

## **SITE VISIT REVIEW REPORT**

<b>APPLICATION NUMBER:</b>	<b>2 P30 CA168524-06</b>
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<b>APPLICATION TITLE:</b>	<b>CANCER CENTER SUPPORT GRANT</b>
<b>APPLICANT INSTITUTION:</b>	<b>UNIVERSITY OF KANSAS CANCER CENTER</b>
<b>COLLABORATING INSTITUTION(S):</b>	<b>STOWERS INSTITUTE FOR MEDICAL RESEARCH CHILDREN'S MERCY HOSPITAL KANSAS CITY</b>
<b>REVIEW GROUP:</b>	<b>NCI SPECIAL EMPHASIS PANEL</b>
<b>MEETING DATE:</b>	<b>FEBRUARY 8-10, 2017</b>
<b>COUNCIL:</b>	<b>MAY 2017</b>

**COMMITTEE BUDGET RECOMMENDATIONS**

**RESUME AND SUMMARY OF DISCUSSION:** In this competitive renewal application from the University of Kansas Cancer Center (KUCC) with consortium partners, the Stowers Institute for Medical Research and Children's Mercy Hospital & Clinics, the overall goals are to translate KUCC discoveries to decrease cancer incidence, morbidity and mortality as well to develop more effective interventions for the KUCC catchment area to mitigate the impact of cancer. Support is requested for four research programs, five shared resources, Senior Leadership, Planning and Evaluation, Developmental Funds, Administration, Clinical Protocol and Data Management, Protocol Review and Monitoring System, and Early Phase Clinical Research Support.

KUCC has made important progress across the entire spectrum of cancer research, including basic, clinical, translational, and population research, and has been highly effective in identifying solutions that specifically address the needs of the catchment area. Dr. Roy Jensen, the Center Director, has demonstrated strong leadership with remarkable success in the development and implementation of strategic initiative for growth of translational and interdisciplinary research. The addition of Children's Mercy Hospital & Clinics as a new consortium partner provides important opportunities to accelerate the development of novel strategies for the treatment of pediatric cancers. Although the breadth and depth of cancer-focused research at KUCC has increased, there continue to be missed opportunities for the two population science programs to develop tighter linkages with each other as well as with the other KUCC research programs.

The Cancer Biology (CB) research program is rated excellent. The program includes strong basic science projects translated to clinical trials and led by a superb group of investigators who continue to be highly productive with an increased publication rate. However, insights from basic science could more effectively inform strategies for cancer control, prevention and survivorship research if this program interacted more closely with the two population science research programs. The Cancer Control and Population Health (CCPH) research program, rated excellent to outstanding, has been highly productive, with smoking cessation continuing to be the strongest area of programmatic focus. However, there is limited state-of-the-art research in the unique underserved patient populations in the catchment area and missed opportunities to integrate precision health care initiatives into programmatic research. The Cancer Prevention and Survivorship (CPS) research program, rated excellent to outstanding, is led by an exceptionally well-qualified new leadership team and has been highly effective in developing a portfolio of clinical prevention trials and in diversifying the organ-based focus of the program to colon, bladder and other solid tumors. However, potential to conduct biomarker-driven clinical trials in the minority underserved patient populations in the catchment area and interact more closely with CCPH and CB members would strengthen the scientific impact of the program on the catchment area. The Drug Discovery, Delivery and Experimental Therapeutic (D3ET) research program, rated very good to excellent, provides a platform to foster translational research, with some of the drugs developed by this program currently in early phase clinical trials. However, there is a relative low percentage of NCI funding and the depth of interaction between the two program leaders and among members is not clear. The D3ET research program would benefit from recruiting clinical investigators who have experience and expertise in cancer therapeutics and early phase drug development.

The four research programs are supported by five shared resources: The Biospecimen Shared Resource and the Transgenic and Gene-Targeting Shared Resource are rated exceptional to outstanding, the Biostatistics and Informatics Shared Resource is rated excellent to outstanding, and the Clinical Pharmacology Shared Resource and the Lead Development and Optimization Shared Resource are rated very good. The shared resources are cost-effective and provide high quality services to the research programs. The leaders and the staff are well qualified and the facilities are appropriate. However, the number of clinical trials and patient accrual linked to the Clinical Pharmacology Shared Resource is limited, and the true potential of the Lead Development and Optimization Shared Resource in facilitating the cancer center research program has yet to be realized.

The Clinical Protocol and Data Management (CPDM), rated outstanding to excellent, provides effective management and oversight for cancer clinical trials conducted by cancer center investigators. The Data and Safety Monitoring Plan is rated acceptable. The Inclusion of Women, Minorities and Children in clinical research are each approved. The Early Phase Clinical Research Support (EPCRS) is rated excellent to very good to outstanding. Four of the proposed early phase clinical studies are well aligned with the translational observations derived from the clinical efforts of the center. However, some of the proposed clinical studies are not highly innovative. The Protocol and Review Monitoring System (PRMS) is approved. An effective review process is in place, assuring high scientific quality of the clinical studies performed at the center and monitoring of their progress. However, PRMS should continue to focus on prioritization of clinical trials and monitoring and closing of poorly accrual trials.

The administration and organizations components are very strong. Senior Leadership, rated excellent, includes a group of highly qualified and experienced leaders. However, there are still concerns as to the relatively high number of Associate Directors and the potential overlap of their roles and responsibilities. Planning and Evaluation, rated excellent, includes superb advisors and has produced a well-developed strategic plan for the center. Developmental Funds, rated excellent, have been effectively utilized by the center to support innovative cancer research, develop shared resources, and recruit new faculty members. However, it is unclear how the future plans for Developmental Funds are directly driven by the overall strategic initiatives of the center. Furthermore, the role that Dr. Calvet would play as a Research Staff Investigator in helping the center achieve its scientific objectives above and beyond his own research is not well developed. Administration, rated excellent, shows clear evidence of significant contribution toward the effectiveness of the KUCC.

All the six Essential Characteristics are met and rated as follows: Institutional Commitment is rated exceptional; Physical Space, Cancer Focus and the Center Director are rated outstanding; and Organizational Capabilities and Transdisciplinary Collaboration and Coordination are rated excellent.

Overall, the KUCC is well positioned on an increasingly upward trajectory to foster collaborative and transdisciplinary cancer research with high relevance to the underserved populations in the catchment area. Dr. Jensen is an outstanding physician-scientist who is well qualified to serve as Director. The strong and effective leadership of Dr. Jensen and his team, combined with robust institutional support are major strengths. However, the CCPH and CPS research programs have not effectively strengthened linkages with each other as well as with the other two research programs. While there is still room for continued growth, maturity, and innovation across the entire spectrum of cancer research, the KUCC is clearly poised to make important achievements in cancer research and patient care over the next several years. This application is rated as excellent to outstanding and support for five years is appropriate.

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**OVERALL DESCRIPTION (provided by applicant):** The University of Kansas Cancer Center (KUCC) is a matrix cancer center that includes: The University of Kansas Medical Center campuses in Kansas City, Wichita and Salina, the University of Kansas in Lawrence and via consortium agreement, the Stowers Institute for Medical Research and Children's Mercy Kansas City. In 2015, 187 members of KUCC accounted for \$13.4M of NCI funding and a total of \$61.2M in overall cancer-related funding, an increase of \$10M during the previous funding period. Roy A. Jensen, MD, who is supported by a strong, nationally recognized leadership team, leads KUCC. Over the last four years substantial progress has been made broadening partnerships with communities throughout the KUCC catchment area, boosting recruitment of physician-scientists, augmenting clinical research and early-phase clinical trials, advancing education for the next generation of scientists and health care providers and heightening influence for KUCC researchers in the national scientific community. KUCC has established four specific aims to ensure KUCC leads in the fight against cancer:

1. Leverage unique institutional and regional assets to become a leading academic institution for transforming discoveries from the laboratory into new anticancer drug therapies;
2. Provide the optimal environment to focus the power of precision medicine, basic science inquiry, drug discovery and development, and behavioral interventions to decrease cancer incidence, morbidity and mortality;
3. Be a nationally recognized leader in partnering with key stakeholders, community advocates and regional leaders to develop, promote, and foster the adoption and implementation of research-based cancer prevention, diagnosis, treatment, control, and survivorship practices throughout the KUCC catchment area to mitigate the impact of cancer; and
4. Provide leadership in envisioning, developing and implementing a thoughtful, comprehensive strategy to educate the next generation of physician-scientists and allied investigators in cancer research, treatment, prevention and control.

To accomplish these goals KUCC has four research programs: Cancer Biology, Cancer Control and Population Health, Cancer Prevention and Survivorship, and Drug Discovery, Delivery and Experimental Therapeutics. In addition, KUCC supports the Clinical Trials Office, five established shared resources - Biospecimen, Biostatistics and Informatics, Clinical Pharmacology, Lead Development and Optimization and Transgenic and Gene-Targeting – along with three developing shared resources – Cell Authentication and Pathogen Screening, Health Communications Research and Nutrition.

**Project Narrative:** KUCC aims to leverage unique regional scientific assets to build a nationally significant cancer research center that will become a leading institution for transforming discoveries in the laboratory into new therapeutic approaches. KUCC will expand its depth, breadth and impact and strive to become an NCI-designated comprehensive cancer center that meets the needs of the more than 4.4M Americans who live within the 92,000 square miles of the KUCC catchment area.

## **CRITIQUE:**

**OVERALL CRITIQUE:** The University of Kansas Cancer Center (KUCC) was established in 2004 as part of the strategic plan initiated by the Dean of the University of Kansas Medical Center (KUMC) and combined with an expansive university, community, and regional effort. In 2004, Dr. Roy Jensen was recruited from the Vanderbilt-Ingram Comprehensive Cancer Center to be the founding Director of the Kansas Cancer Institute, which was subsequently re-named the KUCC. Under his strong and effective leadership, the center received NCI-designated status with the approval of its first NCI Cancer Center Support Grant (CCSG) in July 2012. The center has created a consortium that includes the University of Kansas Medical Center (KUMC), University of Kansas Hospital (KUH), University of Kansas School of Pharmacy at Lawrence, Stowers Institute for Medical Research in Kansas City, and most recently, Children's Mercy Hospital. This consortium brings together expertise in research and clinical care at KUMC, clinical facilities and oncology network of KUMC, skills in medicinal chemistry and drug development from the School of Pharmacy, excellence in basic science from the Stowers Institute, and

now clinical care and research at Children's Mercy Hospital. The center is to be commended for including Children's Mercy as the newest member of their consortium given the significant strengths of this institution for pediatric oncology experimental therapeutics program and its key role as a member of the Children's Oncology Group. Moreover, Dr. Jensen played a critical role in the recent recruitment of Dr. Tom Curran to be Executive Director of the Children's Research Institute at Children's Mercy Hospital. Dr. Curran is a highly accomplished investigator who has made important scientific discoveries in characterizing the key signaling pathways involved in the development of pediatric brain tumors, and he should be an effective partner for Dr. Jensen.

The KUCC serves a catchment area of 120,000 sq. miles that encompasses 123 counties and includes 4.4 million people within the state of Kansas and western Missouri. Located in Kansas City, Kansas, the KUCC is between 190 and 594 miles from the nearest 5 current NCI-designated cancer centers. Notably, 40% of the patients seen by KUCC come from western Missouri.

At the time of the 2012 CCSG review, the center was viewed as having strengths in basic, clinical, and translational research with translational output from basic science into hypothesis-driven, investigator-initiated clinical trials being viewed as a high priority. The present CCSG application represents the center's first competitive renewal and requests funding for years 6-11. The center continues to undergo a positive upward trajectory that has led to continued growth expansion in basic, clinical, translational, and population research. Based on updated data presented at the site visit, total peer-reviewed funding has increased from \$46.45 million in CY 2011 to \$54 million in CY 2016 with an increase in NCI funding from \$11.16 million in CY 2011 to \$12.85 million in CY 2016. Multi-investigator peer-reviewed funding has also increased from 23 multi-PI grants in CY 2012 to 30 in CY 2016. Thirty-seven new members have been recruited over the past five years, which has included several key senior recruits: Dr. Chen, Chair of Radiation Oncology; Dr. Curran, Executive Director, Children's Research Institute; Dr. Khabele, Director, Gynecologic Oncology; Dr. Maliski, Dean, KU School of Nursing; and Dr. Soper, Foundation Distinguished Professor of Chemistry and Mechanism Engineering. As presented at the site visit, accrual to treatment clinical studies at the center increased from 242 in 2012 to 390 in 2016. A major focus has been placed on the development of early-phase institutional clinical studies, and when compared to 2012, there indeed has been a significant increase in the number of patients enrolled on investigator-initiated phase I/II clinical trials. Despite these improvements in patient accruals, continued focus will need to be placed on developing innovative clinical trials that are the direct translation of KUCC science and/or discoveries into the clinic.

In the current grant application, four scientific programs are presented, which remain the same since the 2012 CCSG review. These programs are: Cancer Biology (CB), Cancer Control and Population Health (CCPH), Cancer Prevention and Survivorship (CPS), and Drug Discovery, Delivery and Experimental Therapeutics (D3ET).

