Report on the Status of the SPORE Program

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Translational Research Program
DCTD
BSA/NCAB Presentation
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The Specialized Programs of Research Excellence (SPORE) program, which began as an appropriation from Congress, is in its 23rd year.

- SPOREs are specialized center grants to support multi-project, interdisciplinary, and in some cases, multi-institutional, translational research involving both basic and applied scientists, that results in diverse new approaches to the prevention, early detection, diagnosis and treatment of human cancers.

- There are now 50 fully funded SPOREs, and 6 on interim funding, in 19 states, 27 institutions plus 1 consortium, and including 17 organ sites or highly related cancers.

- NIDCR co-funds one head and neck SPORE grant.

- Most are in Cancer Centers and build upon their institutional resources.

- PAR-14-031 expires in September 2014; a new Program Announcement is required for receipt of applications for January 2015.
Unique Features of SPOREs

• All scientific projects must be translational and have a human endpoint within 5 years.

• Team science approach; at least one basic and one clinical/applied co-leader must head each project.

• Flexibility to terminate projects and to add projects within funding period. This allows the PI to move rapidly to refocus research based upon new knowledge and opportunities in the field.

• Career Development Program: not a training program. Allows basic and clinical scientists to become involved in translational research.

• Developmental Research Program for cutting-edge pilot studies, high risk/high payoff studies, and initiation of collaborations; these are short-term projects with potential to become full scientific projects, if successful, either in the SPORE (20%) or as an independent peer-reviewed grant (26%).

• Biospecimens/pathology CORE is required: a source of research specimen and analytic services. SPOREs must share specimens among other SPOREs and with the general scientific community, when appropriate. >1600 SPORE samples have been sent to TCGA and others were sent to the International Cancer Genome Consortium. Many R01s depend upon biospecimen resources in SPOREs

• SPOREs must collaborate.

• Involve input from patient advocates. Advocates often are included in the External Advisory Boards.
Changes in the SPORE Program since 2008

- Scientific Collaboration component added as required by the CTAC Guidelines Harmonization WG
- Elimination of weighting factors (70/30) in review in order to emphasize scientific projects
- “Required project” mandatory for only the 4 major malignancies
- IND-directed toxicology may be included as a 5 year human endpoint
- Related groups of cancers may include those that are related by an activation pathway or other oncogenic mutations across organ sites
- Option for NCI to support only 3 projects in cases where the overall impact score is within the funding range, but one or more projects is significantly less meritorious; in this case, the budget for the deleted project(s) is removed
- Administrative supplements have been eliminated; PIs are encouraged to use established NCI mechanisms to support Phase 2 and 3 clinical trials
<table>
<thead>
<tr>
<th>Organ Sites Funded</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
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<tbody>
<tr>
<td>Breast</td>
<td>9*</td>
<td>6</td>
<td>6</td>
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<td>Prostate</td>
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<td>6*</td>
<td>8§</td>
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<td>7</td>
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<td>5</td>
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<td>Ovarian</td>
<td>5*</td>
<td>4</td>
<td>4</td>
<td>5</td>
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<td>Bladder</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Skin</td>
<td>4</td>
<td>4*</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Brain</td>
<td>3*</td>
<td>4</td>
<td>4*</td>
<td>5</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>4*</td>
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<tr>
<td>Lymphoma</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Endometrial</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Cervical</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Kidney</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Leukemia</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
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<td>Myeloma</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>2*</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total SPOREs</strong></td>
<td>65 (includes 3 interim funding)</td>
<td>62 (includes 1 interim funding)</td>
<td>56 (includes 3 interim funding)</td>
<td>56 (includes 6 interim funding)</td>
</tr>
</tbody>
</table>

In 2010, 2011, 2012, and 2013 one H&N SPORE was funded by NIDCR

*One grant in the group on interim funding

§Two grants in the group on interim funding
SPORE EVALUATION

Science and Technology Policy Institute (STPI) May 2011 to April 2014

CTAC Working Group: January 27, 2014

CTROC approval: March 4, 2014

CTAC approval: March 12, 2014

SPL approval: April 22, 2014
SPORE Program Evaluation: Stage 1

An evaluation of the SPORE program was performed by Science and Technology Policy Institute (STPI) based on a Statement of Work that included 11 questions: 1 overarching and 10 based on specific aspects of the SPORE Program.

