

# Kidney Cancer Research Program

## Strategic Plan

### 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,<sup>1</sup> 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.

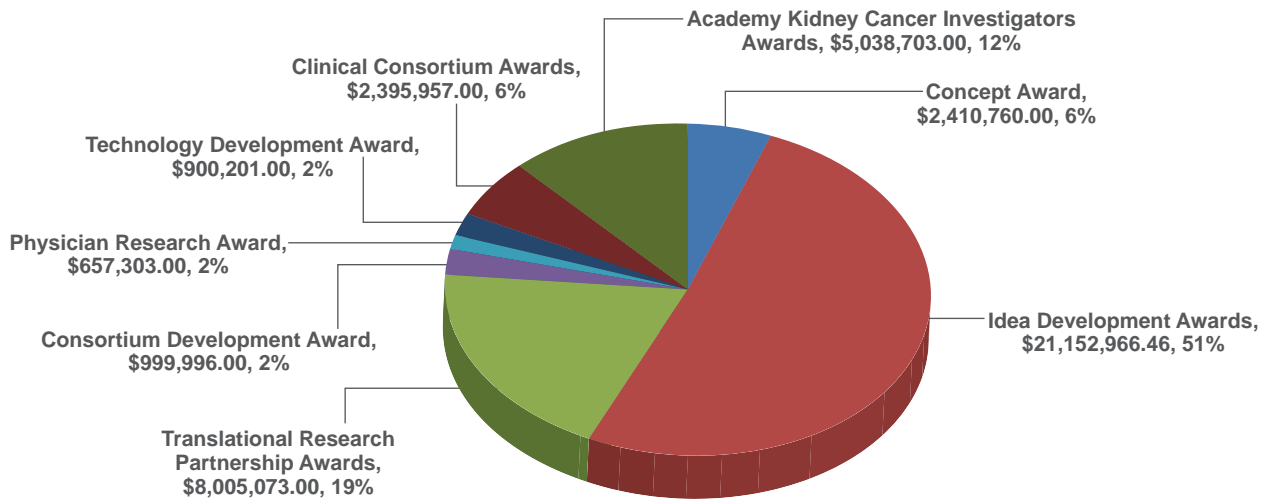
### KCRP BACKGROUND AND OVERVIEW

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. In the inaugural year, a stakeholders meeting (summary available online<sup>2</sup>) 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. Since then, congressional appropriations to the KCRP have totaled \$135M, including \$15M, \$20M, and \$40M from FY18 through FY20. In FY21 KCRP received an additional appropriation of \$50M to conduct kidney cancer research.

During the first Vision Setting meeting in FY17, the Programmatic Panel developed the KCRP vision and mission statements listed below. The Programmatic Panel also recommended funding mechanisms to address several unmet gaps, as identified during the Stakeholders meeting. The vision and mission statements as well as the funding opportunities that are offered are reviewed annually and amended based on the current state of the science in kidney cancer research and patient care. FY17 funding opportunities focused on innovation (Concept Award, Idea Development Award [with both Established and Early-Career Investigator options]); translational studies (Translational Research Partnership Award); and investment in the infrastructure to foster clinical research collaborations to advance patient care (Consortium Development Award). FY18 saw the KCRP expand investment in early-career physician scientists (Physician

