biomarker projects.

For projects with only an intervention objective, nearly two-thirds (65%) proposed conducting clinical safety or efficacy testing, split almost evenly between testing a SPORE-developed modality and a modality developed by others, while 57% proposed preclinical studies or other activities directed at developing or refining a modality in advance of clinical studies. Smaller percentages of the projects, 18% and 25% respectively, proposed identifying or confirming an interventional target while 68% proposed mechanism-of-action studies primarily combined with other activities.

For projects with only a biomarker objective, 74% involved identification of a biomarker and 45% involved confirmation of a biomarker. About 24% proposed human testing, while 9% proposed to develop a biomarker-based clinical test. Again, 40% proposed mechanism-of-action studies primarily combined with other activities.

The figures on the next page indicate that intervention project activities are concentrated in the later stages of early translational research (bottom of the chart) while biomarker project activities are concentrated earlier in the translational research process (top of the chart). In these figures, each row captures the number of projects that have a particular combination of intended translational activities.

⁴ “Modality” means any compound, device, or method with a defined clinical purpose.

Translational Activity “Footprints” for Intervention-Only Projects

# of Projects	MOA Only	Identify Target	Confirm Target	Develop Intervention	Clinically Test Intervention
11					
6					
3					
3					
2					
1					
2					
8					
6					
6					
8					
6					
16					
45					
17					

Note: “MOA” stands for “mechanism of action.”

Translational Activity “Footprints” for Biomarker-Only Projects

# of Projects	MOA Only	Identify Biomarker	Confirm Biomarker	Develop Biomarker Test	Test in Humans
4					
40					
17					
2					
3					
6					
2					
5					
10					
1					
6					
1					
4					

Note: “MOA” stands for “mechanism of action.”

Clinical Trials (Chapter 4)

The clinical trial analysis was designed to address two study questions. The first concerned reaching the goal of a “human endpoint,” and the second addressed the extent of SPORE clinical trial activity. To achieve a consistent frame of reference across the program, the analysis was limited to trials that arose from the research projects conducted by each SPORE during the five-year award cycle analyzed. However, those trials could be conducted either during or after the award period and could be designed and led by SPORE investigators or designed and led by an external party based on SPORE project results.

These trials were identified using two sources. The first was the SPORE PIs, who described relevant clinical trials in their one-on-one discussions with STPI researchers and often provided lists of trials either in advance of or following those discussions.⁵ The second was analysis of progress reports and the subsequent competitive renewal application for references to clinical trials associated with projects conducted during the five-year award cycle. Note that the number of SPORE-related clinical trials reported almost certainly represents a minimum or a “floor” for the five-year award cycles analyzed due to the limitations described in Chapter 4 on page 4-2.

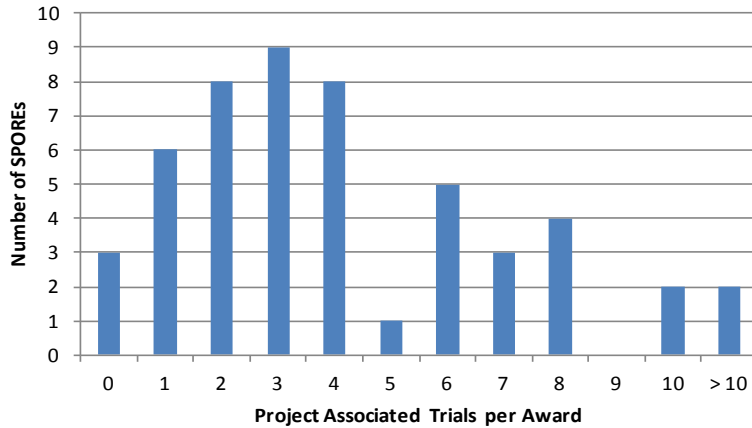
After confirming that each clinical trial identified from these two sources was linked to a SPORE research project, the resulting project-associated trials were analyzed from two perspectives — the extent of clinical trial activity and the character of the trials in terms of phase, type of intervention, funding source, and current status. Some SPORE PIs also provided information on clinical trials conducted in association with Career Development and Developmental Research projects. Although descriptive information on these trials reported by the PIs is presented in Chapter 4, Section E, no attempt was made to systematically analyze this category of trials.