Examples:

– **Overarching:** What specific concepts or scientific findings that arose from SPORE research have had an impact on the practice of oncology?

– How well have the SPOREs been meeting the translational research goal of reaching a human endpoint within the five-year funding period?

– How well have basic and applied scientists worked together on the design and implementation of individual research projects?

– 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 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?

– How well have the SPOREs fostered translational research careers?

– How have the SPOREs used the Developmental Research Program for pilot studies?

Data collected and analyzed from SPOREs that were active in 2004 and after, and that completed at least one 5-year award cycle by mid-2011.
Major Advances (67) of the SPORE Program Identified in the STPI Report

Advances Accepted into Clinical Practice (out of 24 identified)
- Enzalutamide (MDV3100) for Late-Stage Prostate Cancer (CDP)
- Novel Agents and Regimens for Multiple Myeloma
- Diagnostic Test for EML4-ALK Translocation in Non-Small Cell Lung Cancer (NSCLC) Patients
- Predictive Assay for Lung Cancer Response to Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitors
- Chromosomal 1p/19q Deletion as an Oligodendroglioma Prognostic/Predictive Marker
- Screening and Monitoring in Endometrial Cancer and Hereditary Non-Polyposis Colorectal Cancer (HNPCC)/Lynch Syndrome

Advances in Late-Phase Human Testing (out of 29 identified)
- Heat Shock Protein Peptide Complex (HSPPC) 96 Vaccine for Brain Cancer (CDP/DRP)
- Transmembrane Protease, Serine 2 (TMPRSS2) Gene Fusions as Prostate Cancer Detection and Risk Markers

Advances with Broad Clinical Potential (out of 11 identified)
- Sensitivity and Resistance to EGFR Tyrosine Kinase Inhibitors in Lung Cancer
- Risk Factors and Disease Subtypes in Breast Cancer

Landmark Population Studies (out of 3)
- Identified in African American Men 8q24 as a Prostate Cancer Risk Locus (especially in younger men.)
In November 2013, CTAC approved the formation of a working group to evaluate the SPORE program. A working group of subject matter experts met on January 27, 2014. They deliberated about the value of the SPORE Program to the NCI and provided recommendations about the re-issuance of the PAR for January 2015 applications.

**Report**

- Presented by CCCT to CTROC on March 4, 2014
- Presented by the WG Chair, Dr. Nancy Davidson, to CTAC on March 12, 2014

**The value of the program to NCI:**

It remains important for the NCI to have a funding program focused exclusively on translational research.

The SPORE program represents a longstanding effort that has been successful in filling this niche and in which the NCI should take pride.

**Recommendation for re-issuance of the PAR:**

The SPORE Program Announcement should be re-issued and the program should continue in its current configuration with minor modifications.
Recommendations and Modifications

- **Recommendations**
  - Language in the PAR concerning “groups of highly related cancers” be modernized, expanded, and made more explicit, to make it clear that these “groups” include SPOREs organized around common biological pathways or other novel cross-cutting themes that traverse organ sites.
  - From time to time, the NCI might consider encouraging SPORE applications focused on NCI-wide research priorities (e.g., recalcitrant cancers) through a Notice to the PAR or by other means. However, no set-aside funds should be generated for these applications.
  - The 5-year requirement to reach a human endpoint should be continued; the current definition is well-crafted and understood.
  - Investigators should be credited for creative use of collaborations to complete project aims and to handoff for downstream development.
  - The current practice of awarding SPOREs based on the quality of the science as judge by peer review should continue and arbitrary limits on the number of SPOREs in each organ site should not be set.
  - There should not be a limit on the number of consecutive 5-year terms for which a SPORE can be renewed. There has been a reasonable percentage of new SPOREs in recent years and about 50% of projects funded in competitive renewals are new (not extensions of previous aims.) Rigorous peer review is the best way to ensure the quality of renewing awards.
  - The flexibility option was strongly endorsed as a unique feature that should be continued.
Recommendations and Modifications

