INTRODUCTION

The Congressionally Directed Medical Research Programs (CDMRP) represents a unique partnership among the U.S. Congress, the military, and the public to fund innovative and impactful medical research in targeted program areas. In 2015, an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine was assembled to evaluate the CDMRP’s two-tier review process and its coordination of research priorities with the National Institutes of Health (NIH) and the Department of Veterans Affairs (VA). As part of their final report, the committee recommended that each CDMRP program “… develop a strategic plan that identifies and evaluates research foci, benchmarks for success, and investment opportunities for 3–5 years into the future,” and that these strategic plans “should specify the mission of the program, coordination activities with other organizations, research priorities, how those priorities will be addressed by future award mechanisms, how research outcomes will be tracked, and how outcomes will inform future research initiatives.”

In response to these recommendations, this document presents the current strategy for the CDMRP’s Kidney Cancer Research Program (KCRP). The KCRP Strategic Plan identifies the high-impact research goals most important to its stakeholders while providing a framework that is adaptable to changes in the medical research environment. This plan has been formulated to provide greater clarity of the program’s goals over time to the public and other stakeholders. Funding for the KCRP is congressionally appropriated on an annual basis; therefore, there is no guarantee of future funding. The KCRP Strategic Plan will be reviewed during the program’s annual Vision Setting meeting and updated as necessary.

KCRP BACKGROUND AND OVERVIEW

Kidney cancer research has been funded by the CDMRP for many years as a congressionally directed topic under the Peer Reviewed Medical Research Program (PRMRP) and the Peer Reviewed Cancer Research Program (PRCRP). During the fiscal years that kidney cancer was a topic under the PRMRP (fiscal year 2006 [FY06], FY08-FY09), $2.7 million (M) was invested. The kidney cancer topic area was then included in the PRCRP. From FY10 through FY16, the PRCRP invested over $9.8M in kidney cancer research. In FY17, Congress directed $10M to kidney cancer research in the Department of Defense appropriation, thus establishing the KCRP. For the inaugural year, a Stakeholders meeting was held to gain an understanding of the current landscape in kidney cancer research and patient care and to build a program that would fill outcomes and knowledge gaps in kidney cancer. A summary of the FY17 KCRP Stakeholders meeting is available online.

The funding mechanisms that were offered by the FY17 KCRP encompassed several unmet gaps as identified during the Stakeholders meeting. Funding opportunities focused on innovation (Concept Award, Idea Development Award (with both established and early career investigator options)); and translational studies (Translational Research Partnership Award). After in-depth discussion about how the field of researchers and clinicians could advance patient care, the FY17 KCRP Programmatic Panel recommended a short and mid-term investment strategy with the Consortium Development Award (CDA) and a potential FY19 Consortium Award if Congressional funds are appropriated for the KCRP. The CDA is an infrastructure-based research award that allows investigators from multiple sites to collaborate and construct a working clinical consortium that merges team science with clinical outcomes. The CDA builds the base of the future for the KCRP to establish a fully realized clinical consortium. If funds are available in FY19, the KCRP will offer a Consortium Award with the aim to encompass
correlative studies (such as biomarker identification, development of novel strategies, and generation of new treatment avenues in immunotherapy and beyond) and clinical trials. The synergy of clinical trials with supportive laboratory research will reveal new areas to research as well as advance the field of kidney cancer patient care. Figure 1 shows the percentages of the KCRP’s research dollars invested in each award mechanism in FY17.

In FY18, the KCRP continued its commitment to innovation and translational research, as shown in Figure 2. In addition, the KCRP Programmatic Panel members recommended increased investment in early-career physician scientists (Physician Research Award) and in exploiting emerging technologies (Technology Development Award).

Figure 1. FY17 KCRP Percent Research Dollars Invested per Award Mechanism

Figure 2. FY18 KCRP Recommended Percent Research Dollars Invested per Award Mechanism

VISION: To eliminate kidney cancer through collaboration and discovery

MISSION: To promote rigorous, innovative, high impact research in kidney cancer for the benefit of Service members, Veterans, and the American public

RESEARCH AND FUNDING ENVIRONMENT

Renal cell carcinoma (RCC) is the sixth most common cancer in men and the seventh most common cancer in women in the United States. Kidney cancer is twice as common among men as it is in women and is more common among African Americans. The estimated number of new U.S. cases in 2017 was 63,990, representing 3.8 percent of all new cancer cases. The majority of RCC cases are sporadic; only 2% to 3% are hereditary. RCC has increased since the 1970s by an average of 3% per year for Caucasians and 4% per year for African Americans. RCC is primarily diagnosed in senior patients with a median age of diagnosis of 64. The most common type is clear cell RCC (75% of all kidney cancers). The second most common subtype is papillary RCC (type 1 and type 2) at 15%. The third most common subtype is chromophobe RCC.