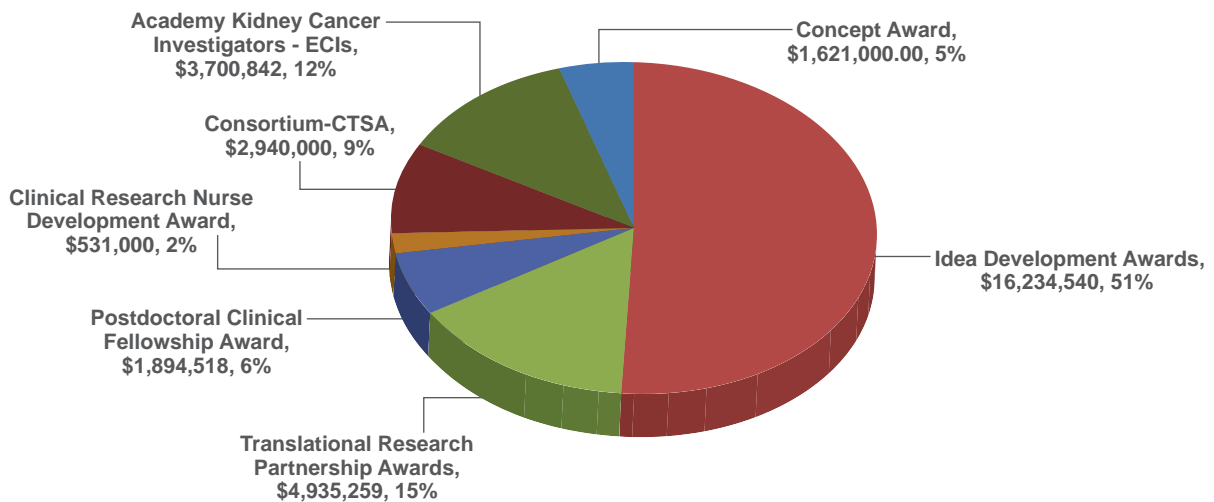
Research Award) and in exploiting emerging technologies (Technology Development Award). In FY19, the KCRP continued its commitment to innovation and translational research, and the KCRP Programmatic Panel members additionally recommended investment in two major initiatives: (1) attracting and fostering career-long interest in kidney cancer research and professional development (Academy of Kidney Cancer Investigators Award [Dean and Early-Career Investigator options]) and (2) synergizing clinical trials and supportive laboratory research (correlative studies) to reveal new research areas and advance the field of kidney cancer patient care (Clinical Consortium Award). **Figure 1** shows the percentages of the KCRP's research dollars invested in each award mechanism in FY17-FY19.

**Figure 1. FY17-19 KCRP Percent Research Dollars Invested per Award Mechanism**



In FY20, KCRP offered funding mechanisms designed to foster innovative research, provide opportunities for early-career investigators, mentor and prepare young investigators for productive kidney cancer research careers within a virtual Academy, support collaborations between clinicians and scientists, and establish a preeminent clinical trials consortium to speed development of promising new therapies, as shown in **Figure 2**. The KCRP Programmatic Panel members recommended adding two training awards, one focused on establishing a clinical research nurse training program (Clinical Research Nurse Development Award), and the other to attract talented postdoctoral and/or clinical fellows in kidney cancer-focused research (Postdoctoral and Clinical Fellowship Award). The FY20 data is based on recommended awards still under negotiation.

**Figure 2. FY20 KCRP Recommended Research Dollars Investment per Award Mechanism\***



\*FY20 awards are still under negotiation.



**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.<sup>3</sup> 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 2021 was 76,080, representing 4.1 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.<sup>4</sup> The most common type is clear cell RCC (around 75% of all kidney cancers). The second most common subtype is papillary RCC (type 1 and type 2) at around 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.<sup>5,6</sup> Cigarette smoking, historically more prevalent among Veterans, is the strongest known risk factor for the development of renal cell carcinoma.<sup>7,8</sup> Other unique occupational exposures that cause kidney cancer, such as ionizing radiation or chemical and/or hazardous materials, can occur during active service, though the disease may not appear until later in life. This results in Veterans being more frequently affected than their U.S. civilian counterparts. According to a 2014 report by the Centers for Disease Control and Prevention, U.S. Marines and their families stationed at Camp Lejeune, North Carolina, have a 35% higher risk of contracting kidney cancer than civilians due to contaminated drinking water.

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.