The Cancer Biology (CB) research program is led by Dr. Kristi Neufeld (KU-Lawrence) and Dr. Linheng Li (Stowers Institute), and this program was rated excellent. The affiliation with the Stowers Institute has substantially strengthened this program. Program leadership is outstanding, and members of this program are well funded and productive with high impact publications. Inter-programmatic publications have also improved since the previous CCSG review. Several basic observations have been made that have advanced cancer knowledge, and there are several examples of CB science/discoveries that have been translated to investigator-initiated clinical trials. Minor weaknesses relate to the still relatively modest level of NCI and cancer-relevant funding compared to total program funding. Concerns also exist about the cohesion and integration of the four program themes and the cancer focus especially as it relates to the somewhat strained linkage between cancer and polycystic kidney disease and cancer and alcohol liver disease. There also appear to be missed opportunities for this program to work more closely with the two population science programs as insights from basic laboratory studies could more effectively inform strategies for cancer control, prevention, and survivorship research. As the center is

focused on achieving comprehensive status, focused efforts to identify collaborative interactions between this program and the two population science programs will be important.

The Cancer Control and Population Health (CCPH) research program is led by Dr. Ellerbeck and Dr. Christie Befort and was rated excellent to outstanding. The program has grown in membership and in scientific productivity, and smoking cessation continues to be a strong area of programmatic focus. The program has also been successful in making the critical linkages with the underserved patient population in their catchment area. However, there are minor concerns including the lack of thematic cohesion within the program, the somewhat limited hypothesis-driven research in the unique underserved patient populations in the catchment area, and the inadequate genetic epidemiology studies. There are also missed opportunities to interact more closely with the other population science research program, CPS, as well as with the other KUCC research programs. Several of these same concerns had been raised at the previous 2012 CCSG review, which have not been adequately addressed in the current application.

The Cancer Prevention and Survivorship (CPS) research program is led by Dr. Dan Dixon and Dr. Jennifer Klemp and was rated excellent to outstanding. The CPS research program has been strengthened by the recruitment of new program leadership, development of a portfolio of clinical prevention trials, and efforts to diversify the program's organ-based focus with efforts in colon cancer, bladder cancer, and other solid tumors. The research efforts focused on obesity is a programmatic strength. However, there are some minor weaknesses that temper overall impact, and they include a limited number of clinical investigators who conduct clinical prevention trials, missed opportunities to conduct mechanistic, biomarker-driven clinical trials in the minority underserved patient populations in the catchment area, and missed opportunities to interact more closely with members in the CCPH research program as well as with the two other KUCC research programs.

The Drug Discovery, Delivery and Experimental Therapeutics (D3ET) research program was rated very good to excellent. This program is led by Dr. Alan Gamis and Dr. Scott Weir. Since the previous CCSG review, there has been a significant increase in program members and an increase in intra- (29%) and inter-programmatic (23%) publications as well as a high level of inter-institutional collaborations (54%). The unique aspect of this program is that it provides a tremendous opportunity for center members to develop novel drugs in an academic environment. Over the past five years, four drugs developed by D3ET have or will soon to be introduced in to phase I-II trials. Moving forward, it will be important to focus on the development of investigator-initiated, hypothesis-driven clinical trials. Minor concerns relate to the reduction in cancer-relevant funding, the relative low percentage of NCI funding, and the lack of peer-reviewed extramural funding by the two program co-leaders. There are also missed opportunities for this program to interact with CB and the two population science programs. Finally, the program would benefit from recruiting a cadre of clinical investigators who have experience and expertise in cancer therapeutics and early-phase drug development as well as identify a co-leader with specific clinical expertise in cancer therapeutics and early-phase clinical drug development.

In the current application, five shared resources are proposed for CCSG support. In general, they provide important support for the cancer center membership and help to facilitate the science conducted by the center investigators. However, there is some unevenness in impact and quality of some of the shared resources, which was an issue previously raised in the 2012 CCSG review. The leadership is encouraged to continue to carefully monitor shared resource quality and impact.

The Biospecimen Shared Resource was rated exceptional to outstanding as it is a growing and increasingly vital part of the cancer center, widely used by multiple research programs and investigators, and is directed by strong leadership. The number and diversity of the specimen collection has substantially increased during this funding period, and standard operating procedures are in place. Another impressive strength is that this shared resource now provides annotated clinical information on



every sample that has been collected with the development of the Curated Cancer Clinical Outcomes Database.

The Biostatistics and Informatics Shared Resource was rated excellent to outstanding as it provides important services for KUCC investigators. Dr. Gajewski is the new leader of this facility, and he is supported by eight additional biostatistical research faculty members. The biostatistics personnel are involved in development of grant applications, design of clinical trials, development of relevant statistical methodology, analysis of data, manuscript writing, and educational activities. Additional strengths of this resource also include the widespread use by KUCC members for grant submissions and a large number of projects involving data science expertise.

The Clinical Pharmacology Shared Resource was rated very good. This is a new facility since 2012 and is made up of three parts, the correlative laboratories, the bioanalytical laboratory, and the PK/PD unit. The publication record highlighting core usage is also surprisingly limited as are the number of clinical trials and patient accruals that might be linked to this shared resource. Minor concerns relate to the relatively limited number of funded investigators who make use of the facility, with usage heavily weighted towards members of the D3ET research program.

The Lead Development and Optimization Shared Resource was rated very good. This resource is unique as few NCI-designated cancer centers maintain this kind of shared resource, and at a conceptual level, its potential value for identifying novel targets and developing useful drugs is substantial. The three components of this shared resource include a high throughput screening (HTS) facility, medicinal chemistry, and a biotechnology, innovation, and optimization facility (BIOC). However, there appears to be only a limited number of scientific projects with few examples of HTS successes that have been supported by this facility. Additional concerns relate to the ineffective coordination and oversight of the various processes involved in this shared resource, and the true potential of this resource in facilitating center science has yet to be realized.

The Transgenic and Gene-Targeting Shared Resource was rated exceptional to outstanding. This is a new shared resource since the previous CCSG review, and it is an institutional core facility that is housed on the main KUMC campus. This facility provides centralized and comprehensive technical services for the production of novel transgenic and gene-targeted models and genetically altered pluripotent stem cells, and the cancer center support of this facility allows for the development of specific initiatives relevant to cancer research. This is clearly a strong core that is critical to expanding the scope and breadth of the KUCC research efforts.

The KUCC Clinical Protocol and Data Management (CPDM) was rated outstanding to excellent as it maintains a central clinical trial office that provides comprehensive support services for all cancer-focused clinical protocols, and is under very effective and strong leadership. The leader of the clinical trials operation, Dr. Williamson, was particularly impressive at the time of the site visit. It has an outstanding organizational structure, which provides an appropriate level of oversight and management of clinical studies. As identified during the site visit, there appear to be some clinical trials conducted by groups within the center that may not be under the oversight of the CPDM. In response to several questions formulated by members of the site visit, the site visit team was left with the impression that it is possible for some cancer-focused clinical trials to be opened and not be under the direct oversight and coordination of the CTO. This has the potential to create unevenness in the management and conduct of studies, and create fragmentation in the oversight process. The CPDM needs to consider bringing all cancer-focused clinical trials under the umbrella of the KUCC CPDM to ensure consistency, high quality, and oversight of the conduct of clinical research.

The Data Safety and Monitoring System received an acceptable rating. However, several issues need to be address. One issue relates to the need for more seasoned, senior clinical investigators to serve on the DSMC as there appears to be a relatively large number of junior faculty on the committee. In

addition, because of the increased oversight that is required for clinical studies deemed to be very high risk, the DSMP needs to require that the number of patients audited should be increased from the stated “no less than 10%”. In fact, for phase I clinical studies, all enrolled patients need to be audited. The DSMP describes a process for requesting corrective actions that is primarily driven by the auditor. When major deficiencies are identified through the audit process and corrective actions are required and planned, the DSMC minutes should reflect the resolution of the corrective actions.

The plans for Inclusion of Women, Minorities, and Children in Clinical Research were each approved.

The Protocol Review and Monitoring System was approved as it has all of the appropriate policies, procedures, and staff in place. However, the PRMS will need to continue to focus on prioritization of clinical trials and maintaining rigorous standards in monitoring and closing poorly accruing trials.

Early Phase Clinical Research Support (EPCRS) was rated excellent to very good to outstanding. Four of the early phase clinical studies proposed for future EPCRS support appear well aligned with the translational observations derived from the clinical/translational efforts of the center. At the site visit, it was noted that there has been a significant increase in phase I accruals since 2012, suggesting that the patient population exists to conduct the proposed new studies. However, there was lack of innovation of some of the proposed studies. Additionally, the inclusion of the nivolumab/afatinib clinical trial that would not be considered appropriate for this particular funding mechanism as it is being conducted by the NCI-ETCTN phase I network. For the EPCRS, the Center Director and Senior Leadership need to continue to focus on developing innovative investigator-initiated clinical trials coming from KUCS science and/or discoveries.

In terms of the organization and administration components, Senior Leadership was rated excellent. As had been raised at the previous CCSG review in 2012, there are still concerns as to the relatively high number of Associate Directors and the potential overlap of their roles and responsibilities. In the executive session with the Director, the specific criteria used in the selection of the Associate Directors was not sufficiently articulated. During this session, concerns were also raised as to the appropriateness of having Dr. Fabian serve as Associate Director of Clinical Research given that her more recent research focus has been on cancer prevention studies as opposed to therapeutic intervention clinical trials and early-phase clinical trials.

Planning and Evaluation was rated excellent. The continued upward growth of this geographically fragmented center is the result of careful planning and evaluation. The leadership structure, internal and external advisory boards, along with various meetings and retreats among programs have led to well-developed strategic plans for the center as a whole and for the scientific programs and shared resources. However, it will be important for the center to develop a more focused mechanism to monitor progress and the benchmarks of success.

Developmental Funds was rated very good as its use during the previous funding period has had a positive impact on the recruitment of faculty, support of pilot projects, and the development of shared resources. Impact is diminished, however, as it was not entirely clear as to how the future plans for Developmental Funds were being directly driven by the overall strategic priorities of the cancer center.

Funding for Dr. Calvet as a Research Staff Investigator was not approved. While Dr. Calvet is clearly a leading expert in polycystic kidney disease, the cancer focus of his research remains unconvincing. Moreover, the definable and special role he would play in helping the center achieve scientific objectives above and beyond his own research, was not well articulated.

Funding for Dr. McGuirk as a Clinical Staff Investigator was approved as his roles fulfill the NCI criteria for this element.

Administration was rated excellent, reflecting a highly developed infrastructure that effectively supports the mission of the cancer center. KUCC administration continues to provide important services, management expertise, and strong program support for the center's research. Since the previous CCSG review, there have been significant improvements in centralized storage of data that has allowed effective management of membership, publications, pilot projects, core facilities utilization, and they have implemented the iLab Solutions, an integrated shared resource management system. However, impact is diminished through a lack of rigor around communications, limited documentation of program meetings that was provided for the site visit team, and an insufficient updated Strategic Plan coming out of the strategic planning retreat in October 2016.

All of the Essential Characteristics were met. Institutional Commitment was rated exceptional. Physical Space, Cancer Focus, and Center Director were rated outstanding, and Organizational Capabilities and Transdisciplinary Collaboration and Coordination were rated excellent.

In summary, during the previous five-year funding period, there has been substantial improvement in this center. The growth of KUCC is highlighted in the upward trajectory of NCI support and cancer-relevant peer-reviewed funding, in the number of high impact publications, and recruitment of talented investigators in key scientific areas that will provide new and exciting research opportunities. The KUCC and its investigators have continued to make important discoveries across the entire spectrum of cancer research, including basic, clinical, translational, and population research. Over the past five years, the center has shown continued growth and maturation, and there are on-going collaborations between bench and clinical scientists across the research programs. There are several examples where KUCC science and laboratory-based discoveries have provided the basis for innovative translational and clinical studies. However, there continue to be missed opportunities for the two population science programs to develop tighter linkages with each other as well as missed opportunities for these two programs to interact more effectively with the two other KUCC research programs. Although the breadth and depth of cancer-focused research at KUCC has increased, it is clear that there is still room for continued growth, maturity, and innovation including more robust transdisciplinary collaborations across the entire spectrum of cancer research. It will be critically important for the Center Director and his Senior Leadership team to continue to focus on detailed strategic planning and to effectively implement the strategic vision of the center.

An effective and strong Center Director, a solid and stable Senior Leadership team, a strong group of Program Leaders, and a remarkable record of exceptional institutional support are to be credited with the achievements of this relatively young center and provide a high level of confidence that further growth and maturation will occur. The center serves a unique patient population in the U.S. and provides tremendous added value and major impact on the oncology care for the community and its catchment area. In particular, the center has done an extremely impressive job in characterizing its catchment area, made effective use of stakeholder engagement strategies to guide research, and has been investigating solutions that specifically address catchment area cancer issues. The KUCC is an important and excellent regional center for cancer research and care, and it continues on a positive upward trajectory with outstanding potential.

Overall, this application is rated excellent to outstanding, and support for five years is recommended.