- **Modifications**
  1. **Required Project:** Early detection, Prevention, or Population Science
     - **Issues:** Importance of these projects; “level playing field”
     - **Majority:** All SPORE applications should be required to have at least one project in one of these areas
     - **Minority:** No requirement, but should be encouraged to include these areas
     - **Minority:** Keep requirement as is: for breast, prostate, GI, and lung

     **Resolution: Discussion with DCTD, DCP, and DCCPS Directors**
     - It is still important for SPOREs to include translational research projects in early detection, prevention, and population science
     - For some organ sites or pathway-focused SPOREs the requirement might be a barrier to entry because of incidence of the cancer, expertise not available, or the cost of the project
     - Trans-NCI discussions continue in order to ensure a level playing field.
       Current thinking: requirement should be eliminated and instead inclusion of one or more of these projects should be encouraged and, if possible, incentivized.
     - The definitions of these projects are being re-examined by experts in DCP and DCCPS to make sure they are not too restrictive or too broad.
Recommendations and Modifications

- **Modifications (continued)**
  2. Developmental Research Program (DRP) and Career Development Program (CDP)

  Consensus that both the DRP and CDP are valuable features of the SPORE Program and should be continued

  - For maximum flexibility in using funds for these programs, the DRP and CDP funds should be consolidated into a single pool from which the PIs in consultation with their External Advisory Board would be able to direct funds to each program based on the best CDP candidates or the best DRP projects.

  **Resolution: Discussion within the TRP/DCTD and at CTROC**

  - This recommendation to merge the budgets will be incorporated into the next PAR, but in order to make sure that each program maintains integrity and one does not subsume the other, each component will be reviewed separately.

  - Important because of the requirement in the CDP that the PI makes a special effort to recruit qualified women and minorities.
Significant Accomplishments in the Last 2 Years
### Bladder

**SPORE PI:** Dinney  
Identified, using whole genome mRNA profiling of 73 fresh-frozen specimens, and validated, using 57 FFPE specimens, 3 molecular subtypes of muscle-invasive bladder cancer that share features with basal and luminal breast cancer. One subtype expressed an activated wild-type p53 gene signature (“p53-like”) and these were resistant to frontline neoadjuvant platinum-based combination chemotherapy. It should now be possible to identify patients who will not benefit from neoadjuvant chemotherapy, relying on molecular characteristics. *Cancer Cell* 25, 2014, 152.

### Brain

**SPORE PI:** Berger  
Followed up on a promising pilot study of recurrent glioblastoma (GBM) patients who underwent surgical resection and were then treated with a vaccine of autologous tumor-derived peptides bound to a 96kD chaperone protein (HSP96) and showed 11/12 individual patient-specific immune responses. Now they performed a Phase II single arm study of this vaccine and reported >90% of patients surviving >6 months, comparable to the best outcomes with bevacizumab. This has led to a Phase II, 3 arm trial comparing this vaccine alone, vaccine plus bevacizumab, and bevacizumab alone in surgically resected recurrent GBM patients. *Clin Cancer Res* 19, 2013, 205; *Neuro-Oncology* 16, 2014, 274. *(NCT01814813)*

### Breast

1. **Arteaga**  
   2. **Ingle**  
   1. Performed comprehensive molecular analyses on the residual disease of 74 triple negative breast cancers after neoadjuvant chemotherapy and compared them with matched pretreatment biopsies. Diverse molecular lesions and pathway activation were discovered; 90% contained an alteration potentially treatable with currently available targeting agents. *Cancer Discovery* 4, 2014, 232.  
   2. Demonstrated that the molecular mechanism of endoxifen (a secondary metabolite of tamoxifen) action in ER+ breast cancer cells differs from those of 4HT (an early metabolite of tamoxifen) and ICI -182 780 (a pure anti-estrogen) and that the induced gene expression in all three were significantly different and, in the case of endoxifen, concentration dependent even in the presence of tamoxifen, suggesting that endoxifen may result in antitumor activity in patients refractory to tamoxifen. *PLOS ONE* 8, 2013, e54613