Extent of Clinical Trials Designed and Led by SPORE Investigators

Of the 51 SPORE awards analyzed, 48 (94%) included research project-associated trials designed and led by SPORE investigators for a total of 221 trials. However, as shown below, the number of trials per award varied substantially and two awards were especially high outliers with 16 project-associated trials each. There were also substantial differences in the mean number of clinical trials conducted per SPORE in different disease areas. The hematological SPOREs had the largest number, in excess of 8 per award, while the gastrointestinal and ovarian SPOREs were the lowest at 2.5 per award. In the other disease areas, the average ranged from 3.7 (lung) to 5.5 (skin). Three SPORE

⁵Because the PI provided information was so critical to the completeness of the data, the four SPORE awards for which PI discussions could not be held are excluded from the clinical trial analysis.

awards had no clinical trials, two gastrointestinal and one breast (see Chapter 4, Figure 4B-2).



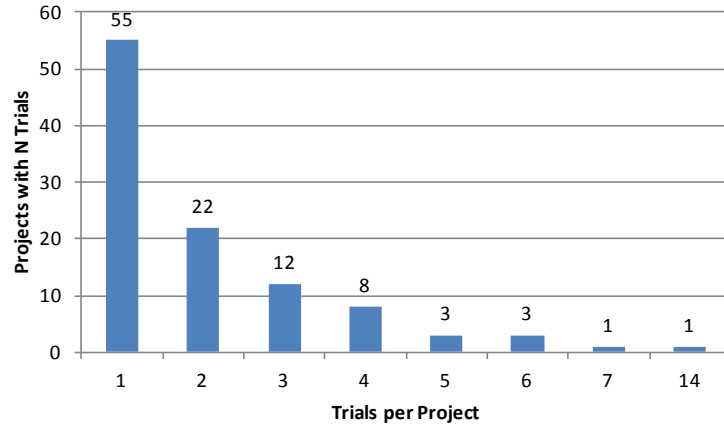
Research Project-Associated Trials per SPORE Award

In order to analyze the degree to which SPORE projects involved clinical trials, it proved useful to consider the intervention-focused and biomarker-focused projects separately.⁶ Not surprisingly, a much higher percentage of the intervention projects had associated clinical trials than the biomarker projects (59% versus 10%). For the intervention projects, there was some variation in the percentage of projects with trials by disease area (see Chapter 4, Figure 4B-4).

In terms of trials per research project, the 221 SPORE trials were conducted through a total of 105 projects⁷ or 2.1 trials per project on average. The figure below shows that just over half the projects had one trial while 5% had more than five trials.

⁶ For this analysis, projects with both an intervention and a biomarker objective were included in the intervention category.

⁷ This number includes both intervention and biomarker projects.



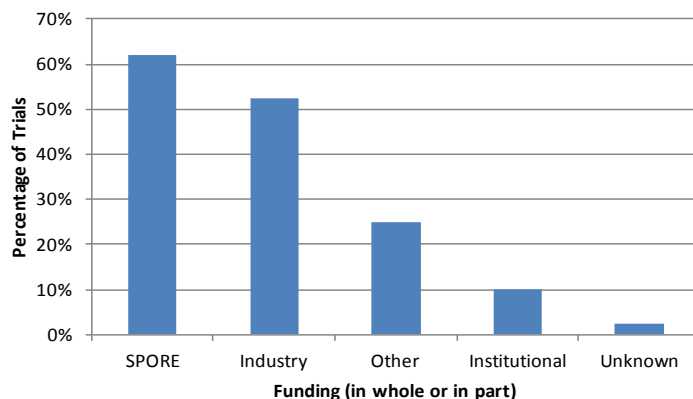
Trials per Research Project

Character of Clinical Trials Designed and Led by SPORE Investigators

The 221 SPORE trials designed and led by SPORE investigators were distributed evenly over phase I trials (43%) and phase II trials (41%) with another 9% being phase I/II and 3% randomized phase II (see Chapter 4, Table 4C-1). In terms of the type of intervention, nearly three-quarters (73%) involved drugs or biologics while the next largest category was immunotherapy at 22%. Gene therapy and chemoprevention trials each represented only 2% (see Chapter 4, Table 4C-2).