#### **Criterion Scores:**

Significance: 3, 3, 3; Investigator(s): 2, 3, 3; Innovation: 3, 3, 3; Approach: 3, 3, 3; and Environment: 2, 2, 3

**Significance:** The KUCC and investigators continue to make important scientific and clinical discoveries in basic, translational, and population sciences to the benefit of a diverse population in their local catchment area. The addition of the pediatric component into the consortium is a noted strength

as well as their efforts and impact on the community. However, the interactions across the scientific programs remain a work in progress.

**Investigators:** During this funding cycle, there have been changes in leadership, in particular, with the creation of a new position the Center Deputy Director and a new AD for Clinical Research. Senior leaders and program leaders are highly qualified and committed to the mission of the center. The center has maintained a rigorous alignment of members to maximize programmatic interactions. In addition, there is an important number of faculty to enhance the science and management of the center, although recruitment of key leaders for strategic initiatives in immunotherapies and medical oncology are yet to be realized.

**Innovation:** In the past funding period, the center has aimed to broaden partnerships with communities throughout the KUCC catchment area, boost recruitment of physicians and scientists, augment clinical research and early-phase clinical trials, and some efforts to advance education and training for the next generation of scientists and health care providers. The research to achieve these goals is organized around four scientific programs with some weakness in the innovation of the clinical trial efforts.

**Approach:** The overall strategy, structure, and organization are well reasoned and effective. Efforts to increase translational activity have been modestly effective. There have been important investments in clinical trials infrastructure and clinical facilities. Additional opportunities to increase the scope and relevance of clinical trials to the science of the programs should be embraced.

**Environment:** Facilities and institutional commitment are strong and support the research activities very effectively. The center also receives strong support from the University and the Medical Center, and it plays an important role in cancer care in the eastern Kansas metropolitan area and throughout the state.

## COMPREHENSIVENESS

The KUCC has become much stronger in many areas since attaining its NCI designation five years ago. The center has broadened its expertise through new recruits and programmatic growth as well as by leveraging the expertise of members of the consortium. The addition of Mercy Children's Hospital as a new consortium member is viewed as a valuable addition and is anticipated to accelerate the development of novel strategies for the treatment of pediatric cancers. While the breadth of the four scientific programs is emerging, deficiencies in the robustness and innovativeness of the drug development and clinical efforts have compromised the attainment of significant depth in the clinical area. The CCPH research program has made significant inroads into the minority, underserved and rural populations of the catchment area. Efforts to identify and address the existing health disparities of this community have begun and are expected to increase with the recent recruitment of an Associate Director of Health Disparities. The delivery of care to communities across the catchment area is facilitated by the establishment of the Midwest Cancer Alliance and development of novel resources such as the PIVOT Program. While the levels of inter-and intra-programmatic interaction are robust, as is evident from joint publications, missed opportunities for interactions across all of the programs exist, in particular, between the population science-based and basic research programs. As a result, the number of transdisciplinary team-based collaborations and grants is modest. Training and education initiatives include a successful Summer Student Training Program, establishment of two new formal graduate training programs in Cancer Biology and Biostatistics and a close relationship with the Postdoctoral Association at KUMC. Several K grants have been awarded to trainees and Continuing Medical Education is occurring via the Midwest Cancer Alliance. Training grants (i.e., T32 training grants) would aid in solidifying these activities but have not been obtained to date. Overall, the KUCC has made significant progress during its first review cycle. However, continued growth to address weaknesses in several areas, most notably the robustness of scientific and clinical investigation,

missed opportunities for transdisciplinary collaboration and enhanced scientific innovation are needed prior to achieving comprehensive status. This process can also be facilitated by the implementation of a clear strategic vision.

**Assessment:** [to be determined at the NCI Special Emphasis Panel meeting]

**THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:**

**PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE** (Also, see the heading, Data and Safety Monitoring)

**DATA AND SAFETY MONITORING PLAN: ACCEPTABLE**

**INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE** (Also, see the heading, Inclusion of Women in Clinical Research.)

**INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE** (Also, see the heading, Inclusion of Minorities in Clinical Research.)

**INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE** (Also, see the heading, Inclusion of Children in Clinical Research.)

**VERTEBRATE ANIMAL (Resume): ACCEPTABLE**

**BIOHAZARDS: ACCEPTABLE**

**ADDITIONAL REVIEW CONSIDERATIONS**

**RESOURCES SHARING PLANS:** The Resource Sharing Plans of the University of Kansas Cancer Center (KUCC) are appropriate and are in line with NIH policies and expectations of the broader research community for resource sharing. They satisfactorily address HIPAA issues, transfer of human tissue and IRB regulations in this regard.

**Data Sharing Plan:** The application does address the NIH Policy on Data Sharing. **ACCEPTABLE**

**Sharing of Model Organisms for Biomedical Research:** The application does address the NIH Policy on Sharing of Model Organisms for Biomedical Research. **ACCEPTABLE**

**Genome-Wide Association Studies (GWAS):** The application does address the NIH Policy on Genome-Wide Association Studies. **ACCEPTABLE**

**RESEARCH PROGRAMS**

**Cancer Biology Research Program**

**DESCRIPTION** (provided by applicant): The scientific goal of the Cancer Biology research program (CB) is to understand the molecular mechanisms that define normal and neoplastic cell growth in order to identify and characterize molecules, pathways and processes that are involved in tumor development, growth and progression that can serve as useful biomarkers and/or as new cellular targets for cancer therapeutics and prevention. CB represents the basic science initiatives of The

University of Kansas Cancer Center (KUCC) and is unified by member utilization of molecular, biochemical and cell-based approaches to understand normal and cancer cell behavior. The Specific Aims of CB are: 1) to promote collaboration that enhances discovery of the mechanisms underlying tumor development, progression and malignant behavior; and 2) to leverage basic science discoveries to inspire pre-clinical and clinical development of novel cancer therapies. CB has 49 full members and 12 associate members from 17 departments located at KUMC, KU-Lawrence and Stowers. In 2015, CB garnered nearly \$17 million in cancer-related, peer-reviewed funding (\$2 million from NCI, \$12.2 million other NIH). CB members have published 617 articles since 2012 of which 144 (23%) had intra-programmatic, 128 (21%) had inter-programmatic and 315 (51%) had inter-institutional collaborations. These publications have been cited over 5,600 times, have an average journal impact factor (JIF) of 7.3 and 167 (27%) have a JIF $\geq$ 8. CB is jointly led by Kristi Neufeld (KU-Lawrence) and Linheng Li (Stowers), who bring complementary scientific expertise in cell biology, stem cell biology, biochemistry and translational research, leadership experience and diverse institutional representation. Danny Welch, Associate Director for Basic Science & Education and Jim Calvet, KUCC Research Staff Investigator, round out the leadership team and represent KUMC. Intra- and inter-programmatic collaborations are fostered by research retreats, seminars, research symposia and targeted pilot funding. CB has taken advantage of historical strengths in the study of three tumor sites over-represented in either incidence or mortality rate in the KUCC catchment area population (GI, kidney and hematopoietic). But rather than a disease-based thematic organization, CB members have expertise that can be organized into four discipline-based themes: 1) Cancer Cell Biology and Stem Cell Biology; 2) Cell Proliferation, Differentiation and Death; 3) Chromatin Organization and Transcriptional Regulation; and 4) Signaling Pathways and Development.

**CRITIQUE:** The Cancer Biology research program (CB) was established 10 years ago, and the specific aims remain the same as the last site visit. The membership has grown from 32 to 48 full members, and 11 to 13 associate members. Funding has remained constant (currently at nearly \$15.9 million in cancer-related, \$1.7 million from NCI), while the number and the citations of publications have increased for a similar time frame (from 447 to 829 papers), as well as the inter- and intra-programmatic publications (7 to 20%, 15 to 23%), indicative of increased collaborative integration of the center. The number of shared resources users by program members has increased from 15 to 38.

The mechanism to facilitate the identification of new targets included the organization of interactions with Drug Discovery, Delivery and Experimental Therapeutics (D3ET) research program, including documented seminars, symposium, planning and working group interactions. The outcome has been to identify and pursue translational of several new targets including Akt Ser 552,  $\beta$ -catenin Ser 552 (low dose daunorubicin in AML and ALL), small molecule MSI inhibitors, and DNA methylation derived neutrophil to lymphocyte ratio as a marker for cancer survival.

Interactions between members of this consortium center is facilitated by videoconferencing of seminars, rotating meetings between the sites, and program retreats. Consortium members include Children's Research Institute at Children's Mercy, which engages new distinguished faculty, including Dr. Tom Curran, who serves on the internal advisory board and a new member of CB who has expertise in childhood malignancies, and clinical translation, in particular, medulloblastoma. At the last site visit, the cancer focus of the program had appeared to be diluted through contributions of significant research in polycystic kidney disease and liver injury. In response, the rationale is now given that autophagy is a focus of the liver injury studies and autophagy is a driver of malignancies. The rationale for the inclusion of the polycystic kidney disease research includes the reduced incidence of malignancy amongst polycystic kidney disease patients and the focus of the studies on mechanisms governing aberrant proliferation in the disease. A second minor weakness is that the program could be better integrated with the other research programs. Although the process to facilitate interactions with D3ET were described at the site visit, the process to promote interactions with the population science programs was less clear.

KUCC supported the recruitment of 5 CB faculty members and the development of CB relevant technologies (shRNA libraries, next gen sequencing, and ChIP-seq). The plan is to recruit an additional five faculty members.

In summary, CB has been highly productive with important high impact discoveries with leadership that is thematically aligned and actively involved. Although cancer focus of the grants has been enhanced through an active process of review by leadership, the proportion of funding from NCI remains modest (\$1.7 million /\$15.9 million) and the predominant sources of program funding remains research of polycystic kidney disease and liver disease. As the center is focused on comprehensive status, deliberate efforts to further integrate CB with the population science programs will be important in the coming years.

**Program Leader(s):** CB is jointly led by Dr. Kristi Neufeld (KU-Lawrence) and Dr. Linheng Li (Stowers Institute). Each has responsibility for leading themes within the program related to their specific expertise. Dr. Neufeld is a new program leader, who joined KU in 2003, with a research focus on the APC gene in colon cancer. Dr. Li was program co-leader at the last review, has participated in guiding the program, and is well known for important and fundamental contributions in the domain of stem cell and stem cell niche interactions. The representation by leaders from distinct sites of the cancer center assured representation at multiple meetings since the last site renewal. Meetings of the co-leaders with Dr. Welch (Associate Director for basic science), and Dr. Jim Calvert (KUCC scientist representing KUMC) has occurred at least bi-annually. An additional feature that contributes to program cohesiveness is the role of the Steering Committee that includes members of all three campuses who meet semi-annually to evaluate scientific directions and identify emerging fields and technologies for consideration by CB.

**Assessment:** Excellent merit

**Budget:** 10% effort for Dr. Neufeld and 10% (without salary) for Dr. Li is recommended as requested.

### **Cancer Control & Population Health Research Program**

**DESCRIPTION** (provided by applicant): The Cancer Control and Population Health (CCPH) research program in The University of Kansas Cancer Center (KUCC) brings together an interdisciplinary team of researchers focused on: 1) identifying new strategies to improve smoking cessation and enhance the capability of clinical systems to deliver proven smoking cessation services; and 2) advancing the science of translating cancer control into communities and clinical practice, with a particular emphasis on addressing the needs of the KUCC catchment area. The 35 members of the CCPH program come from 14 departments in six schools across four campuses. These members represent a rich mix of expertise, including psychologists, sociologists, neuroscientists, primary care physicians, oncologists, epidemiologists, biostatisticians, anthropologists, economists, pharmacists, communication specialists and health services researchers. Program members are supported by \$13.4M in total annual funds, including \$3.6M from the National Cancer Institute. CCPH members have published 341 articles since 2012 of which 111 (33%) had intra-programmatic, 69 (20%) had inter-programmatic and 243 (71%) had inter-institutional collaborations. Since the creation of CCPH, program members have made remarkable progress in developing the infrastructure to conduct cancer control research in our region among underserved, rural, American Indian, African American and Latino communities. With this infrastructure in place, in 2015 CCPH members enrolled 1,929 people, including those from underserved communities in the KUCC catchment area, into cancer control research studies. Specifically, 1,603 to interventional research studies. Paralleling this growth in infrastructure has been a significant growth in cancer control funding, program membership and scholarly productivity. CCPH program activities support both intra- and inter-programmatic interactions through translational research seminars, a visiting scholars program, research symposia and research working groups. A strong mentoring program has helped junior faculty procure training grants and minority supplements. CCPH research

efforts have led to a better understanding of the cancer control needs in the KUCC catchment area, improved capacity to analyze the needs of affected and at-risk populations, better strategies for the design and delivery of cancer control messages and improvements in the delivery of tobacco control, cancer screening, physical activity and obesity treatment programs at the level of both the clinical practice and the community at large.

**CRITIQUE:** The Cancer Control and Population Health (CCPH) research program consists of 33 members from 17 departments who reside on three campuses, and the majority of program members are associate or full professors. Since the last review, Dr. Christie Befort was appointed co-leader of the program with Dr. Edward Ellerbeck remaining as the other co-leader. This change has resulted in a major emphasis on obesity, weight loss interventions, and survivorship in rural populations. Strong representation of membership from the Department of Preventive Medicine and Public Health as well as Biostatistics is evident. Total funding is listed as \$12.7 million, \$3.9 million of which is from the NCI. This level of NCI funding is close to that of the previous cycle with fewer members. However, a large percentage of the investigators do not have funding currently.