### Cervical

**SPORE PI:** Wu  
Demonstrated that although intramuscular vaccination of high-grade cervical intraepithelial neoplasia (CIN2/3) patients with a therapeutic HPV E6/E7 vaccine caused only modest changes in the immune response as measured in the blood, pronounced CD8+T cell changes were observed in the target lesion microenvironment. Patients with this response might be monitored and avoid resection as they have a better prognosis. *Sci Transl Med* 6, 2014, 221ra13
<table>
<thead>
<tr>
<th>Organ Site</th>
<th>SPORE PI</th>
<th>Accomplishments</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Fuchs</td>
<td>Identified BCL-XL plus MEK inhibition as an effective strategy in KRAS mutant cancer models using a pooled shRNA-drug screen designed to find genes that when inhibited cooperate with MEK inhibitors to kill KRAS mutant tumors. <em>Cancer Cell 23, 2013, 121. Collaboration between 2 SPOREs; collaboration with industry</em></td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td>Sidransky</td>
<td>Discovered membranous expression of PD-L1 on tonsillar crypts, the site of initial HPV infection in HPV-associate head and neck squamous cell carcinomas, and a high level of PD-1 expression on tumor infiltrating lymphocytes, which explains why these cancers evade the immune system, persist and grow despite their immune-rich environment. <em>Cancer Research 73, 2013, 1733.</em></td>
</tr>
<tr>
<td>Leukemia</td>
<td>Byrd</td>
<td>Conducted a multicenter Phase 1b/2 trial with ibrutinib (BTK inhibitor) in patients with relapsed or refractory CLL or small lymphocytic lymphoma. At 26 months, the PFS rate was 75% and the OS was 83%. Response was independent of stage of disease, number of previous therapies, and the 17p13.1 deletion. <em>N Engl J Med 361, 2013, 31. Collaboration of 2 SPOREs and industry partner (NCT01105247)</em></td>
</tr>
<tr>
<td>Lung: NSCLC</td>
<td>1.Bunn 2. Johnson</td>
<td>1. Studies employing second biopsies from ALK+ lung NSCLC patients who either progressed on crizotinib or became resistant to crizotinib revealed secondary mutations (4 different mutations) in the ALK kinase domain or the presence of several oncogenes (Kras or EGFR activating mutations) in the same sample. <em>Clin Cancer Res. 18, 2012, 1472</em> 2. Similar studies were performed by a second SPORE group that demonstrated amplification of the ALK fusion protein or activation of KIT as the cause of resistance to crizotinib, <em>Sci Transl Med 4, 2012, 120ra17</em></td>
</tr>
<tr>
<td>Lung: SCLC</td>
<td>Minna, Bunn, Baylin</td>
<td>Comparing 36 primary SCLC and adjacent normal tissue pairs, 17 matched SCLC and lymphoblastoid lines, 4 additional primary tumors and 23 cell lines, the PIs found that G to T transversions predominated consistent with the effects of tobacco carcinogens on DNA; high prevalence of inactivating mutations of p53 and RB1 were confirmed; Kras mutations were not found; mutations in FLT1, FLT4, KDR, and KIT were found. A major finding was that SOX2, a transcription factor, was amplified in 27% of the samples; aberrant SOX2 expression is implicated in reprogramming mature cells to pluripotency. <em>Nature Genetics 44, 2012, 1111 Collaboration between 3 SPOREs</em></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Forman</td>