SPORE trials are often funded from multiple sources. The figure below shows the percentage of trials receiving at least partial funding from any of four different sources — the SPORE award itself, industry, the SPORE host institution, and a composite category that includes foundation awards, other government awards, and various miscellaneous awards.⁸ Over 60% of the trials received at least some funding from the SPORE awards or supplements while over 50% received at least some industry funding. Funding from foundations, other government sources, and other miscellaneous funding sources contributed to 25% of the trials, while SPORE host institutions supported 10%.

⁸ Of the 221 SPORE trials, funding information could be determined for 216 (98%).



Percentage of Trials with Different Funding Sources

As might have been expected, industry funding is heavily weighted to drug/biologic trials whereas SPORE, host institution and other government, foundation, etc. funding contributes a larger share for the more experimental intervention types (see Chapter 4, Figure 4C-2). In terms of specific funding categories, trials funded completely by industry account for 24%, while trials funded totally by the SPORE and trials with a combination of SPORE and industry funding each account for another 21% (see Chapter 4, Table 4C-3).

Extent and Character of Trials Designed and Led by External Parties

Across the SPORE program, 15 trials were identified that are “hand-offs” to external parties for further development. Among these were three phase III trials including a chemoprevention trial conducted jointly by industry and a NCI Clinical Trials Cooperative Group and two therapeutic trials, one supported by industry⁹ and one by two of the Cooperative Groups (see Chapter 4, Table 4D-1 for trial details). The nine external phase II trials all tested either drugs or biologics. Five trials were conducted by the Cooperative Groups, three by industry and one by the DOD Prostate Cancer Clinical Trials Consortium. The three phase I trials included two funded by industry (one of which was an immunotherapy trial) and one funded by the SPORE’s host institution.

Non-Clinical Trial Research Activities (Chapter 5)

To fully address the study question concerning success in reaching a “human endpoint,” the degree to which SPORE research projects involved human observational studies or the use of human biospecimens was determined through analysis of competitive applications and progress reports for the 55 SPORE awards.

⁹ The industry trial resulted from a project conducted under a Career Development award.

Observational Studies

Of the 55 SPORE awards, 89% involved observational studies in some way although only 28% of the projects did so. For 79% of those projects, the observational studies were designed, conducted, and funded by the SPORE while for the remaining 21% SPORE investigators conducted research with biospecimens or data obtained from an observational study conducted by an external party. Not surprisingly, a much higher percentage of biomarker projects¹⁰ involved observational studies than did intervention projects (52% versus 10%).

Use of Biospecimens

All of the 55 SPORE awards included some use of biospecimens while 86% of their projects did so. Over 60% of these research projects obtained some or all of their specimens from SPORE specimen banks or other repositories while use of specimens from SPORE clinical trials, non-SPORE clinical trials and observational studies (both SPORE and non-SPORE) were less prevalent at 33%, 22% and 26%, respectively.¹¹ Not surprisingly, virtually all (97%) of the projects with a biomarker objective used biospecimens. However, more than 80% of the intervention-only projects also used biospecimens as did 91% of the mechanism-of-action projects.

Collaborations (Chapter 6)

The two study questions on collaboration encompass both collaboration between basic and applied researchers in the conduct of SPORE research projects and collaborations between SPORE investigators and external parties. Information on collaboration between basic and applied researchers was gathered from discussions with SPORE PIs while data on external collaborations was derived from analysis of both the competitive applications and progress reports and the PI discussions.

Collaboration between Basic and Applied Researchers

PIs generally credit the SPORE with bringing together researchers from disparate backgrounds into a team-based translational research environment where basic and clinical researchers both contribute and where research results are handed back and forth. Specific contributions of the SPORE awards in enhancing collaboration included creating a common language, facilitating development of interdisciplinary investigators, and bringing new investigators into translational research. Several PIs also credited the

¹⁰ For this analysis, projects with both an intervention and a biomarker objective were included in the biomarker category.