The goal of the CCPH is to address the needs of minority and underserved rural populations in the catchment area by focusing on tobacco control and cancer control interventions. Significant progress has been made in establishing relationships with the minority, underserved, and rural populations in the catchment area. The smoking cessation research (Theme 1) is strong and of high impact, with publications in high impact journals. There is evidence of both depth and breadth with tobacco research spanning development and implementation of smoking cessation interventions, biology and pharmacology of tobacco control and implementing novel strategies in different clinical contexts, including the development of implementation processes (the dissemination and implementation science). Program members propose to increase smoking quit rates by tailoring interventions to meet the needs of distinct subgroups of smokers, including those not prepared to quit, rural and minority populations, and hospitalized subjects. Overall, the studies under this theme are solid and well-funded, but some of the research seems to lack innovation. This concern was noted during the last review.

Theme 2 focuses on implementing cancer control strategies into clinical settings by establishing interventions to promote cancer screening, reduce obesity and address health literacy and the evaluation of CBPR methods. While most publications are not high impact in their respective fields, pockets of excellence do exist. Notable is Dr. Greiner's innovative theory-based intervention study that incorporated implementation strategies to promote colorectal cancer screening in an ethnically/racially diverse population. Efforts by Dr. Befort provide a key interface with the CPS research program. Building on her obesity treatment trials, Dr. Befort is now collaborating with Drs. Ellerbeck, Greiner, and Gajewski to test real-world clinical implementation of three models of delivery for obesity treatment in the rural primary care settings (36 sites). Attention to the low HPV vaccination rates in the catchment area (lowest in the country) have lagged and are just starting to be addressed. It is unclear how the translational tools that are being developed to assess activity versus sedentary behavior and nutritional literacy, and promote community health are going to be used to augment ongoing studies conducted by other investigators.

Overall, the CCPH should be commended for their progress in securing a significant presence in the underserved populations in the catchment area. Numerous efforts to enhance cancer awareness and screening are underway that have been tailored to the Latino, African American, and American Indian populations. It is clear that a substantial amount of time has been invested in advocating for health awareness and equity in the community and with local and state officials. It is unfortunate that the investigators have not embraced the opportunity to conduct novel research in these unique populations. However, the dissemination and implementation science work in this theme is important and an area of strength on which to build. While the program would clearly benefit from having a genetic epidemiologist onboard, as recommended by the EAB, it is disappointing that the need for this



expertise has not been realized, considering the important role that genetic variability contributes to racial/ethnic diversity and response to interventions.

The number of articles published by members of the CCPH (N=442) has more than doubled since the last review cycle (N=141). A significant proportion of these publications are intra-programmatic (32%), while fewer (21%) are inter-programmatic; intra-programmatic publications rates are lower than that reported for the previous cycle. Five of 28 grants are multi-PI and a U54 to support the Kansas Community Cancer Health Disparities Network has expired. Two U58 grants to fund activities in the Latino and Indian populations will end later this year. A deficiency in transdisciplinary interactions during the last review has been addressed through joint meetings with members of the other programs. It would also be beneficial to have program members meet more often than every 3-6 months and enhance interactions with the CPS research program. Mentoring activities, the majority of which are unstructured, have led to numerous K and F awards and successfully leveraged several junior faculty members to independence. Dr. Cupertino's research trajectory is an example of how successful mentoring through a K01 award resulted in an R01 funded randomized trial to test a text messaging intervention targeting Latino smokers.

During the last grant cycle, a total of 10,064 individuals were accrued to CCPH studies. Of these, 1,312 were recruited to a single breast study funded by the ACS. This is a dramatic reduction from the number of minority and underserved participants who were enrolled during the last grant cycle. No explanation for this decline was given.

The CCPH adds value to the KUCC by establishing meaningful partnerships with underserved groups in the catchment area. In return, the center has given the program \$50K in discretionary funds, invested in start-up packages for four new recruits to the program, and provided incentives to retain three additional faculty members. An Associate Director for Health Equity (Dr. Maliski) has been appointed. In addition, the center provided funds to supplement a PCORI grant and some R awards. Furthermore, the program is developing a health communication shared resource that will support development and testing of novel cancer control interventions as well as dissemination and implementation research. Future plans are appropriate; however, plans for integrating precision medicine initiatives are encouraged as they are timely yet appreciably underdeveloped.

In summary, the major strength of the CCPH is the ability of its members to establish significant relationships with partners in rural and underserved communities in the catchment area, dissemination and implementation of science work, and practice changing and health-policy related research. The program has grown in members as well as productivity, with smoking cessation continuing to be the strongest area of programmatic focus. Weaknesses include limited state-of-the-art research in the unique populations in which members have gained trust, and missed opportunities in precision health care such as translation of genetics/genomics/epigenetic knowledge and incorporation of biomarkers into programmatic research. Lastly, initiatives to enhance research funding and strengthen collaborations with members of the other KUCC scientific programs, in particular the CPS research program, are strongly encouraged.

**Program Leader(s):** Dr. Ellerbeck is Chair of the Department of Preventive Medicine and Public Health and a Professor in the Department of Internal Medicine at the University of Kansas. He has served as co-leader of the CPC research program for the past 11 years. Dr. Ellerbeck has extensive experience in the area of cancer prevention and control, most notably the area of smoking cessation. He actively participates in the mentoring of junior faculty and has received awards in this regard. He is funded currently by a PCORI grant that will be ending soon, in addition to serving as a co-investigator on several other awards. His strong leadership skills and expertise in clinical medicine and health services research and vision for strengthening dissemination and implementation science in the catchment area are assets to the program. Dr. Befort is an Associate Professor in the Department of Preventive Medicine and Public Health and co-director of the Breast Cancer Survivorship Program at KUCC. She

was previously a member of the CPS research program and was appointed co-leader of the CCPH in 2015. She is currently funded to develop strategies to implement weight control in rural primary care settings. She actively mentors junior investigators in grant preparation and writing. The leaders have distinct expertise and are both highly experienced and qualified to lead the CCPH.

**Assessment:** Excellent to outstanding merit

**Budget:** Recommend approval as requested.

### **Cancer Prevention & Survivorship Research Program**

**DESCRIPTION** (provided by applicant): Cancer Prevention and Survivorship (CPS) focuses on pre-cancerous biology and its translation into initial testing of new prevention strategies, as well as interventions aimed at improving the quality of life for cancer survivors. In the Pre-Cancerous Biology and Risk Biomarkers theme, research centers on tissue changes that serve as indicators or predictors of malignant transformation and potential targets for developing new preventive strategies. In the Prevention and Survivorship Translational Research theme, basic scientists from the Pre-Cancerous Biology and Risk Biomarkers theme work with behavioral and clinical researchers for early testing of new strategies. CPS is unique from Cancer Control and Population Health (CCPH) in that CPS focuses on the discovery of new biomarkers and early phase testing of prevention and survivorship interventions using high-risk individuals, whereas CCPH focuses on implementation of known effective strategies. CPS has 21 full and 10 associate members from 16 departments/divisions with expertise in cancer biology, medical and surgical oncology, radiation biology, gastroenterology, nursing, clinical health psychology, nutrition, exercise physiology and biomedical informatics. In 2015, CPS increased the number of NCI (12) and total peer-reviewed (29) funded grants from 6 and 24 since 2011, the previous CCSG submission. Seven of the peer-reviewed grants are multi-PI awards, up from one. NCI and total peer-reviewed funding increased from \$1,804,303 and \$6,244,484 to \$3,098,479 and \$11,890,377. From 2012-2015, over 800 patients were accrued to 15 intervention trials. Twelve of these trials were investigator-initiated and three peer-reviewed funded. Kansas and Missouri have high rates of adult obesity. Thus, many of the CPS interventional trials focus on physical activity and weight reduction, in close collaboration with catchment area partners. CPS members have published 382 articles since 2012 of which 164 (43%) had intra-programmatic, 127 (33%) had inter-programmatic and 204 (54%) had inter-institutional collaborations. Forty-five publications (12%) had a journal impact factor  $\geq 8$ . CPS contributes to KUCC with significant leadership (Director and three ADs, Chair PRMC, Co-chair SWOG Survivorship Committee) and highly translational biomarker based early phase prevention and survivorship trials often with parallel animal studies. The SWOG chair position helps move promising pilots into larger co-operative group trials. KUCC contributes to CPS both through shared resources and pilot funding. In the future, CPS will continue to build on its strengths of novel pre-cancerous models, new risk and response biomarkers, high-risk cohorts for early phase trials, energy balance and natural products in chemoprevention trials. CPS will increase collaborations with CB to expand biomarker research in metabolomics, with D3ET to develop natural product analogues for primary prevention and with CCPH to increase disparity and catchment area-relevant research, as well as educational initiatives and mentoring.

**CRITIQUE:** Cancer Prevention and Survivorship (CPS) research program (formally Cancer Prevention) focuses on pre-cancerous biology and its translation into initial testing of new prevention strategies, as well as interventions aimed at improving the quality of life for cancer survivors. CPS has 20 full and 10 associate members from 16 departments/divisions with expertise in cancer biology, medical and surgical oncology, radiation biology, gastroenterology, nursing, clinical health psychology, nutrition, exercise physiology and biomedical informatics. Membership is slightly increased from the 2011 review (18 full and 9 associate members). CPS has two themes. Theme 1, Pre-Cancerous Biology and Risk Biomarkers, focuses on identifying predictors of malignant transformation and potential targets for new preventive strategies. In Theme 2, Prevention and Survivorship Translational Research, basic scientists

from the Pre-Cancerous Biology and Risk Biomarkers Theme work with behavioral and clinical researchers to test new prevention and survivorship strategies.

Future directions for CPS include: 1) building on its strengths of novel pre-cancerous models, 2) new risk and response biomarkers, 3) high-risk cohorts for early phase trials, 4) developing energy balance and natural products in chemoprevention trials. CPS will increase collaborations with CB to expand biomarker research in metabolomics, with D3ET to develop natural product analogues for primary prevention and with CCPH to increase disparity and catchment area-relevant research, as well as educational initiatives and mentoring.

Since the past review in 2011, total peer-reviewed funding has increased from \$7,733,455 to \$12,384,805, and CPS has increased the number of NCI funded grants, total peer-reviewed, and multi-PI peer-reviewed grants. However, many of these grants have expired or are about to expire; of 29 peer-reviewed grants listed 15 will have expired at the time of this review; this includes 8 grants from NIH. Clinical trials are being conducted in collaboration with investigators in other programs and accrual to interventional trials, while still low, has increased from 477 to 807 (total accrual 2013). However, the program includes a limited number of clinicians to conduct clinical prevention trials.

CPS members published 471 articles since 2012 of which 44% had intra-programmatic, 33% had inter-programmatic and 56% had inter-institutional collaborations. Forty-five publications (12%) had a journal impact factor  $\geq 8$ . This is increased from the 2011 review where (from 2006 – 2010) program members had 204 peer-reviewed manuscripts related to prevention or survivorship (with 25% intra-and 24% inter-programmatic); the average Journal Impact Factor was 4.23, and the average number of times a publication was cited was 14.07.

From 2012-2015, over 800 patients were accrued to 15 intervention trials. Twelve of these trials were investigator-initiated and three peer-reviewed funded. Kansas and Missouri have high rates of adult obesity. Thus, many of the CPS interventional trials focus on physical activity and weight reduction, in close collaboration with catchment area partners.

At the prior 2011 review, there were many strengths identified but there were also several key missed opportunities. Investigators have made substantial progress in expanding trials and biomarkers to other organ sites. Dr. Klemp has provided strong efforts in building the survivorship program. There remain, however, missed opportunities in reaching underserved populations and developing biomarkers that match the exceptional opportunity provided by the rich clinical material available to program investigators.

Investigators in Theme 1 study events in the laboratory with the goal of understanding the molecular mechanism(s) underlying initiation and/or progression of breast, prostate, pancreas, and colon cancer. As highlighted in the prior review, Dr. Behold and his colleagues have developed a mouse model of DCIS in which human epithelial cells are injected into the mammary duct of an immune-compromised mouse. The investigators aim to use this mouse model to develop predictive markers of progression and are considering using the mouse model to predict whether a BRCA1 mutation carrier might progress to invasive breast cancer. As noted in the prior review, given the extraordinary wealth of Dr. Fabian's cohort, it is unclear why biomarkers are not first identified in humans and then mechanisms elucidated in mouse models. Dr. Fabian and her group are focusing on the impact of weight loss and exercise and breast cancer risk reduction. These studies are highly productive. Work by Dr. Fabian's team has identified that mammary adiponectin/leptin ratios increase with weight loss and are investigating the role of CD68+ macrophages in adipose tissue inflammation and breast cancer risk. Drs. Anant and Weir (D3ET) have isolated marmelin and demonstrated its chemopreventive activity in colon cancer preclinical models through inhibition of the cancer stem cell marker kinase DCLK1; this work has resulted in a multi-PI R01. Drs. Behbod, Valdez, and Christenson (CB) have shown that the miR-146 family (miR-146b) is involved in hormonal maintenance of breast alveolar cells and may

provide a missing link in the molecular pathways implicated in hormonal regulation of breast cancer (work published in *J Cell Sci*, 2013).