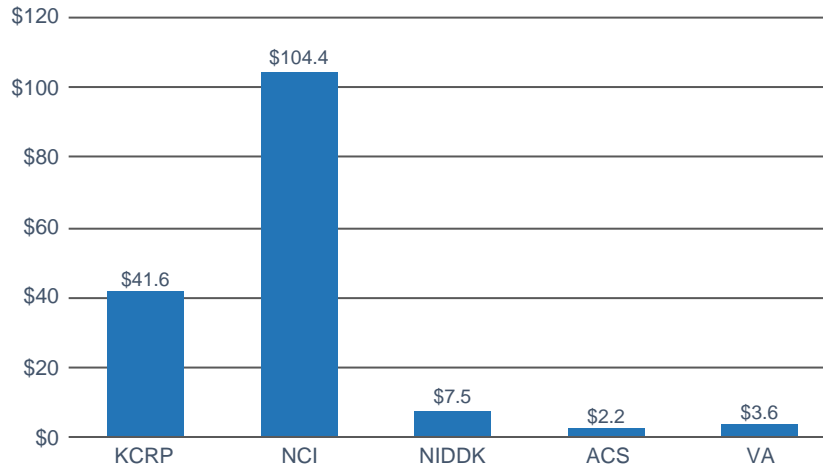
Drugs that target vascular endothelial growth factor (VEGF) or its receptor are standard therapy.<sup>9</sup> Commonly, sunitinib or pazopanib are used first. Other anti-VEGF agents, such as axitinib and cabozantinib, have taken a role in the refractory space. More recently, nivolumab, a programmed cell 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.<sup>10</sup> Adjuvant therapy using sunitinib was recently approved by the U.S. 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.<sup>3</sup> For stage I cancer larger than 4 cm and for stage II and III tumors, radical nephrectomy is generally necessary.

## RESEARCH FUNDING LANDSCAPE

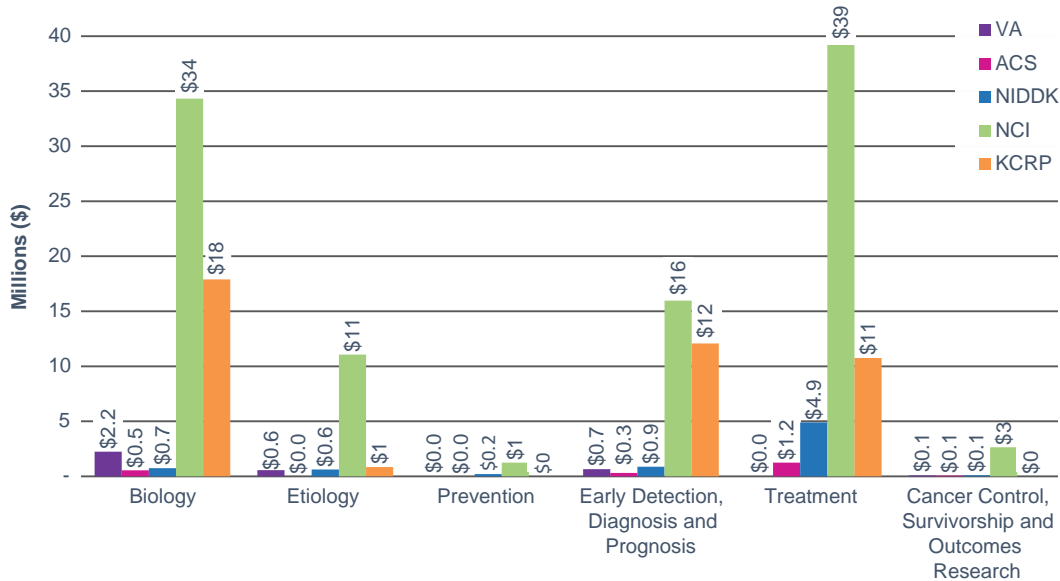
Federal government agencies National Cancer Institute (NCI), National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), and VA, along with the congressionally directed KCRP and the non-profit American Cancer Society (ACS) are the largest funders of kidney cancer research. The total investments from FY17 – FY19, by the indicated funding organization, with a minimum of 50% relevance to kidney cancer are shown in **Figure 3**. The Common Scientific Outline (CSO)<sup>11</sup> data from the International Cancer Research Partnership (shown in **Figure 4**) illustrate the total funds invested between FY17 – FY19 across the CSO spectrum for the KCRP, NCI, NIDDK, ACS, and VA. The majority of the NCI investment since 2017 has been in treatment, followed by research in kidney cancer biology. The KCRP's investment in biology and early detection, diagnosis, and prognosis addresses the identified need to develop a better understanding of the biology of kidney cancer and early detection techniques to assist the patient community.



**Figure 3. FY17-FY19 Agency Investments on Kidney Cancer**



**Figure 4. Comparative Investment (\$) by CSO: FY17 – FY19**



**PRIVATE KIDNEY CANCER FUNDING INITIATIVES**

**Action to Cure Kidney Cancer<sup>12</sup>**

- Has directly funded kidney cancer research since 2006; since then, it has provided 22 grants to 10 researchers totaling \$427,282.50.