<td>Demonstrated that STAT3 or BCL-XL is knocked down by specific CpG(class A)- siRNAs in TLR9+ B-cell lymphomas and other hematologic malignancies. These TLR9-agonists are, on the other hand, immunostimulatory and non-toxic for normal cells. <em>Blood, 121, 2013, 1304.</em></td>
</tr>
<tr>
<td>Organ Site</td>
<td>SPORE PI</td>
<td>Accomplishments</td>
</tr>
<tr>
<td>------------</td>
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</tr>
<tr>
<td>Myeloma</td>
<td>Anderson</td>
<td>Showed antitumor efficacy of a ubiquitin-specific protease-7 inhibitor, P5091, in <em>in vitro</em> studies and in xenografts of multiple myeloma. This agent does not target the proteasome itself, but induces apoptosis in myeloma cells resistant to bortezomib therapy. The study provides the underpinning for clinical evaluation of this class of agents alone or in combination with lenalidomide, or an HDACi, or with dexamethasone and is important because dose-limiting toxicity and development of resistance limit long-term use of bortezomib. <em>Cancer Cell</em> 22, 2012, 345.</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Boyd</td>
<td>Showed that although a whole-tumor GVAX vaccine alone had no effect, combining it with PD-1:PD-L1 blockade, decreased the immune suppressive environment (Tregs, MDSCs) and allowed the expansion and activation of TILs. <em>Cancer Research</em> 73, 2013, 6900. <em>Developmental Research Program; collaboration with a P01</em></td>
</tr>
<tr>
<td>Pancreatic</td>
<td>Petersen, Tepper, Carbone</td>
<td>Discovered that in pancreatic cancer development, mutant Kras requires the expression and activation of ligand-dependent EGFR. Without EGFR activity, mutant Kras activity is insufficient to induce MEK/ERK activity which is required for epithelial transformation. <em>Cancer Cell</em> 22, 2012, 304. <em>Collaboration of 3 SPOREs</em></td>
</tr>
<tr>
<td>Prostate</td>
<td>Chinnaian</td>
<td>Discovered a long noncoding RNA (lncRNA) on chromosome 2q31, named SChLAP1, that is highly expressed in 25% of prostate cancers and is associated with ETS gene fusions and higher Gleason Scores—histological measures of tumor aggressiveness. In SChLAP1 knockdown experiments, it was shown that genes regulated by this lncRNA were inversely correlated with the SWI/SWF chromatin modifying complex functions (including a tumor suppressor function). <em>Nature Genetics</em> 45, 2013, 1392. <em>Collaboration of SPORE and EDRN.</em></td>
</tr>
<tr>
<td>Skin</td>
<td>Kupper</td>
<td>Demonstrated intrinsic resistance to Braf inhibition in melanoma is due to stromal cell secretion of hepatocyte growth factor (HGF) that results in the activation of MET, reactivation of MAPK and PI3K-AKT pathways. Dual inhibition of Braf and either HGF or MET resulted in a reversal of drug resistance. A similar resistance mechanism was found in a subset of BRAF mutant colorectal and glioblastoma cells lines. <em>Nature 487, 2012, 500. Collaboration between SPORE and Foundation.</em></td>
</tr>
</tbody>
</table>
RESERVE SLIDES
Translational research uses knowledge of human biology to develop and test the feasibility of cancer-relevant interventions in humans and/or determines the biological basis for observations made in individuals with cancer or in populations at risk for cancer.