There is new strength in prevention of GI cancers. Dr. Dixon, Weir (D3ET), and Roy (D3ET) using the high throughput screening (HTS) facility have identified flavonoid compounds as modulators of the COX2/PGE2 pathway in colon cancer preclinical models. Drs. Bansal, Rastogi, Sharma, and Christenson (CB) have identified miRNAs associated with Barrett's Esophagus progression and demonstrated the feasibility of using this biomarker in a phase II study. Drs. Subramaniam and Anant have identified chemoprevention dietary interventions that modulate miRNA expression in colorectal cancer patients along with work by Dr. Dixon who identified a common COX-2 polymorphism that interferes with miRNA regulation and serves as a biomarker of COX-2 overexpression.

Investigators in Theme 2 conduct early phase primary prevention trials using drugs or natural products or behaviors (such as weight loss and physical activity) with minimal side effects. Drs. Fabian, Kimler, Carlson (fatty acid analysis), and Sullivan (diet composition) found that women with lower levels of serum omega-3 fatty acids were more likely to have hyperplasia with atypia on RPFNA; pilot trials of six months of 3.4 g EPA and DHA combined (4g Lovaza) showed a significant decrease in Ki-67, and a significant decrease in atypical cytomorphology. Substantial tissue proteomic effects were observed with omega-3 fatty acids (Dr. Mills, MD Anderson) (Fabian, *Cancer Prev Res*, 2015, 8:912 and 8:922). An NCI funded pilot (R21CA117847 Fabian) of 12-months of SDG 50 mg/day indicated reduction in Ki67, decrease in pS2 and increase in BRCA1 mRNA in benign breast tissue obtained from high risk premenopausal women by RPFNA (Fabian, *Breast Cancer Res*, 2010). These studies resulted in a multi-PI Komen Promise grant (KG101039) in which 12 months of SDG was compared to placebo with a primary endpoint of change in Ki-67 in a multisite trial (Drs. Fabian, Hursting, Petroff, Kimler, Klemp, and Yeh); parallel animal studies were conducted (Drs. Petroff and Hursting). Drs. Sharma, Rastogi, and Bansal have been instrumental in developing and testing narrow band imaging that provides greater mucosal detail for visualizing the at-risk esophagus than traditional white light endoscopy.

Other efforts of investigators in this theme develop survivorship trials to prevent or reduce common side effects from local or systemic therapy (cognitive dysfunction, cardiac dysfunction) and/or improve the quantity or quality of life. Investigators have developed exercise interventions to combat obesity. CPS exercise physiologists and nutritionists (Drs. Donnelly, Sullivan, and Carlson) developed exercise interventions in average cancer risk adolescents and adults (R01HL111842, R01HD079642) and then adapted these interventions for prevention in high risk (Fabian, Kimler, Klemp, Sullivan, Donnelly R21CA121106) and cancer survivors (Befort, Klemp, Fabian, R01CA155014). Dr. Befort (CCPH), along with other CPS members, Drs. Klemp, Fabian and Sullivan, targeted overweight/obese breast cancer survivors in both the KUCC catchment and adjacent areas to deliver a phone-based behavioral weight loss intervention. Drs. Hamilton-Reeves, Klemp, Befort (CCPH), and Thrasher (D3ET) have assessed the impact of weight loss before and weight maintenance after prostate cancer surgery on obesity-driven prostate cancer biomarkers. In a collaborative trial between CPS and CCPH investigators [Drs. Fabian, Kimler, Klemp, Dixon, Carlson, Umar (CPS); Drs. Savage, Martin, Befort, and Fridley (CCPH)], investigators tested the combination of weight loss and omega-3-FA; primary endpoints were feasibility, weight loss induced biomarker modulation, reduction in weight re-gain, and differences in fMRI at six months between omega-3 fatty acids and placebo; accrual is complete; results are pending. Dr. Kluding, an exercise physiologist, is examining the effects of exercise on diabetics with peripheral neuropathy (R01DK064814) and will ascertain if this will be able to be safely translated into a trial for cancer survivors with peripheral neuropathy from taxol and other agents. Dr. Smith (R01HD049615) is continuing to study the effects of hormonal deprivation on pain including vaginal and pelvic pain.

Program members have developed a strong translational program in obesity. This is an important problem that affects the catchment area; Kansas ranks 9<sup>th</sup> in adult obesity and 13<sup>th</sup> in obesity amongst teens. Obesity is a factor in development and outcome after diagnosis of three of the four most

common cancers (breast, colon and prostate) in the KUCC catchment area. Rural residents are often challenged in access to weight loss and survivorship services. A CDC grant, Kansas Survivor Care Quality Initiative (KSCQI), in partnership with the Kansas Department of Health and Environment, (Klemp, CDC 6 NY58P006113-01-01) addresses the quantity and quality of life among Kansas cancer survivors. The purpose of this project is to increase both survivor and clinician knowledge of cancer follow-up care, screening and preventive lifestyle behaviors, and awareness/increased participation in chronic disease prevention and control programs (e.g., tobacco cessation, cancer screening, weight control). The Greater Plains Collaborative (GPC) (IRB#00003138) is a network (PCORNET) of health systems in 12 states committed to a shared vision of improving healthcare delivery through ongoing learning, adoption of evidence-based practices, active research dissemination and data sharing. The GPC is led by KUMC (Waitman, PI) and focuses on breast cancer and obesity.

The program has made a strong beginning in developing clinical trials that impact key catchment area issues such as obesity. However, there are significant missed opportunities. The most important missed opportunity is the need to work with CCPH to serve unique populations in the catchment area (e.g. Native American, African Americans). These missed opportunities were cited at the last site visit and have not been adequately addressed. Collaborations with CCPH could facilitate rapid transfer of clinical observations to laboratory experiments, and promising discoveries in the laboratory to innovative behavioral and medical applications in prevention, detection, diagnosis, treatment, and survivorship. The inadequate interface markedly decreases the impact the program has on the catchment area.

In summary, the program has made strong progress in diversifying its efforts in GI cancer and expanding its portfolio in survivorship. The addition of Dr. Dixon and Dr. Klemp as leaders provides new areas for growth in the program. The program has strengths, particularly Dr. Fabian's efforts in breast cancer chemoprevention, Dr. Dixon's efforts in GI, and Dr. Klemp's efforts in survivorship. Recent biomarker studies improve the mechanistic depth of the clinical studies. Inter- and intra-programmatic collaborations are strong. The program has improved its interface with other programs. There are, however, opportunities that remain. There are missed opportunities, particularly: 1) the need to strengthen the interface with CB, and 2) the importance of working with CCPH to impact diverse at-risk populations (e.g. Native American, African Americans). These missed opportunities were cited at the last site visit and have not been fully addressed. While funding has increased, many of the funded grants have expired or will expire soon. The biomarker portfolio has increased in sophistication, but many studies still use relatively simple endpoints (e.g., Ki-67 or cytokine ratios). Additional scientific depth of analysis and interface with CB would bring new insights into cancer initiation. Collaborations with CB could markedly strengthen the scientific impact of the program on the catchment area.

**Program Leader(s):** Dr. Carol Fabian has led the program since its inception. With Dr. Fabian moving towards retirement, there has been a significant change in program leadership. Dr. Dan Dixon, PhD, was recruited as the basic science program co-leader in 2013. Dr. Dixon's research focus is in post-transcriptional regulation of oncogenic mRNAs by RNA binding proteins and microRNAs in colon. In April 2016, Dr. Jennifer Klemp, MPH, PhD, a clinical health psychologist, with research interests in cancer survivorship, replaced Dr. Fabian, who became AD for Clinical Research. Both leaders are well qualified to lead the program and have complementary scientific strengths; their roles and responsibilities as program leaders are clearly delineated. Dr. Dan Dixon, PhD is an Associate Professor who joined KUCC in 2012 and has served as CPS co-leader since 2013. His research focus is on colorectal cancer prevention. He currently serves as a standing member of NCI Subcommittee J – Career Development Panel and the USAMRMC (DOD) Peer Reviewed Cancer Research Program Programmatic Panel. He also serves on the Editorial Board of Cancer Research. While Dr. Dixon brings key strengths in GI cancer, he is not a PI on a R01 grants. Dr. Jennifer Klemp, PhD, MPH, was mentored by Dr. Fabian and has extensive experience in primary and secondary cancer prevention. As the Director of Cancer Survivorship at the University of Kansas Cancer Center and across the State of Kansas, she coordinates a multi-disciplinary program that serves cancer survivors from the greater

Kansas City area and across the state. Her clinical practice is focused on cancer genetics and her clinical research has focused on quality of life, quality improvement and technology, cancer genetics, and behavioral interventions in primary and secondary prevention populations. Most recently, she has evaluated cardiovascular risk factors and developed strategies to assess and modify these risk factors. Dr. Klemp brings important expertise to the program in survivorship but does not have independent R01 funding.

**Assessment:** Excellent to outstanding merit

**Budget:** The budget is recommended as requested.

### **Drug Discovery, Delivery, & Experimental Therapeutics Research Program**

**DESCRIPTION** (provided by applicant): The Drug Discovery, Delivery and Experimental Therapeutics (D3ET) research program integrates a broad range of research areas that contribute to the discovery and delivery of new cancer therapeutic strategies, identification of companion biomarkers, translation of the most promising therapeutic strategies to the clinic and the evaluation of these strategies in experimental therapeutics trials. D3ET is organized around three, central highly-integrated scientific themes: 1) Discover and Deliver New Cancer Therapeutic Strategies; 2) Develop New Cancer Therapeutic Strategies; and 3) Evaluate New Cancer Therapeutic Strategies in Experimental Therapeutics Trials. D3ET has 60 members (33 PhD's and 27 MD's), including 39 full and 21 associate members. Membership reflects a range of senior and early-stage investigators with 20 Professors, 13 Associate Professors and 17 Assistant Professors. D3ET members are drawn from 25 departments across Children's Mercy, The University of Kansas in Lawrence and The University of Kansas Medical Center in Kansas City, providing a rich environment for discipline diversity and team science. During the reporting period (CY15), 51% of the 39 full members serve as principal investigators on externally funded, peer-reviewed grants. From 2012-2015, the D3ET program achieved a strong and growing cancer-focused research portfolio. In 2015, D3ET members conducted research on 36 cancer-relevant, peer-reviewed projects representing \$9.1M in extramural funding, including \$3.1M in funding obtained directly from the National Cancer Institute (NCI). The 15 NCI funded grants represented 35% of total peer-reviewed funding. D3ET has grown clinical research primarily by members successfully obtaining grants from industry to support clinical trial activities. The D3ET program has made impressive progress in publishing its research, and increasing intra-programmatic and inter-programmatic collaborations. Between 2012 and 2015, D3ET members published 617 cancer-relevant publications, including 67 papers with a journal impact factor of  $\geq 8$ . Twenty-nine percent of D3ET published research over this time period represented intra-programmatic collaborations and 23% involving inter-programmatic collaborations. Consistent with its research themes and objectives, 51% of D3ET publications included external industry, academia, government or disease philanthropy collaborators. Alan Gamis, MD (Children's Mercy) and Scott Weir, PharmD, PhD (KUMC), who bring complimentary scientific expertise in drug discovery, development and experimental therapeutics and strong track records of mentorship, jointly lead D3ET. Steve Williamson, MD, Medical Director for the Clinical Trials Office and D3ET member, completes the leadership team representing adult cancer experimental therapeutics.

**CRITIQUE:** The Drug Discovery, Delivery and Experimental Therapeutics (D3ET) research program was established in 2006, and in the last funded period, the program has grown from 22 full and 28 associate members to 39 full and 20 associate members. The program draws its strength from membership of a large number of faculty members with expertise in medicinal chemistry, pharmaceutical chemistry, pharmacology, toxicology, and therapeutics, headed by Dr. Weir who spent 20 years in pharmaceutical industry and a new co-program leader, Dr. Gamis, who directs Hematology/Oncology and Bone Marrow Transplantation at Children's Mercy Hospital. The goal is to discover, deliver, and evaluate new cancer therapeutic strategies by faculty members from diverse campuses, including the University of Kansas, Lawrence, the School of Pharmacy, the KU Medical

Center, and Children's Mercy Hospital. In 2015, D3ET had \$13.4 million in total cancer-related funding, including \$2.8 million in funding obtained directly from the NCI. This is reduced from the last renewal, which listed \$3.1 million from the NCI. Although there are some concerns regarding the reduction in cancer funding since 2010, the narrative does state that D3ET has established growth in clinical research, primarily by members obtaining funding from industry to support clinical trial activities. From 2012-2015, the D3ET program states that its proportion of cancer-focused research efforts expanded; with 15 NCI funded grants represented 35% of total peer-reviewed funding.