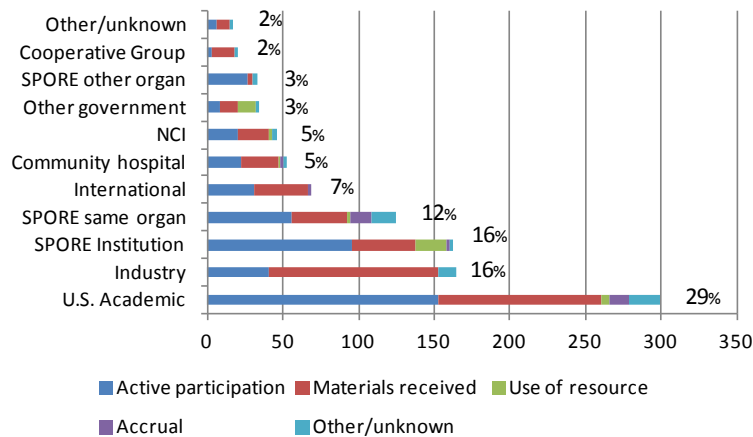
¹¹ The percent usage totals more than 100% because many projects used more than one source of biospecimens.

SPORE program with promoting an overall culture of collaborative research and enhancing research collaboration at their institutions more generally.

Collaboration with External Partners

Analysis of applications and progress reports identified a total of 1,022 external collaborations associated with the 311 SPORE projects.¹² Not surprisingly, the number of collaborations per project was highly variable with a substantial right tail to the distribution. Sixty-five of the projects (21%) had no identified collaborations whereas another 26% had five or more collaborations including one project with 22 (see Chapter 6, Figure 6C-1). In terms of purpose, 45% of the external collaborations involved active participation in SPORE research while 41% involved receipt of materials or data from collaborators (see Chapter 6, Figure 6C-2).

As shown in the following figure, SPORE external collaborations involved a wide variety of organizational types. The most prevalent at 29% was U.S.-based academics who are neither affiliated with the SPORE program nor at the SPORE’s host institution. Collaborations with industry and non-SPORE investigators from the SPORE’s host institution each represented another 16% while collaborations involving investigators from two or more SPOREs in the same organ site comprise 12%.



External Collaborations by Collaboration Purpose and Collaborating Organization Type

The figure also shows that different types of collaborating organizations emphasize different types of collaborative activities. As might be expected, 50% or more of

¹² These include 38 projects initiated through exercise of the flexibility option in addition to the 273 originally proposed projects.

academic collaborations involved active research participation whereas industry collaborations primarily involved providing materials or data to the SPORE.

Key Types of External Collaboration

The analysis revealed four categories of external collaboration that are particularly critical to the success of SPORE research. The first is research collaborations among SPOREs within a disease area, especially for clinical trials, epidemiological studies and the collecting and sharing of samples. PIs were generally enthusiastic about the value of in-person meetings and regularly scheduled conference calls in facilitating these collaborations. The second category was collaborations with industry, which many SPORE PIs viewed as the most valuable type of collaboration. Important industry contributions included access to drugs or biologics, manufacturing and formulation of clinical materials, clinical trial funding, and participation in SPORE research projects.

Collaborations with the NCI-funded Cooperative Groups, although not prevalent, did play a key role in certain SPORE research projects. The most frequent collaboration involved providing specimens from Cooperative Group trials to SPORE investigators. The two other, less frequent, collaborations involved either Cooperative Group trials based on SPORE preclinical or early clinical trial data (see Chapter 4, Section D) or the conduct of integral biomarker studies by SPORE investigators in association with Group trials.

The fourth critical collaboration category was that with various disease-specific phase I/II clinical trials consortia such as the Translational Breast Cancer Research Consortium, the Prostate Cancer Clinical Trials Consortium, the Melanoma Research Foundation Breakthrough Consortium and the NCI Adult Brain Tumor Consortium as well as with several national and international biomarker consortia.

Programmatic Activities (Chapter 7)

Analysis of SPORE programmatic activities addressed four separate study questions covering the flexibility option, the Career Development Program, the Developmental Research Program, and Core Services.

Flexibility Option

Under the flexibility option, SPORE PIs, in the midst of an award cycle, can terminate and replace projects that are either not progressing toward their translational objectives or have been completed ahead of schedule. To gather data on this distinctive aspect of the SPORE program, applications and progress reports were analyzed to identify projects that were either terminated or newly initiated, and qualitative insights regarding the value of the flexibility option were obtained from SPORE PI discussions.

