

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,¹ 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.² In FY18 and FY19, the KCRP received additional appropriations of \$15M and \$20M, respectively, bringing the total KCRP investment budget to \$45M in its first 3 years.

The funding mechanisms that were offered by the KCRP during its first 2 years addressed several unmet gaps, as identified during the Stakeholders meeting. 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). **Figure 1** shows the percentages of the KCRP's research dollars invested in each award mechanism in FY17 and FY18 (FY18 data based on recommended awards still under negotiation).



In FY19, the KCRP continued its commitment to innovation and translational research, as shown in **Figure 2**. Additionally, the KCRP Programmatic Panel members 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. FY17 and FY18 KCRP Percent Research Dollars Invested per Award Mechanism

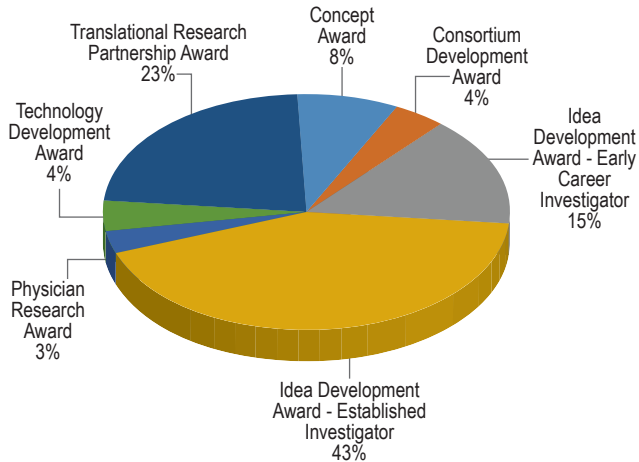
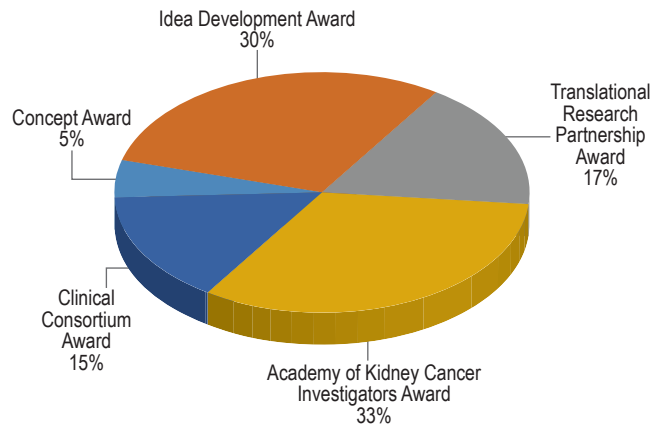


Figure 2. FY19 KCRP Recommended Percent Research Dollars for Investment per Award Mechanism



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.³ 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% 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 64.⁴ 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.^{5,6}

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.⁷ 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.⁸ 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.³ For stage I cancer larger than 4 cm and for stage II and III tumors, radical nephrectomy is generally necessary.

RESEARCH FUNDING LANDSCAPE

The National Institutes of Health (NIH) invested \$89.7M in awards with a minimum of 50% relevance to kidney cancer research from FY15 to FY18. The Common Scientific Outline⁹ data from the International Cancer Research Partnership (shown in **Figure 3**) illustrate the amounts invested by the NIH in each research area. A comparison of the FY17 and FY18 KCRP investment into each category is shown in **Figure 4** (these data include budget estimates for FY18 awards that were under negotiation during the draft of this document). The majority of the NIH investment since 2015 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. FY15-FY18 NIH Common Scientific Outline Investment

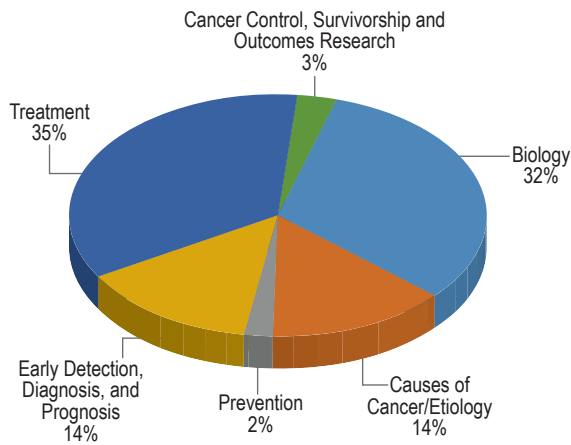
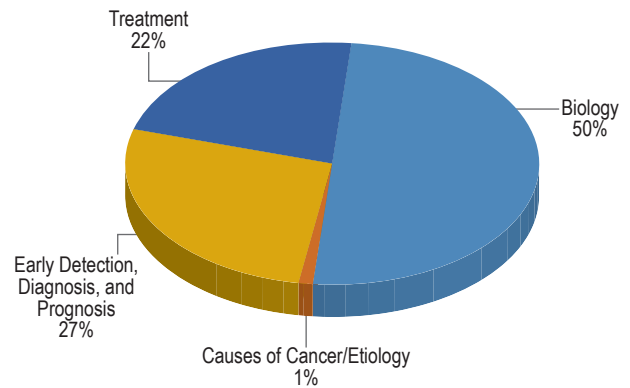