Sixty-five percent of patients are initially diagnosed with localized disease that is confined to the kidney, and nearly 35% will be diagnosed with disease that has spread beyond the kidney, with 16% having spread to distant organs. Patients diagnosed with localized disease who receive surgery and have low-risk disease have a 5-year disease-specific survival rate of 97%. Survival rates for patients with disease that has spread beyond the kidney drop sharply to 8% for high-risk patients, 18% for intermediate-risk patients, and 41% for low-risk patients.

Rare kidney cancer subtypes include renal medullary carcinoma, collecting duct carcinoma, and MiT family translocation carcinomas, among others. Renal medullary carcinoma, in particular, is a highly lethal tumor that generally affects young African-American patients with sickle cell trait and is characterized by mutations in the SMARCB1 gene.

Lifestyle factors are associated with the disease (smoking, obesity, low physical activity, hypertension, diabetes mellitus, and consumption of beef, fatty food, and black tea). Some evidence suggests that environmental factors, including pollutants, may increase risk for kidney cancer.
Most kidney cancers are discovered through incidental findings using computerized tomography or magnetic resonance imaging of the abdomen to diagnose other medical complaints. There are no specific and selective biomarkers for kidney cancer. Renal mass biopsy is imperative for definitive treatment of subtype, but is generally only done when the treatment plan may need to be revised due to suspected infection or metastatic spread.

Drugs that target vascular endothelial growth factor (VEGF) or its receptor are standard therapy. Commonly, sunitinib or pazopanib are used first. Other anti-VEGF agents, such as axitinib and cabozantinib, have taken a role in the refractory space. More recently, nivolumab, a programmed cell death protein 1 (PD-1) inhibitor that acts to stimulate a patient’s anti-cancer immunity, was approved for use in refractory RCC and has become a standard treatment based on its tolerability and clinical activity. Adjuvant therapy using sunitinib was recently approved by the Food and Drug Administration for high-risk patients. For stage I cancers smaller than 4 cm, options include active surveillance with possible delayed intervention; percutaneous ablative procedures, such as radiofrequency ablation and cryoablation; and surgery, such as partial nephrectomy, or less commonly, radical nephrectomy. For stage I cancer larger than 4 cm and for stage II and III tumors, radical nephrectomy is generally necessary.

RESEARCH FUNDING LANDSCAPE
The NIH funded $155.5M in kidney cancer research from FY14 to FY17. Common Scientific Outline (CSO) data from the International Cancer Research Partnership, shown in Figure 3, illustrate the amounts invested by the National Cancer Institute (NCI) in each research area. The comparison of the FY17 KCRP investment into each category is shown in Figure 4. The majority of the NCI investment since 2014 has been in treatment, followed by research in kidney cancer biology and etiology, respectively. FY17 KCRP investment in biology and early detection, diagnosis, and prognosis demonstrates the identified knowledge gaps and growing need to develop an understanding of the biology of kidney cancer and ways to answer the patient community with early detection techniques.

PRIVATE KIDNEY CANCER FUNDING INITIATIVES

<table>
<thead>
<tr>
<th>Fund</th>
<th>Description</th>
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<tr>
<td>Action to Cure Kidney Cancer</td>
<td>Action to Cure Kidney Cancer has directly funded kidney cancer research since 2006 and, since then, has provided 11 grants to seven researchers, totaling $382,282.50.</td>
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<tr>
<td>KCCure</td>
<td>$100,000 has been awarded to Dr. Wayne Marasco at Dana Farber Cancer Center.</td>
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<tr>
<td>Kidney Cancer Association</td>
<td>Funds research in urology and clinical oncology through the Young Investigator Award to support physicians and scientists transitioning from a fellowship program to a faculty appointment.</td>
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<tr>
<td>American Cancer Society</td>
<td>$4,228,245.82 has been awarded in kidney cancer research between 2009 and 2017.</td>
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<tr>
<td>Alex’s Lemonade Stand Foundation</td>
<td>$602,566.45 has been awarded in kidney cancer research between 2014 and 2017.</td>
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STRATEGIC DIRECTION

KCRP OVERARCHING STRATEGIC GOALS

Increase understanding of the biology of kidney cancer
Understanding the biology of kidney cancer could impact research along the entire cancer care spectrum from basic/etiology to prevention, detection/diagnosis, prognosis, treatment, and survivorship. The KCRP addresses this need by encouraging innovative ideas with high-impact approaches that move the field toward the KCRP's vision of eliminating kidney cancer. While other cancer research has begun to delve into personalized medicine, the question of what drives kidney cancer development and metastasis has become a barrier to progress. Improved understanding of genetic, epigenetic, or environmental risk factors may help diagnose patients earlier and, as a result, improve their prognosis. The focus on RCC propels the field forward; yet, investigations into the rarest forms of kidney cancer could have implications that may impact the entire field. Hence, the KCRP's goal of understanding the biology of kidney cancer encompasses, not only the spectrum of research, but also different forms of kidney cancer.