Of the 55 SPORE awards, 28 (51%) were identified as having made some use of the flexibility option during the five-year period analyzed for each award. In 19 of these 28 awards, only one project was involved while four awards terminated four or more projects each. Across these 28 awards, 36 projects were terminated and 38 new projects were initiated, affecting 13% of the original 273 projects.

PIs praised the flexibility option as an effective management tool that allows a SPORE to focus on its most promising translational opportunities. They also viewed it as keeping investigators “on their toes” and focused on making translational progress.

Career Development Program

To analyze implementation of the Career Development Program (CDP), data were gathered on the professional profile of the CDP awardees, their subsequent career progression, and the nature of their current research. These objective data were then supplemented by discussions with the SPORE PIs to gather more perceptual, qualitative insights. Because meaningful analysis of the career progression of CDP investigators requires tracking over an extended period, the decision was made to gather data on all CDP investigators supported over the lifetime of each of the 55 awards.

In terms of the professional profile of CDP investigators, 20% hold both MD and PhD degrees while 45% have only a PhD and one-third only an MD. At the time of award, 37% were Assistant Professors while another 22% each were non-tenure track faculty or postdoctoral/clinical fellows.

With regard to career progression, subsequent National Institutes of Health (NIH) research funding could be identified for 38% of the CDP investigators. Of the remaining 62%, 21% applied for but did not receive an award while 41% did not appear in IMPAC II (NIH’s database of information on extramural applications and awards) and hence never submitted an application to NIH. It was not feasible to determine subsequent research funding from foundations, industry, or other government agencies. Current position titles for 39% of CDP investigators are indicative of an academic promotion while titles for 46% indicate no change in position since receiving the CDP award.¹³ Based on available information, 64% continued to perform research in the disease area of their CDP awards while 22% did not.¹⁴

With regard to publications, 71% of CDP investigators appeared as authors on at least one SPORE publication. In terms of relative contribution to SPORE publications, CDP investigators are authors on 41% of the 7,997 publications associated with the 55 SPOREs, appearing as first author on 11% and last author on 13%. Moreover, 14% of the

¹³ Current titles could not be determined for the remaining 14%.

¹⁴ There was insufficient evidence to make a determination for the remaining 13%.

CDP investigators (110 individuals) were listed as authors on 6 to 10 SPORE publications while 15% were authors on more than 11 publications. There are 25 CDP investigators with over 30 SPORE publications (see Chapter 7, Figure 7B-4).

Although the majority of SPORE PIs held a positive opinion of the Career Development Program, the PIs were about equally divided on whether they would continue making CDP awards if not required. The primary reason for continuing was the ability to bring early stage investigators into a community of researchers focused on translational research in a specific disease area where they are given access to a wide range of physical and intellectual resources for advancing their careers. The ability to leverage outside funding to supplement the awards was also seen as an advantage. The primary reasons for not continuing were that equivalent translational training can be obtained through other mechanisms and the awards are too small to be meaningful.

Developmental Research Program

To analyze implementation of the Developmental Research Program (DRP), application documents and progress reports were used to determine the degree to which DRP projects were promoted to full SPORE research projects or received non-SPORE follow-on funding. These objective data were then supplemented by discussions with the SPORE PIs to gather more perceptual, qualitative insights. Because the transition of DRP projects to full research projects either within the SPORE or funded by other sources may occur beyond any particular grant period, data collection and analysis spanned the entire lifetime of the SPORE awards.

Of the 1,618 DRP projects conducted across the lifetime of the 55 SPORE awards, 136 were promoted to full SPORE projects. This was estimated to represent approximately 20% of all the SPORE research projects conducted by those awards since their inception. Another 26% of DRP projects were documented to have received non-SPORE follow-on funding. Although the conversion of DRP projects to full SPORE research projects could be determined with a reasonable degree of certainty, there are several important limitations to the data on other types of follow-on funding (see Chapter 7, Section C).

Many SPORE PIs had strongly positive views about the Developmental Research Program overall and explicitly stated they would allocate funds to the program even if it were not a requirement. The primary perceived benefit was that DRP awards bring new investigators, particularly basic scientists, into cancer research related to a particular disease site. DRP awards are also viewed as a cost-effective way to pursue high-risk ideas and generate additional NIH and non-NIH funding for projects related to their disease area. Finally, as with the CDP awards, the ability to leverage institutional and outside resources to fund more DRP projects was an added advantage.