The following types of human endpoints are acceptable to qualify SPORE projects as translational and programmatically responsive:

- Early phase clinical trials of new investigational drugs and biologics, experimental procedures, medical devices, or combinations thereof, or
- Early phase clinical trials of new combinations or new uses of the FDA-approved agents and devices, or
- Discovery and development of biomarkers, only when measurements are made in human specimens, or directly in human subjects, or
- IND-directed toxicology studies* conducted following a pre-IND meeting with the FDA in which the plan proposed by the investigators is acceptable to the FDA, or
- Population, behavioral, or psychosocial studies, when these studies address mechanistic aspects of the biology of the disease, or
- Clinical studies that lead to laboratory studies which address new clinical hypotheses.
Types of Grants Funded

- Type 1: Same PI
- Type 1: New PI
- Type 2: Same PI
- Type 2: New PI

Chart showing the number of competing grants funded by type over fiscal years 2010 to 2013.
Required Project Definitions

- **Early Detection:** An early detection project is one that develops and/or tests an assay (biological or imaging) that determines the presence of an early invasive cancer or detects a pre-cancerous lesion, for which a subsequent intervention is established or for which an experimental intervention will be performed. This includes early detection of a new primary in a “cancerized field” (an area of epithelium surrounding an excised or treated primary tumor that contains genetically transformed, but histologically normal cells that are predisposed, perhaps because of continual carcinogenic insult, to subsequent tumor development.) Testing for metastases or recurrence of the primary tumor is not early detection and is therefore not acceptable. Although screening and early detection are sometimes used interchangeably, screening is the application of the assay in general populations and is beyond the scope of a SPORE project.

- **Prevention:** A prevention project investigates a medical, surgical, or lifestyle intervention that has as its aim the reduction of cancer incidence in individuals at risk. A project that addresses the prevention of a second primary tumor is also appropriate. A project that addresses prevention of cancer recurrence is not acceptable. A therapeutic vaccine in a no-evidence-of-disease state would not be considered secondary prevention, but rather a therapeutic intervention (i.e., adjuvant therapy.) However, a project that develops a vaccine that targets “at risk” lesions (e.g., Barrett’s esophagus or DCIS) is acceptable.

- **Population Science:** A population science project aims to understand the causes and distribution of cancer in diverse populations, supports the development and delivery of effective interventions to reduce cancer risk, mortality and morbidity, as well as social costs of cancer, and monitors and explains cancer trends in all segments of the population. Such projects in the SPORE may focus on samples in the general population, individuals at risk for cancer, or cancer patients. Unlike clinical trials with their specific exclusion criteria, population studies should be sufficiently representational to allow for substantial external validity, i.e., generalized inferences to the target populations in the studies. Likewise, population studies that focus on biomarkers may not draw on specimens from a convenience sample, but instead must be based on samples that allow for inferences to the target populations. Population Science required project may draw upon already existing population science resources or may develop new cohorts in order to examine a specific translational research question developed in collaboration with basic, clinical, and population science investigators.

- For each required project, there must be a laboratory component addressing relevant mechanistic aspects of human cancer biology. The project may involve genetic, epidemiological, behavioral, social, applied, and surveillance studies.
Research Project Trial Characteristics

Table 5C-1. SPORE Trial Distribution by Phase

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<th>Trial Number</th>
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<tr>
<td>I</td>
<td>95</td>
<td>43%</td>
</tr>
<tr>
<td>I/II</td>
<td>20</td>
<td>9%</td>
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<tr>
<td>II</td>
<td>89</td>
<td>40%</td>
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<tr>
<td>Randomized II</td>
<td>6</td>
<td>3%</td>
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<tr>
<td>Unknown</td>
<td>9</td>
<td>4%</td>
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<tr>
<td>Total</td>
<td>221</td>
<td>100%</td>
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Table 5C-2. SPORE Trial Distribution by Intervention Type

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<tr>
<th>Intervention Type</th>
<th>Number of Trials</th>
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<tr>
<td>Drug/Biologic</td>
<td>162</td>
<td>73%</td>
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<tr>
<td>Gene Therapy</td>
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<td>2%</td>
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<tr>
<td>Immunologic</td>
<td>49</td>
<td>22%</td>
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<tr>
<td>Chemoprevention</td>
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<td>2%</td>
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Table 5C-4. Status of SPORE Trials—Fall 2011

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<tr>
<th>Trial Status</th>
<th>Number of Trials</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Completed</td>
<td>132</td>
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<tr>
<td>Ongoing</td>
<td>56</td>
<td>25%</td>
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<tr>
<td>Terminated</td>
<td>16</td>
<td>7%</td>
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<tr>
<td>Unknown</td>
<td>17</td>
<td>8%</td>
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Note: Analysis of 221 SPORE trials.

Figure 5C-1. Percentage of Trials with Different Funding Sources