Figure 4. KCRP Historical Common Scientific Outline Investment



PRIVATE KIDNEY CANCER FUNDING INITIATIVES

Action to Cure Kidney Cancer¹⁰	Has directly funded kidney cancer research since 2006; since then, it has provided 22 grants to 10 researchers totaling \$427,282.50.
KCCure¹¹	Funds high-impact, high-risk kidney cancer research and has awarded two grants totaling \$200,000 to two researchers since 2017.
Kidney Cancer Association¹²	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 (awards data not available).
American Cancer Society¹³	Awarded \$7,054,869 in research funding with at least partial applicability to kidney cancer between 2009 and 2018.
Alex’s Lemonade Stand Foundation¹⁴	Awarded \$1,123,993 in kidney cancer research funding between 2015 and 2018.



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

Integration of bench research with bedside care is crucial to translational research and the acceleration of promising ideas in kidney cancer into the clinical arena. The KCRP aims to support basic, technology development, and translational research in order to move innovative concepts to clinical applications. 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. By investing in the infrastructure to access and rapidly deploy clinical trials that bring novel advances to the treatment of kidney cancer, the KCRP will enable the greater research community to focus on exciting and innovative avenues of research that will improve patient care.

Grow the field and increase collaboration in the area of kidney cancer

Kidney cancer research would benefit tremendously from an infusion of new talent and expertise, expansion of participation by physician scientists, and trans-disciplinary research that builds on advances made in other fields. In addition to growing the field via encouraging inclusion of varying expertise, fostering collaborations that cross both translational (bench to bedside to community and back) and disciplinary boundaries holds great promise for advancing impactful research and improving the care of patients with kidney cancer.

INVESTMENT STRATEGY

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

- Investment in early-career investigators (laboratory scientists and physician scientists)
- Investment in highly innovative, untested, potentially groundbreaking novel concepts in kidney cancer research
- Investment in translational research between clinicians and research scientists
- Investment in technology development
- 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. The KCRP plans to build on early successes via mechanisms that expand and translate program investments.



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 Goals of the KCRP

25% Funded portfolio invested in innovated and impactful research for the development of new approaches in kidney cancer research and patient care
25% Funded portfolio invested in the development of early-career scientists and physician scientists for productive careers in kidney cancer research
15% Funded portfolio invested the advancement of the development of technology in kidney cancer
35% Funded portfolio invested in translational research partnerships and collaborative clinical research and trials (consortium)

REFERENCES

1. *Evaluation of the Congressionally Directed Medical Research Programs Review Process*. 2016. The National Academies of Sciences, Engineering, and Medicine. The National Academies Press. Washington, DC.
2. Fiscal Year 2017 Kidney Cancer Research Program Stakeholders Meeting Summary. 2017. Available at http://cdmrp.army.mil/kcrp/pdfs/Summary_of_Stakeholders_Meeting-KCRP%202017_FINAL.pdf.
3. *Cancer Stat Facts: Kidney and Renal Pelvis Cancer*. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Available at <https://seer.cancer.gov/statfacts/html/kidrp.html>.
4. *Key Statistics About Kidney Cancer*. 2018. American Cancer Society. Available at <https://www.cancer.org/cancer/kidney-cancer/about/key-statistics.html>.
5. Saint-Jacques N, et al. 2014. Arsenic in Drinking Water and Urinary Tract Cancers: a Systematic Review of 30 Years of Epidemiological Evidence. *Environ Health*. 13:13-44.
6. Saint-Jacques N, et al. 2018. Estimating the Risk of Bladder and Kidney Cancer from Exposure to Low Levels of Arsenic in Drinking Water, Nova Scotia, Canada. *Environ Health*. 110:95-104.
7. *Immunotherapy for Kidney Cancer*. American Cancer Society. Available at <https://www.cancer.org/cancer/kidney-cancer/treating/immunotherapy.html>.
8. *FDA Approves Nivolumab and Ipilimumab Combination for Advanced Kidney Cancer*. 2018. National Cancer Institute. Available at <https://www.cancer.gov/news-events/cancer-currents-blog/2018/kidney-cancer-fda-nivolumab-ipilimumab-first-line>.
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>).
10. *Direct Funding*. Action to Cure Kidney Cancer. Available at <http://www.ackc.org/direct-funding/>.
11. *KCCure Kidney Cancer Research Grant Program*. KCCure. Available at <https://kccure.org/grants/>.
12. Kidney Cancer Association website: <https://www.kidneycancer.org/>.
13. International Cancer Research Partnership website: <https://www.icrpartnership.org/>; American Cancer Society website: <https://www.cancer.org/>.
14. International Cancer Research Partnership website: <https://www.icrpartnership.org/>; Alex's Lemonade Stand Foundation website: <https://www.alexslimonade.org/>.