Core Services

Information on the number and types of core services associated with the 55 SPORE awards was collected from application documents and progress reports. Discussions with SPORE PIs then provided qualitative information concerning the value of these core services, their integration with those of the Cancer Center, and current practice in providing biospecimens to non-SPORE investigators.

A biospecimen/pathology core is required for all SPORE awards and 98% also had a biostatistics core. Other common core services included a clinical core (35%) and an animal model core (22%). Two-thirds of the SPOREs funded at least one other core specific to their research needs including genomics, informatics, proteomics, and biomarkers. The SPORE PIs view the biospecimen/pathology core as a unique strength.

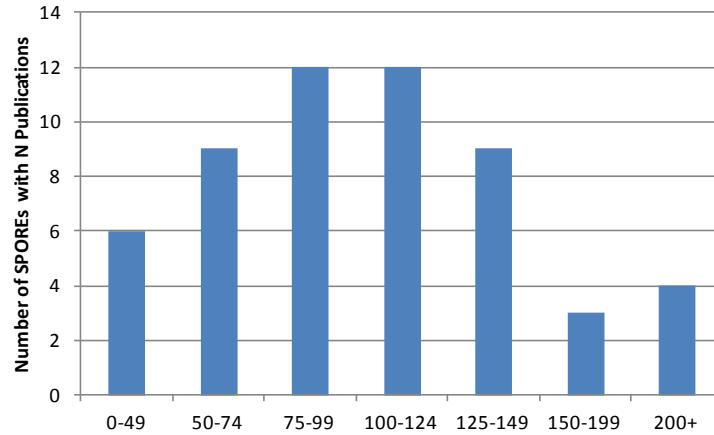
According to the PIs, SPORE core services, especially biostatistics, are often fully or partially integrated with those of the host Cancer Center. However, integration of the biospecimen/pathology core was often not practical. In some cases, the Cancer Center could not provide a sufficient level of immunohistochemistry and specimen banking services. In other cases, the organ site requires specialized skills in specimen acquisition and storage that were not available in the general Cancer Center core.

Almost all SPOREs have a formal process for reviewing outside requests for SPORE-derived specimens and most of them frequently provide specimens to non-SPORE investigators. Unfortunately, most SPORE progress reports do not contain comprehensive or standardized data on the number and types of biospecimens provided or to whom they were provided. Therefore, no quantitative analysis of the provision of biospecimens to non-SPORE investigators was possible.

Publications (Chapter 8)

The NIH RePORTER data system contains 5,655 publications published since 2004¹⁵ that acknowledge one or more of the 55 SPORE awards. Taking into account publications acknowledging multiple SPOREs, there is an average of 105 publications per SPORE. The distribution pattern for the number of publications per SPORE in the period January 2004 through March 2011 is shown in the figure on the next page. The distribution is relatively symmetric around a median of approximately 100 publications per award. Not surprisingly, all four of the highest-publishing SPOREs were among those that received their Type 1 awards before 2000.

¹⁵ The study question specified post-2004 publications.



Publications per SPORE: January 2004–March 2011

To determine the extent to which SPORE publications appeared in “high impact” journals, STPI researchers identified 18 biomedical research journals with a journal impact factor of 15 or higher.¹⁶ Between January 2004 and March 2011, 419 SPORE publications appeared in these 18 journals, representing approximately 7% of total SPORE publications in that period (see Chapter 8, Table 8D-1 for publications by journal).

¹⁶ The 18 journals are *Cancer Cell*; *Cell*; *Journal of Clinical Oncology*; *Journal of the National Cancer Institute*; *JAMA*; *The New England Journal of Medicine*; *Nature Biotechnology*; *Nature Genetics*; *Nature Immunology*; *Nature Medicine*; *Nature Methods*; *Nature Nanotechnology*; *Nature Reviews Cancer*; *Nature Reviews Drug Discovery*; *Nature Reviews Immunology*; *Nature Reviews Molecular and Cell Biology*; *Nature*; and *Science*.