**KCCure<sup>13</sup>**

- Funds high-impact, high-risk kidney cancer research and has awarded two grants totaling \$200,000 to two researchers since 2017. In 2019, KCCure doubled funding for Innovation Awards to \$200,000 and will be making awards of \$100,000 and \$50,000 and two awards of \$25,000. The total project funding over the 2017–2019 period will be \$400,000, supporting six awards.

**Kidney Cancer Association<sup>14</sup>**

- 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. In 2019, four awards totaling \$300,000 were made.
- The Advanced Discovery Award was offered for the first time in 2019 to support early detection and innovative treatments for kidney cancer. This mechanism promotes collaboration between clinicians and research-based collaborators. In 2019, two awards totaling \$1M were made. Kidney Cancer Association anticipates awarding two more awards at \$500,000 each in 2020.



## American Cancer Society<sup>15</sup>

- Awarded \$8,222,869 in research funding for kidney cancer research as of March 2020.

## Alex's Lemonade Stand Foundation<sup>16</sup>

- Funded nine awards of various mechanisms (Young Investigator, Epidemiology, Innovation, and Sing-cell Pediatric Cancer Atlas Grants) in kidney cancer research since 2009, for a total investment of approximately \$1,848,837.

## STRATEGIC DIRECTION

### KCRP OVERARCHING STRATEGIC GOALS

- Increase understanding of the biology of kidney cancer
  - Encourage innovative ideas with high-impact
- Develop novel therapeutic strategies for the treatment of kidney cancer
  - Identify new targets
  - Develop pharmacological, immunological, and genetic interventions
  - Optimize prognostic or predictive markers to assist with therapeutic decision-making
  - Repurpose existing and currently approved drugs
- Improve patient care for kidney cancer
  - Integrate bench research with bedside care and emphasize translational research
  - Invest in early career kidney cancer physicians - next generation
  - Facilitate multi-site collaborative clinical research development and clinical trials
  - Eliminate disparities in populations with an unequal burden of kidney cancer
- Grow Integration of bench research with bedside care-translational research
  - Invest in next generation kidney cancer physicians and scientists
  - Facilitate multi-site collaborative clinical research development and clinical trials
  - Encourage experts inside and outside KC to apply knowledge for advancements
  - Foster collaborations that cross translational, disciplinary, and institutional boundaries

### KCRP FOCUS AREAS

- Conduct basic biology research to better understand etiology and cancer progression, metastatic disease, refractory disease and therapeutic resistance, genetic and environmental risk factors and the prevention of kidney cancer.
- Define the biology of rare kidney cancers and develop treatments to improve outcomes and reduce death.
- Identify and develop new strategies for screening, early-stage detection, accurate diagnosis and prognosis prediction of kidney cancers, with examples including biomarkers and imaging.
- Develop novel therapeutic strategies for the treatment of kidney cancer, such as novel drug targets, therapeutic modalities and agents, treatment combinations and drug delivery systems.
- Identify and implement strategies to improve the quality of life of patients.
- Identify and implement strategies to mitigate health disparities, such as access to healthcare, social and cultural factors, environmental factors, and biological contributors.
- Support preparation and development of the next generation of kidney cancer researchers, or cultivate collaborations in kidney cancer research or patient care in alignment with the KCRP Overarching Strategic Goals.

## INVESTMENT STRATEGY

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

- Investment in early-career investigators (laboratory scientists and physician scientists) through the Postdoctoral and Clinical Fellowship, Idea Development - Early Career Investigator, Physician Research, and Academy of Kidney Cancer Investigators 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 and Clinical Consortium mechanisms

## 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 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.

**Table 1. Investment Metric - KCRP Goals Funded FY17-19**

50% Funded portfolio invested in innovated and impactful research for the development of new approaches in kidney cancer research and patient care
18% Funded portfolio invested in the development of early-career scientists and physician scientists for productive careers in kidney cancer research
4% Funded portfolio invested the advancement of the development of technology in kidney cancer*
28% Funded portfolio invested in translational research partnerships and collaborative clinical research and trials (consortium)

\*Technology development was a program goal in FY17 and FY18

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