D3ET is organized around three, central scientific themes: 1) Discover and Deliver New Cancer Therapeutic Strategies; 2) Develop New Cancer Therapeutic Strategies; and 3) Evaluate New Cancer Therapeutic Strategies in Therapeutics Trials. D3ET members are drawn from a wide number of 25 different departments across Children's Mercy Hospital, the University of Kansas in Lawrence and the University of Kansas Medical Center in Kansas City, and they suggest that this diversity is contributory to the efforts to establish team science. During the reporting period (CY15), 51% of the 39 full members serve as investigators on externally funded, peer-reviewed grants. The D3ET program has increased both intra-programmatic and inter-programmatic collaborations. Between 2012 and 2015, with 750 cancer-relevant publications, including 67 papers with a journal impact factor of  $\geq 8$ . Twenty-nine percent of D3ET published research over this time period represented intra-programmatic collaborations and 23% involving inter-programmatic collaborations. Representative of the stated research themes and objectives, 54% of D3ET publications included external industry, academia, government, and disease philanthropy collaborators. Examples of small molecule cancer focus are provided in the program narrative, and there are examples of IIT's that serve the cancer center program membership.

In the last review, the weaknesses of the program included a lack of a coherent programmatic focus and did not have a clearly defined pathway for the clinical translation of novel concepts or agents. In response, strategies were implemented to drive directed translational research. The Target Acceleration Group was initiated to accelerate drug discovery projects from target identification through *in vivo* preclinical proof of principle with help from the Lead Development and Optimization Shared Resource. The Investigator-Initiated Trial (IIT) Steering Committee was also formed to solicit IIT proposals, and to enable and advance hypothesis-driven IITs that could compete for extramural funding. These efforts have paid off to some extent. Examples for bench-to-bedside research include a selective inhibitor of ATPase p97 with two druggable derivatives being licensed and evaluated in two phase I clinical trials in cancer patients with multiple myeloma and solid tumors. Besides small molecule inhibitors, the natural product, gossypol, was discovered to target the RNA-binding protein, MSI1, and it is being validated *in vitro* and *in vivo*. Another significant development is chemically linked hyaluronan-cisplatin that facilitates delivery into the lymphatics *in vivo* and has successfully treated cancer in dogs. Repurposing old drugs for new indications is a focus of this program and an example is the discovery of an FDA-approved topical anti-fungal agent, CPX, to suppress tumor growth by inhibiting the Notch-1 pathway. Its derivative, CPX-POM, is licensed and being evaluated in cancer patients. Stem cell therapy for graft-versus-host disease has an allogeneic mesenchymal stem cell product under development. There is also a focus on BRCA1/2 studies related to breast cancer and exosomes in tumor promotion. Some attempts at immune analysis comes from studies of the role of myeloid-derived suppressor cells in cachexia, and chimeric antigen-receptor-T cell therapy in pediatric and adult cancer patients.

Despite these successes, a number of weaknesses remain. It is unclear what projects are being pursued by the large number of members outside of those involved in the projects mentioned above. The productivity of these members is not well documented, especially in relation to cancer. In addition, only a handful of the members appear to be highly collaborative and of the 60 members, only five members are currently NCI-funded. Although the 2015 tally indicates 36 total peer-reviewed grants totaling \$9.1 million with \$3.1 million from 15 NCI grants, at the end of 2016, six NCI grants and 10 other non-NCI grants have ended, substantially reducing grant support. In total, only 15 members of 60

members are extramurally funded as of January 2017. In addition, most of the clinical trials funded by industry, are thus still suboptimal in terms of innovation. It was not clear how the theme of personalized medicine will be integrated throughout all stages of drug development in the program. The preclinical-to-clinical components of the program, development of predictive biomarkers, and translation to early clinical trials was not always well articulated and was uneven in quality. The integration of the program is not evident, especially with only two cited formal program meetings per year. The list of meetings is not program-based but project-based that only brings limited numbers of individuals on a single topic, often involving a similar set of collaborative individuals. Other meetings listed are seminars by internal and external speakers. Another concern is the lack of extramural funding by both program leaders as PI's.

The program narrative describes a number of ongoing development projects that span early stage target validation to bona fide clinical trials. Some of these appear to have been driven by lead agents developed at KUCC. Moreover, early stage pilot and developmental funds have supported the projects. This is viewed as encouraging. The iterative nature of the project development approach could represent a strength of the program. Precisely how go-no go decisions are employed during this process might require further refinement, but the present approaches do address some of the concerns expressed in the previous review. For example, the group now appears to have established a sustainable pipeline of potential cancer small molecule drug discovery candidates at the chemistry/biology interface. To some extent, this has increased the number of hypothesis-driven IIT's that have the potential (although have perhaps not yet matured) to secure peer-reviewed funding. Finally, there is evidence that KUCC's pipeline of novel cancer therapeutic projects (including immunotherapy) is being expanded. Each of these can be viewed as positive advances.

In summary, the program appears to remain fragmented with isolated pockets of highly innovative research leading to potentially marketable products. The depth of interaction of the two program leaders is not apparent, and with the program members scattered in various geographical locations, an obvious venue is not evident besides webinars for them to interact and form a coherent unit, especially with the clinical members. With better organization, this program could become a highly integrated enterprise to develop much-needed new therapeutics. Moreover, the program would greatly benefit from the recruitment of a cadre of clinical investigators with expertise in cancer therapeutics and early phase cancer drug development.

**Program Leader(s):** The program leaders are Dr. Alan Gamis, MD, Children's Mercy Hospital, who has recently joined Dr. Scott Weir, PharmD, PhD, KUMC, in this capacity. Dr. Scott Weir is a highly-respected expert in pharmacology, who brings a unique set of skills to the program, having risen through the ranks in pharmaceutical industry for 20 years, and then entering academia to build a state-of-the-art Institute for Advancing Medical Innovation at Kansas University. He also serves as the Associate Center Director for Translational Research and sits on prestigious committees such as the NIH NCATS Advisory Council and Cures Acceleration Network Board. Dr. Gamis is the Associate Director of the Division of Hematology, Oncology and Bone Marrow Transplant at Children's Mercy Kansas City, and is board certified in pediatric hematology/oncology and bone marrow transplantation. He has a strong clinical background, but appears to lack expertise in the design and development of early phase drug testing trials. Dr. Steve Williamson, MD, Medical Director for the Clinical Trials Office and D3ET member, completes the leadership team representing adult cancer experimental therapeutics. However, the program might benefit from identifying a co-leader with specific clinical expertise in cancer therapeutics and early-phase clinical drug development.

**Assessment:** Very good to excellent merit

**Budget:** The budget is recommended as requested.



## SHARED RESOURCES

### Biospecimen Shared Resource

**DESCRIPTION** (provided by applicant): The Biospecimen Shared Resource (BSR), led by Andrew K. Godwin, PhD (Director, BSR; Deputy Director, KUCC, and D3ET member) and by Rashna Madan, MBBS, FCAP, FASCP (Assistant Director, BSR) plays a vital role in the University of Kansas Cancer Center (KUCC) by its ethical collection, storage, annotation, and distribution of high quality biospecimens, such as fresh/fresh-frozen tumor tissues of varying histology and bodily fluids (blood, saliva, urine, ascites fluids) which are essential to support translational research and investigator-initiated studies. The BSR also provides expert histopathology support and combines the expertise of pathologists, translational researchers, and technical personnel to produce a comprehensive and focused approach to support the research activities at KUCC. The BSR is overseen by an internal advisory board (IAB) and the director and assistant director, Godwin and Madan, respectively. Colleen Reilly (Project Manager) provides the day-to-day staff supervision and Cassaundra Shipman (Program Development Manager) oversight of participant consenting. The BSR is staffed by four research coordinators who identify participants and administer informed consent, one clinical laboratory supervisor, two lab technicians who handle the processing and banking of biospecimens, one histotechnologist who performs advanced histology services, including histology support for therapeutic clinical trials, and one cancer registrar who performs searches for samples to match user requests and enters clinical information not available electronically into our developing Curated Cancer Clinical Outcomes Database (C<sup>3</sup>OD). Additionally, tissue biospecimen collection is facilitated by pathology assistants, residents and fellows at the KU Hospital and the Indian Creek Campus as part of the KU Health System's commitment to the Cancer Center's BSR. The BSR is fully equipped for biospecimen collection, processing, and distribution, and thus, the BSR adheres to the OSHA laboratory standards for handling cryogenics, ISBER Best Practice for Repositories, and NCI Best Practices for Biospecimen Resources, and has developed Standard Operating Procedures to govern each of these processes. The collection, processing, and distribution of samples by the BSR staff has grown substantially over the past four years (2012-2015) and now includes collections of pediatric sarcomas from ICC and underserved populations from the satellite biospecimen bank at Truman Medical Center, a member of the Midwest Cancer Alliance and the Kansas City safety-net health system. Together, this essential KUCC shared resource, houses over 9,000 tissues and more than 20,000 blood samples (including either single or repeat draws from individuals diagnosed with cancer, benign disease, or no evidence of cancer) from >17,000 participants (enrolled by the end of 2015) and distributed nearly 16,000 specimen aliquots since 2012. In CY15 (the reporting year), the BSR services were used by 74 investigators, 44 who were KUCC members, an increase of nearly 2-fold during the funding period.

**CRITIQUE:** The Biospecimen Shared Resource (BSR) is a continuing shared resource that was well received in the last submission. It remains under the overall leadership of Dr. Andrew Godwin and a new co-leader, Dr. Rashna Madan, has been added. The BSR provides collection, storage, annotation, and distribution of high quality biospecimens as well as histology support. All of the tissue is collected under a single informed consent, and this shared resource has excellent leadership and an internal advisory board.

The volume of samples has grown over the prior funding period by nearly 7-fold and now houses over 9000 tissue samples. Over 16,000 specimen aliquots were distributed since 2012. The BSR provides frozen and fixed tissues (including custom TMA's), blood, serum, and DNA to users as needed. The priority for requests and distribution is clear with 32.5% of the materials distributed to NCI-peer reviewed cancer grants, 27% to junior investigators, and 27% to NIH/NCI funded investigators outside the KUCC.

The BSR remains a growing and increasingly vital part of the cancer center. They have substantially increased the number and diversity of their collection over the past 4 years and appear to have

responded to the critique of the prior submission, which had raised questions about the diversity of the tissue collection and its ability to respond to new initiatives in different tumor tissues. The efforts to collect tissues on under-represented minority individuals is a particular strength, although the accrual, to date, does not show an over-representation of minorities in the collections. Roughly 70% of all unique users for this resource are members of the cancer center, and the number of distributed samples is experiencing impressive growth. Another potential strength of the BSR is the Curated Cancer Clinical Outcomes Database (C<sup>3</sup>OD), which is designed to ethically collect key clinical data on every sample entered into a companion database to provide investigators with annotated clinical information on the samples in the database. The BSR has contributed to national studies of TCGA cancers, particularly in the gynecological area and has performed as a “good citizen” in the national cancer community to complete these key efforts. The quality assurance programs seem to be satisfactory.

The BSR has anticipated many of the likely future directions of core needs. Their genomic efforts and PDX developments are commendable, and future development of hematologic malignancies and sarcoma base will support the centers developing needs. They will face a continuous challenge in the integration of the various consortium components and service of clinical effort that will depend on high quality genomic and immunotherapeutic targeting.

The leadership is exceptional. Both Dr. Godwin and Dr. Madan are highly qualified and appear to contribute sufficient time and effort to successfully perform their duties. The number of individuals involved in the day to day work of tissue bank seems adequate to the tasks at hand.

In summary, the BSR remains an extraordinarily strong and vital part of the cancer center’s mission. The strengths of the BSR include the growth of diversity in the collection and the linkage of clinical data (assuming that this costly and intensive service can be successfully maintained). The future directions might be enhanced by a user survey to better understand how the shared resource might add services to satisfy unmet needs of the cancer center members.

**Assessment:** Exceptional to outstanding merit

**Budget:** The CCSG provides 7.2% of the current budget and the applicant requests an increase to 12.5%, which certainly reflects the usage by CCSG members. The institution continues to support 40%-50% of the core efforts in both the current and the proposed budget. The value added/cost effectiveness of the core remains excellent with modest charge-backs and superior quality output. The budget is recommended as requested.

## **Biostatistics & Informatics Shared Resource**

**DESCRIPTION** (provided by applicant): The Biostatistics and Informatics Shared Resource (BISR) plays an essential role in the research activities of the University of Kansas Cancer Center (KUCC) by supporting the data science needs of KUCC investigators. The BISR is led by Brooke L. Fridley, an accomplished biostatistician with a long-standing commitment to cross-disciplinary collaborations, and includes eight additional faculty members with specialized cancer biostatistics research expertise. The BISR assists KUCC investigators by providing expertise in study design, statistical oversight and analyses, clinical research informatics and data management, electronic data collection, bioinformatics, statistical genomics and investigator initiated clinical trials. The BISR consists of faculty and staff, whose diverse expertise and skill sets span the areas of biostatistics, bioinformatics and informatics. The considerable overlap between these three areas allow researchers to work with a single shared resource for all their data collection, analytics and statistical analysis needs. The synergy between the areas that encompass “data science” enables the BISR to support a wide-range of quality services, and in a timely and cost-effective manner. To support the research activities of KUCC members, the specific aims of this resource are to: 1) provide study design and statistical support and expertise; 2) provide

bioinformatics and statistical genetics support and expertise; 3) provide informatics support for data collection and management; 4) develop and support on-going research enabling technologies, platforms and tools; and 5) educate students, fellows and faculty members of KUCC on data science and reproducible research ideas and methods used in cancer research. During the last cycle of the CCSG grant, BISR services were used by 101 KUCC members for 240 grant submissions (with subsequent awarded grants providing 34% of total support for BISR faculty and staff) and 545 projects involving data science expertise. As an essential shared resource for KUCC, the BSR leverages substantial institutional support and requests only 11% support from the CCSG.

