SPORE Grants: Putting Collaboration Front & Center

SPORE grants have become the cornerstone of NCI's efforts to advance collaborative, interdisciplinary translational cancer research.

September 24, 2019 By Melanoma Research Alliance

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In medicine, sometimes the biggest and most game-changing advancements come from a single person — who through tireless work — arrives at a true 'eureka' moment. This 'go it alone' concept is not only reinforced through television and movies, it's also bolstered in the way the medical community makes research awards, faculty appointments, and publishing rights.

However, more often than not, in research as in life — it truly does take a village to make progress. In recognition of this, the National Cancer Institute established the Specialized Programs of Research Excellence (SPORE) program in 1992 that requires collaborations of teams of scientists across disciplines. SPORE programs can focus on cancer in a specific organ such as the skin or lung, or on cancers that arise in different organs but share common genetic mutations. Since its founding, SPORE grants have become the cornerstone of NCI's efforts to advance collaborative, interdisciplinary translational cancer research that brings basic research findings from the laboratory bench into the clinic. In fact, SPORE awards operate much like MRA Team Science Awards that draw together different areas of expertise; however, SPORE awards are much larger in scope and scale.

What Goes into a SPORE Grant?
SPORE grants are a highly competitive, five-year grant award totaling $11 million from the National Cancer Institute (NCI) that serves as a 'capstone', or external validator, for highly productive and successful research programs. In addition to melanoma (skin cancer), more than twenty other organ sites, systems, and pathway-specific themes are represented in the SPORE program, including: bladder, brain, breast, cervical, and hyperactive RAS tumors.

Housed in the NCI's Translational Research Program, SPORE grants bring together basic, clinical, and applied researchers to rapidly move innovative approaches from bench to bedside. In fact, all SPORE awards are required to reach a human end-point (such as a clinical trial) during the 5-year funding period. All SPORE awards aim to reduce cancer incidence and mortality while improving survival and quality of life.

Melanoma SPORE Grants:
The NCI has awarded five SPORE grants focused on melanoma research to the following institutions: Moffitt Cancer Center, University of Texas MD Anderson Cancer Center, New York University, The Wistar Institute, and Yale University. Each grant award is then divided into several distinct projects addressing topics such as combination therapy, treatment resistance, predictive biomarkers, or the development of altogether new or refined treatment strategies.

The newest grant recipient, New York University (NYU), was awarded its SPORE grant in July 2019. The award is led by Drs. Iman Osman and Jeffrey Weber — both MRA-funded investigators. During their five-year grant term, the NYU team will focus on identifying and validating biomarkers that can help guide melanoma treatment in the adjuvant setting.

Adjuvant therapy, a follow-on treatment delivered after surgery or other 'curative' treatment, helps to reduce the likelihood of melanoma returning. Studies have shown that adjuvant therapy can be very helpful in reducing the risk of recurrence or relapse, but it also exposes patients to risks, including medications that can cause side effects, requires time out of the day, and may cause financial hardship. This is especially important because most patients who are treated with surgery will not go on to relapse. The FDA has approved several drugs for adjuvant therapy for patients with surgically resected, Stage 3 disease with lymph node involvement. Beyond this, doctors have little insight into who needs this therapy, who might be fine without it, and if indicated, which medication is the right fit. NYU's SPORE researchers want to change that.

As a growing body of research continues to show the promise of delivering therapy earlier in the course of melanoma — this insight will only become more important. That's because currently, without any of the predictive biomarkers that NYU researchers aim to develop, for every four patients treated with adjuvant therapy:

- Two patients out of the four were never going to relapse — and thus didn't need additional treatment,
- One patient out of the four does not benefit from the therapy and relapses despite it, and
- One patient benefits.

In short, today, for every patient who benefits from adjuvant therapy — three others will be treated and will see no such benefit. At least such is the case now without better bio-markers to determine the most appropriate candidates for adjuvant therapy.

Researchers involved in NYU's SPORE grant will work to close this gap through four distinct — but related — projects:

- Project One: Defining Predictive Biomarkers in Patients Receiving Checkpoint Immunotherapy Based Adjuvant Therapy

Using clinical data and specimens obtained from Checkmate 915, a Phase 3 clinical trial comparing adjuvant nivolumab with adjuvant combination ipilimumab/nivolumab, the team will identify factors that help predict which patients are most likely to benefit from this therapy. To do this, the team will analyze the gut microbiome, serum factors, and immune cells in the blood from the trial participants.

- Project Two: Genomic Profiling of T-Cells in Immunotherapy-Based Adjuvant Therapy:

Again, using samples from the Checkmate 915 trial, the team will analyze the genome of blood T cells, as well as cells in the tumor microenvironment to identify which patients will benefit from adjuvant checkpoint inhibitor therapy.

- Project Three: Predicting Immune-Related Adverse Events in Patients Treated with Adjuvant Therapy:

Despite their game-changer status, immune checkpoint inhibitors are associated with a suite of side effects that can be long-lasting and lead to treatment disruption and discontinuation. Given only 1 in 4 patients will benefit from adjuvant therapy when delivered broadly, the ability to predict who will develop such side effects is desperately needed. Here, the team aims to do just that by determining whether patients who develop such side effects harbor signs of latent autoimmunity before they are treated. They will also test whether the preventive — what doctors call prophylactic — use of a drug for inflammatory bowel disease will help prevent ipilimumab-associated colitis.

- Project Four: Optimizing the Management of Stage II Melanoma Using miRNA:

Of patients diagnosed with stage 2 melanoma, although unlikely, a small percentage will see their melanoma return at a later date, making selecting which patient's to treat with adjuvant therapy even more critical for this group of patients. The NYU team aims to identify a molecular signature that will help predict which of these patients are most likely to benefit from adjuvant checkpoint inhibitor therapy and then validate their findings in the clinic.

For NYU, this award was a longtime in the making. They started to map out their application more than three years ago, and their extensive biospecimen database — a critical part of their project — has been collecting patient samples for almost two decades. They've also assembled a research team with broad experience in basic, translational, and clinical research.

"Earning the NCI Skin SPORE award in 2019 is a biomarker — a surrogate marker — of the excellence in melanoma treatment and research that NYU has built over the last two decades," says Iman Osman, M.D., Principal Investigator and Director of the SPORE and professor in the Ronald O. Perelman Department of Dermatology. "My colleagues and I have worked diligently to deliver excellence in care and research conduct, build the program through strategic recruitment

of both young and established investigators, and ensuring long-term support of key resources like the biobank. In fact, NYU received MRA's prestigious Team Science Awards in 2010 and 2018, as well as several other MRA awards.

Scientific advancements are built upon the collaborative efforts of scientists across the globe. Grant mechanisms, such as MRA's Team Science or NCI's SPORE awards, provide critical resources that prioritize collaboration and cross-discipline approaches to answer some of the toughest unanswered questions. For the NYU, and the broader melanoma community, the SPORE grant will help researchers determine which patients needs adjuvant therapy, how long they should receive it, and which drug is the best fit for them — critical questions needed to dramatically expand the use of adjuvant therapy.

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