Improve patient care for kidney cancer
Despite the heavy burden of kidney cancer for patients and their families, clinical progress remains stagnant. Integration of bench research with bedside care is crucial to translational research and the acceleration of promising ideas in kidney cancer. The KCRP aims to support translational research in order to move laboratory observations to clinical applications. Research opportunities are critical for early-career physician scientists and address the need to train and fund the next generation of kidney cancer clinicians. Complimentary to supporting physician scientists, the KCRP recognizes the requirement to grow and develop early-career laboratory scientists and, by doing so, increase the research community and ensure that it thrives in the future. A robust research community produces outcomes to continually improve patient care.

Another significant gap for patient care outcomes that the KCRP has acknowledged is the need for facilitation of multi-site collaborative clinical research development and clinical trials. Due to funding constraints and weak infrastructure, the kidney cancer community has, in the past, had only a paucity of multi-institutional clinical trials with the capability to reach out to a large demographic and test potential lifesaving therapies. By investing in and growing the pool of kidney cancer experts, as well as supporting clinical collaborations, the KCRP will help provide the resources needed by the research community to focus on novel avenues of research that will improve patient care.

Enhance technology development for kidney cancer
New approaches to kidney cancer are not always found within the field of kidney cancer research. Encouraging experts in diverse disciplines to apply their knowledge to kidney cancer is key to expanding the potential for advancements in kidney cancer research and patient care. For example, investment in the expansion and integration of telemedicine for patients with limited access to kidney cancer specialists broadens the impact of advancements to a larger demographic. Therefore, the KCRP prioritizes technological development for the future of kidney cancer research and patient care.

INVESTMENT STRATEGY

NEAR- TO MEDIUM-TERM GOALS (2 TO 5 YEARS)

- Investment in early-career investigators (laboratory scientists and physician scientists) through the Idea Development - Early Career Investigator and Physician Research Award mechanisms
- Investment in highly innovative, untested, potentially groundbreaking novel concepts in kidney cancer research through the Concept Award and Idea Development Award mechanisms
- Investment in translational research between clinicians and research scientist through the Translational Partnership Award mechanism
- Investment in technology development through the Technology Development Award mechanism
- Investment in collaborative clinical research efforts through the Consortium Development Award mechanism and the Consortium Award mechanism

MEDIUM- TO LONG-TERM STRATEGIC PRIORITIES/STRATEGY ADJUSTMENTS (5 TO 10 YEARS)
Over the medium to long term, the KCRP will consider expanding its focus to include the additional scientific priorities defined for the program. Their inclusion will be considered and based upon the results of research supported by the program in the near term and the progress made by others in the field.
MEASURING PROGRESS

The KCRP will measure its success in the near term based on successful investments in areas that are important to the program’s strategy. Long-term success will be evaluated based on contributions to the scientific community and follow research linked to KCRP-funded projects.

Progress toward the KCRP’s strategic goals will be measured in multiple ways, including reviewing and monitoring the research outcomes of funded applications. Assessment of the progress made by the KCRP’s research awards will inform the program on its impact and steer changes in the investment strategy in future years. The KCRP’s metrics include, but will not be limited to, reviews of publications, patents, presentations, follow-on funding obtained, and the career advancement of funded investigators.

REFERENCES

9. CSO is a coding system used by public and private organizations in the United States (including the National Institutes of Health), United Kingdom, and Canada to describe research projects (see https://www.lcrpartnership.org/CSO).

Table 1. Investment Metric Goals of the KCRP

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<thead>
<tr>
<th>Metric Goals</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>25% Funded portfolio invested in innovated and impactful research for the development of new approaches in kidney cancer research and patient care</td>
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<tr>
<td>25% Funded portfolio invested in the development of early-career scientists and physician scientists for productive careers in kidney cancer research</td>
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<tr>
<td>15% Funded portfolio invested the advancement of the development of technology in kidney cancer</td>
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<tr>
<td>35% Funded portfolio invested in translational research partnerships and collaborative clinical research and trials (consortium)</td>
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