**CRITIQUE:** The Biostatistics and Informatics Shared Resource (BISR) provides expertise in study design, statistical analysis and oversight, clinical research informatics and data management, electronic data collection, bioinformatics, and statistical genomics. Specific aims of the BISR are to: 1) provide study design and statistical support and expertise; 2) provide bioinformatics and statistical genetics support and expertise; 3) provide informatics support for data collection and management; 4) develop and support on-going research enabling technologies and platforms; and 5) educate students, fellows, and faculty members on data science and reproducible research in cancer.

At the time of the last submission, this shared resource was headed by Dr. Matthew Mayo, who has since been promoted to Associate Director for Shared Resources. In partial response to a prior critique of the need for a sufficient knowledge base to be able to support basic research, Dr. Brooke Fridley was appointed director of the BISR and was the listed director at the time of this submission. Dr. Fridley is an expert in the areas of statistical genomics, cancer genomics, and pharmacogenomics and has extensive experience in the design and analysis of 'omic studies conducted with both microarray and high-throughput sequencing technologies. During the site visit, it was communicated that Dr. Fridley accepted a position as the Chair of the Department of Biostatistics at Moffitt Cancer Center and that Dr. Byron Gajewski was appointed Director of the BISR. Dr. Gajewski has expertise in Bayesian biostatistics, adaptive designs, and validation of measures of patient reported outcomes. Although he has only been at the helm for a few months, he has been a full member of the KUCC since 2009. Dr. Devin Koestler rounds out the leadership team as the Associate Director of the BISR. A former mentee of Dr. Fridley, Dr. Koestler has experience working with different types of 'omic data including genotypic, DNA methylation, microbiome, mRNA and miRNA expression, and Next-Gen sequencing data. Drs. Gajewski and Koestler are joined by six additional PhD level biostatisticians representing a mixture of junior, mid-level, and senior levels with expertise in a wide variety of areas including clinical trials, mixed models, analysis of cell-based assays, Bayesian adaptive designs, psychometrics, meta-analysis, survival analysis, phase I/II clinical trials, and integrative clustering analysis. BISR members appear to be well integrated into the cancer center serving on internal review committees, PRMC, IACUC, and other committees.

This shared resource is housed in the Department of Biostatistics allowing access to additional resources as necessary. Members are divided into statistical expertise subunits including: 1) Bioinformatics, 'Omics, and Analysis and Design; 2) Pharmacological Modeling, High Throughput Screening and Bioassays; 3) Therapeutic Investigator Initiated Trials; 4) Clinical Trial Designs and Analysis Methods; 5) Observational Data and Survivorship; 6) Instrument Development and Psychometrics; and 7) Health Equity and Disparities with individual faculty leading each of this subunits. An additional strength of this shared resource is the economies of scale achieved by researchers having one shared resource for all their data collection, analytics and statistical analysis needs. The BISR is also involved in innovative work as evidenced by the development of an application that predicts when studies will accrue all patients into a study highlighted during the site visit. This program is widely used by investigators and the Clinical Trials Management team to help in recruitment strategies and decisions. The core has a robust collection of tools for electronic data capture including Comprehensive Research Information System (CRIS), REDCap, and OpenClinica. The BISR also receives input from the cancer center IAB as well as an EAB for the Department of Biostatistics. During

the last cycle, BISR services were used by 101 KUCC members for 240 grant submissions and 545 projects (with subsequent awarded grants providing 34% of total support for BISR faculty and staff).

In the previous review, a major concern relating to this resource was the low publication productivity for its size, the weakness of the clinical trials and analysis plans in reviewed protocols, and lower demonstrated level of integration into the basic science and translational efforts. In response to concerns about depth of knowledge in the area of clinical trials, the core has entered into collaboration with Berry Consultants LLC and brought on Dr. Scott Berry as an adjunct faculty member (not included in this budget). This collaboration has facilitated the use of proprietary software used in the development of Bayesian adaptive clinical trials evidenced by two example trials provided in the narrative. The BISR is widely used and well integrated as evidenced by full integration into program areas as well as extensive collaborative publications. This shared resource has also increased their statistical genomics expertise with the addition of Drs. Fridley, Koestler, and Chalise. This additional knowledge base has allowed the core to better serve the basic science programs and resulted in a 2.1- and 1.5-fold increase in usage for the CB and D3ET programs. Although Dr. Fridley has since left, Dr. Koestler has a similar knowledge base. Additionally, Dr. Dong Pei has been recruited (starting in April) to help solidify their knowledge base in Next-Gen sequencing.

Because KUCC investigators are geographically spread over a wide area, there was some concern about the BISR's ability to effectively collaborate. During the site visit, BISR leaders indicated that consultations occur in person (driving by BISR director), via teleconference, and videoconferencing. One remaining concern is the BISR's input into investigator-initiated Trials (IIT). During review, it was discovered that some IITs have uneven statistical input. At the site visit, it was discovered that although a biostatistical investigator is assigned to each IIT, it is up to the individual project leader to engage that investigator. The BISR should consider advocating for a more formalized arrangement to ensure that there is consistent biostatistical involvement in IITs.

In summary, this is a strong shared resource consisting of an experienced team that provides an essential service for KUCC investigators. Services are provided for the majority of KUCC members that have resulted in grant submissions that in turn, now provide funding. A remaining weakness of this shared resource is its impact on IIT and concerns regarding the ability of investigators to overcome the geographic barriers in collaboration. Because of turnover, the current director has had a short tenure in his role. He has, however, the appropriate expertise to be an effective leader and has already implemented important improvements to the BISR. His ultimate long-term impact will be seen over the upcoming years.

**Assessment:** Excellent to outstanding merit

**Budget:** CCSG requested funds only comprise 11% of the resource's total operating budget. The budget is recommended as requested.

### **Clinical Pharmacology Shared Resource**

**DESCRIPTION** (provided by applicant): Established as a University of Kansas Cancer Center (KUCC) developing shared resource in 2012 and selected as an established shared resource in 2015, the Clinical Pharmacology Shared Resource (CPSR) is led by Gregory Reed, PhD. This shared resource has three functional components.

1. Correlative Laboratories - directed by LaToya Berry. The Correlative Laboratories provide GXP-compliant acquisition, processing and storage or shipping of clinical research samples. Following either a sponsor's protocol or CPSR protocols, the staff efficiently and precisely prepares samples from blood (whole blood, serum, plasma or specific blood cell fractions), urine and saliva or processes tissue samples, and then stores or transfers those samples for analysis. The Correlative Laboratories are located near patient treatment areas at the KU Clinical Research Center (KU CRC),

Westwood (The University of Kansas Health System's outpatient clinical facility) and at The University of Kansas Health System's main campus. The Correlative Laboratories also provide scientific and technical support to the community oncology sites and Midwest Cancer Alliance (MCA) sites to assist them in sample acquisition, processing and shipping.

2. Bioanalytical Laboratory - led by Reed. Located at the KU CRC, this GLP-compliant facility prepares biological fluids, cells or tissue samples, and analyzes them for concentrations of drugs, drug metabolites and other small molecule biomarkers. Analyses are performed on two UPLC-tandem quadrupole mass spectrometers, with a combined sample throughput of over 30,000 samples per year.
3. Pharmacokinetics/Pharmacodynamics (PK/PD) Unit – also directed by Reed. Reed performs calculations and modeling using the Phoenix/WinNonlin® software to define and interpret the kinetics of drugs and their actions.

In addition to these study-specific activities, the staff of the CPSR also play a major role in educating future physicians and researchers, as well as nurses and study coordinators currently involved in cancer clinical trials, on the theory and practice of clinical pharmacology and on how those applications of clinical pharmacology result in more powerful and informative results from clinical trials.

**CRITIQUE:** Established as a KUCC developing shared resource in 2012, this facility was selected as an established shared resource in 2015. The Clinical Pharmacology Shared Resource (CPSR) is led by Dr. Gregory Reed and lists three functional components: (1) Correlative Laboratories, directed by Dr. LaToya Berry, provides GLP-compliant acquisition, processing and storage or shipping of clinical research samples. As part of a protocol, staff members prepare samples from blood, urine and saliva or process tissue samples, and then store or transfer those samples for analysis. The Correlative Laboratories are located in areas central to and near patient treatment areas. The Correlative Laboratories also provide scientific and technical support to the community oncology sites to assist (but not necessarily process) in sample acquisition and shipping; (2) Bioanalytical Laboratory - led by Dr. Reed is a GLP-compliant facility for preparation of biological fluids, cells or tissue samples, analyzing them for concentrations of drugs, metabolites and other small molecule biomarkers. Analyses appear to reach a combined sample throughput of over 30,000 samples per year; and (3) Pharmacokinetics /Pharmacodynamics (PK/PD) Unit – also directed by Dr. Reed performs calculations and modeling to define and interpret the kinetics of drugs. In addition, the staff also teach the theory and practice of clinical pharmacology to future medical and graduate students, as well as nurses and study coordinators currently involved in cancer clinical trials.

The resource narrative lists a number of examples where basic pharmacology studies are carried out to supplement existing ongoing trials and enhance the correlative impact of such studies. In most cases, these are important adjuvants and add to the overall value and translational quality of the trials. Overall, there is little doubt that the existence of this type of facility provides value as a commodity in enhancing the translational and inter-disciplinary efforts of the clinicians and scientists in designing and carrying out clinical protocols. Although it should be noted that the basic services offered to achieve this endpoint are fairly limited, reflected by the restricted number of scientific examples provided on the poster presentation, and the relatively small number of in-house users. Even in the context that this is a new shared resource, the total number of investigations appears small, there is a relatively limited number of funded studies using this resource, seemingly heavily weighted towards the D3ET program. The actual number of analyzed samples for the KUCC is not clear from the provided materials and the publication record is limited as are the number of protocols / accruals that might be linked to the use of this shared resource. It appears that a fairly large proportion of the samples are collected and shipped to pharmaceutical companies as part of sponsored non-IIT's. Use of the resource is entirely predicated on investigator-based protocols that are brought to the attention of the director of this shared resource. If 20%-25% of the time and effort for the three named individuals are to be provided through the CCSG, further documentation that 25% of the shared resource work (funded-unfunded) is reasonably linked to the CCSG programs would be required- but this documentation is not provided. One of the

achievements cited in the grant application is an extramural collaboration linked through a co-investigator within the KUCC. The value of the (part 3) PK/PD and (part 2) analytic services offered by the core appear to overlap with other similar services from the Department of Pharmacology and the LDOSR. The quality assurance metrics and results are not clearly communicated beyond compliance with outside standards.

The goals of Aim 2 are listed as to develop, codify, and perform proper acquisition, processing and either short-term storage or shipping of research samples from clinical trials in cancer therapeutics and prevention and cancer population health. While these are all reasonable goals, it would appear that some of them could be coordinated by the tissue biorepository facility. There is discussion about the complementarity of function with other tissue handling cores at KU and while a rationale is provided for separating sample distribution functions, it is not entirely compelling.

Dr. Gregory Reed, PhD, is the Director of the CPSR. He is responsible for the operation and performance of all components and serves as the main contact for the shared resource. Direct supervision and management of the Correlative Laboratories and their staff is delegated to Dr. LaToya Berry. Dr. Reed is responsible for all operations of the Bioanalytical Laboratory and for all functions of the PK/PD Unit. He brings over 35 years of experience with the types of equipment and technologies that are relevant to this facility and he has a GLP-compliant Bioanalytical Laboratory. As Professor in the Department of Pharmacology, Toxicology and Therapeutics in the University of Kansas Medical School of Medicine he already provides instruction for medical students in Chemotherapy and in PK/PD. It appears that much of Aim 5, as related to education will essentially be an extension of standard professional school teaching obligations.

**Assessment:** Very good merit

**Budget:** As a developing resource, no support was provided in the prior grant support period. Over \$529,000 was provided by KUCC (\$269,000) and institutional sources (\$260,000) as well as \$322,000 of fee for service income. The budget requests \$75,908 in CCSG support for Year 1 of the next funding period (7.7% of the projected total) representing 25% T/E for the director and 20% for 2 other senior staff members. The budget is salary-focused, but appears not unreasonable for the services provided. The budget is recommended as requested.

### **Lead Development & Optimization Shared Resource**

**DESCRIPTION** (provided by applicant): The Lead Development and Optimization Shared Resource (LDOSR) is a University of Kansas Cancer Center (KUCC) shared resource composed of three functions: 1) High Throughput Screening (HTS); 2) Medicinal Chemistry (MC); and 3) the Biotechnology, Innovation and Optimization Center (BIOC). Collectively, these three functions allow the LDOSR to accelerate projects from early method development around cancer pathways or targets, through high throughput screening, compound hit prioritization, secondary *in vitro* confirmatory assays, medicinal chemistry optimization, *in vitro* pharmacology testing, *in vivo* pharmacokinetics and drug delivery formulations for *in vivo* preclinical proof-of-concept testing. The LDOSR has modified its composition and activities over the past four years in order to provide the best possible support to KUCC members. The Preclinical Proof of Concept (PPOC) service was eliminated from the LDOSR at the end of 2012 because many KUCC members had similar functionality within their own laboratories. Furthermore, it was realized that the LDOSR would be enhanced by a dedicated medicinal chemistry expert. Therefore, Frank Schoenen joined the LDOSR to provide medicinal chemistry optimization services. In 2014, the LDOSR formed a project management service known as the Target Acceleration Group (TAG). TAG aims to accelerate projects from early method development around cancer pathways or targets and more seamlessly move projects between HTS, Medicinal Chemistry and the BIOC. TAG helps KUCC members navigate the drug discovery, delivery and development process more efficiently.

**CRITIQUE:** The Lead Development and Optimization Shared Resource (LDOSR) is a KUCC shared resource composed of three functions: 1) High Throughput Screening (HTS); 2) Medicinal Chemistry (MC); and 3) the Biotechnology, Innovation, and Optimization Center (BIOC). These three functions are designed to allow the LDOSR to accelerate projects from early method development around cancer pathways or targets, through high throughput screening, compound hit prioritization, secondary assays, medicinal chemistry optimization, *in vitro* pharmacology testing, *in vivo* pharmacokinetics and drug delivery formulations for *in vivo* preclinical proof-of-concept testing. In other words, to iteratively advance in-house leads towards IND status. The services provided by the LDOSR has changed over the past four years. The Preclinical Proof of Concept (PPOC) service was eliminated from the LDOSR at the end of 2012 to eliminate duplicative functions. Dr. Schoenen joined the LDOSR to provide medicinal chemistry optimization services and in 2014, the LDOSR formed a project management service known as the Target Acceleration Group (TAG) designed to accelerate the drug discovery, delivery and development process more efficiently.

Overall, this is a complex multifactorial service with numerous moving parts reliant upon the efficient coordination of iteratively driven processes that are not always adequately addressed in one individual's laboratory. Shared resource structure is maintained through a series of inter-campus meetings and teleconferences. Given the size and complexity of all the moving parts, it became apparent at the site visit that coordination and transitional efficiency provides a practical challenge. Some examples of early hit lead compounds were provided in the narrative and at the poster presentation. There are plans to advance some of these compounds through preclinical testing towards an IND status. Given the variety of issues that could permeate drug discovery and development, this core would certainly have functional importance. The actual organization of the flow of iterative decision networking and the mechanisms used for prioritization was not explained in great detail in the application or at the site visit. The number of cancer center users has increased slightly since the last review cycle, but is still not high, but there was evidence of some cost effectiveness associated with the process.

In summary, this shared resource is conceptually very valuable and has undergone some positive changes since the last review. It has also been somewhat responsive to the concerns raised during the prior review. Usage has broadened slightly to more investigators and there were some examples of cost-effectiveness; however, the graphical representation of usage was cumulative and unclear, since only 59 users appear to be actively involved for the previous year. Other disconnects were also noted. There were very few valuable examples of HTS successes and the examples associated with the other core functions (generally) were viewed by the review committee as neither outstanding nor numerous. Communications between shared resource and program personnel were not well-delineated and how resource involvement was initially instigated seemed to be contingent upon potential user investigators approaching core personnel, rather than the reverse.

Dr. Michael J. Baltezor, PhD, is Director of the LDOSR and Manager of the BIOC function (2.4 calendar months) and provides coordination of the efforts across the two groups within the LDOSR. Dr. Anu Roy, PhD, is Assistant Director of the LDOSR (1.2 calendar months) and is responsible for the HTS activities. Dr. Frank Schoenen, PhD, has recently joined as Manager of the Medicinal Chemistry (MC) (1.2 calendar months) function, which was added to the LDOSR in 2015. Trained as a synthetic organic chemist, Dr. Schoenen has 15 years of pharmaceutical industry experience as a medicinal chemist working in inflammation and cancer therapeutics and high-throughput chemistry at the early stages of drug discovery. These individuals appear to possess the qualifications and experience required to coordinate some of the decision network options required for moving leads forward.

**Assessment:** Very good merit

**Budget:** The overall costs of the various components are high, but the CCSG requested support appears reasonable. The budget is recommended as requested.

### Transgenic & Gene-Targeting Shared Resource

**DESCRIPTION** (provided by applicant): Genetically altered mouse models are important tools for the researchers at the University of Kansas Cancer Center (KUCC). The production and analysis of such models ultimately leads to a better understanding of the nature, progression and functional genomics of tumor formation. They also serve as *in vivo* models for diagnostics and treatment. The Transgenic and Gene-Targeting shared resource (TGTSR), led Jay L. Vivian PhD, supports members of KUCC by providing centralized and comprehensive technical services for the production of novel transgenic and gene-targeted rodents and genetically altered pluripotent stem cells. The TGTSR uses cutting edge methods, state-of-the-art instrumentation, and novel reagents for the generation of these models. The TGTSR, housed at the KUMC campus, has four full time technical staff along with Vivian. The Cancer Center support of the TGTSR allows for the development of specific initiatives in the Facility relevant to cancer research. For example, certain transgenic methods and mutations are particularly relevant to cancer studies, including tissue specific transgene expression, subtle mutations that recapitulate clinically identified variants and somatic mutations and strain-specific nuclear transfer. Emerging technologies, including *in vivo* genome editing methods (e.g., CRISPR/Cas9 and TALE nucleases) are providing a more rapid means of generating these types of novel mouse models of tumor progression. The integration of these continually evolving methods into the 'toolbox' of the TGTSR greatly accelerates the development of animal models of cancer, while also reducing costs to KUCC researchers on all campuses.

**CRITIQUE:** Genetically altered mouse models are important tools for the researchers and the production and analysis of such models ultimately leads to a better understanding of the nature, progression, and functional genomics of tumor formation. They also serve as *in vivo* models for diagnostics and treatment. The Transgenic and Gene-Targeting Shared Resource (TGTSR), led by Dr. Jay L. Vivian, PhD, supports members of KUCC by providing centralized and comprehensive technical services for the production of novel transgenic and gene-targeted rodents and genetically altered pluripotent stem cells. The TGTSR uses cutting-edge methods, state-of-the-art instrumentation, and novel reagents for the generation of these models. The TGTSR, housed at the KUMC campus, has four full time technical staff along with Dr. Vivian. The cancer center support of the TGTSR allows for the development of specific initiatives in the facility relevant to cancer research.

The TGTSR is an institutional support facility providing a centralized service for the production of transgenic and gene-targeted mice for investigators of KUMC, KU-Lawrence, and the surrounding Kansas City research community. As a fee-for-service, the TGTSR provides a full range of transgenic services, including pronuclear injection of nucleic acids (including RNA and plasmid-derived, BAC, and YAC DNA injections) and blastocyst injection of ES cells. The TGTSR has the necessary equipment and space for a range of state-of-the-art embryo manipulation. Most work is done in mouse models, but the TGTSR also has the capacity to support rat embryo manipulation and pronuclear injection. The facility is equipped to offer a range of embryo services, including cryopreservation of sperm, embryos and oocytes and assisted reproductive techniques such as rederivation, *in vitro* fertilization, and intracytoplasmic sperm injection.

The TGTSR also offers molecular biology services of genotyping of mice and screening of ES cell clones, as well as DNA construct preparation, including BAC DNA for microinjection. The TGTSR has generated hundreds of transgenic and knockout mice for studies of cancer, cardiovascular diseases, neurological diseases, kidney diseases, cystic fibrosis, bone morphogenesis, and environmental and reproductive sciences. Finally, the core contains Pluripotent Stem Cell manipulation, Embryo Manipulation, Pluripotent stem cell culture stations, and a Molecular Biology lab are all contained in this core.



This shared resource is new since the last CCSG review. However, it appears to be a very strong core that is critical to expanding the scope and breath of the KUCC research portfolio. In summary, the TGTSR clearly meets the goals set forth by the KUCC, and it is very well placed to make important advancements in the next five-year cycle.

**Assessment:** Exceptional to outstanding merit

**Budget:** The budget is recommended as requested.

## **CLINICAL PROTOCOL & DATA MANAGEMENT (CPDM)/CLINICAL TRIALS OFFICE & DATA AND SAFETY MONITORING**

### **Clinical Protocol and Data Management**

**DESCRIPTION** (provided by applicant): The Clinical Protocol and Data Management (CPDM) function at the University of Kansas Cancer Center (KUCC) resides within the Clinical Trials Office (CTO). The CTO, led by Stephen Williamson, MD (Medical Director of the CTO and Early Phase Clinical Research Program) and Hobs Apell, (Senior Executive Director) provides comprehensive support services that span the life cycle of cancer clinical trials from concept through manuscript. The CTO provides a central location for protocol management and reporting. There is a strong emphasis on assuring data integrity and compliance as well as emphasis on the education and training of CTO staff and investigators. There is also a strong emphasis on achieving timelines for rapid submission and activation of protocols while observing all regulatory requirements. To further translational research and mentorship goals, the Investigator-Initiated Trial Steering Committee (IITSC) was established in 2015. The IITSC, chaired by Williamson, and Scott Weir, PharmD, PhD (Associate Director for Translational Research), was formed to mentor and educate junior investigators and to support the acceleration of scientific discovery of novel therapeutics through the conduct of investigator-initiated clinical trials. Over the last four years, substantial progress has been made broadening clinical research partnerships with communities throughout our catchment area. Three major changes have expanded the composition of clinicians participating in the clinical trials process. The first change results from the incorporation of a large private practice oncology group by the University of Kansas Health System, a group now defined as the KUCC community oncology program. The second change is the expansion of the outreach network of KUCC, known as the Midwest Cancer Alliance (MCA), which is a membership fee-based network of hospitals and physician groups located across the KUCC catchment area. Many MCA centers serve as affiliate sites to cooperative group sponsored trials and investigator-initiated trials conducted by KUCC as the Primary Center. The third change results from the 2015 consortium agreement with Children's Mercy incorporating their clinicians into KUCC programs. The CTO has enabled a steady increase in clinical trials accrual at KUCC since receiving NCI Designation. Accrual to Intervention clinical trial protocols increased overall by 21% (2,097 accruals in 2012 to 2,544 accruals in 2015). Accrual to Interventional investigator-initiated trials (IIT) increased by 12% (1,140 accruals in 2012 to 1,275 accruals in 2015). Notably, in 2015, institutionally sponsored IITs accounted for nearly 50% of all KUCC intervention clinical trial enrollments. Accrual to Industrial Sponsored Interventional Trials increased more than 160% (96 accruals in 2012 to 256 accruals in 2015). In summary, the CTO has facilitated significant growth of clinical research, while implementing cost-effective processes to ensure that the research activities have scientific merit, protect safety, and maintain scientific integrity.

**CRITIQUE:** Currently, the Clinical Protocol and Data Management (CPDM) at KUCC resides within the Clinical Trials Office (CTO). The CTO provides comprehensive support services that span the life cycle of cancer clinical trials from concept through manuscript. It also ensures data integrity and compliance as well as provides education and training of CTO's staff and investigators. Over the past funding period, the CPDM has made substantial progress in broadening clinical research partnerships with communities throughout our catchment area. Three major changes have been made: 1) Incorporation

of a large private practice oncology group by the University of Kansas Health System, a group now defined as the KUCC community oncology program; 2) Expansion of the outreach network of KUCC, known as the Midwest Cancer Alliance (MCA), which is a membership fee-based network of hospitals and physician groups located across the KUCC catchment area. Many MCA centers serve as affiliate sites to cooperative group sponsored trials and investigator-initiated trials conducted by KUCC as the Primary Center; 3) Establishment of a consortium agreement with Children's Mercy incorporating their clinicians into KUCC programs. Additional positive changes are structuring data management around disease sites, introduction of a regulatory affairs FTE within the CTO, multiple site accrual, and implementation of eCRF's for investigator-initiated trials.

As a result of these changes, accruals to therapeutic trials has increased by 21% in 2015 compared to 2012 (2,097 accruals in 2012 to 2,544 accruals in 2015). Accruals to interventional investigator-initiated trials (IIT) increased by 12% (1,140 accruals in 2012 to 1,275 accruals in 2015). Of note, in 2015, institutionally sponsored IITs accounted for nearly 50% of all KUCC intervention clinical trial enrollments. Accrual to industry-sponsored interventional trials has also increased significantly (more than 160%: 96 accruals in 2012 to 256 accruals in 2015).

In parallel to this growth, the level of complexity in the management of clinical trials has also increased given the establishment of partnership with community practices and hospitals within the KUCC catchment area. Questions that remains are which processes are in place to make sure that clinical trials are offered through this network of practices and hospitals and what quality control and metrics are in place as well as safeguards to protect patients enrolled in clinical trials in locations other than the KUCC main cancer clinic/hospital. A major concern that was conveyed during the site visit was the fact that some trials conducted by groups within the center may not be under the direct oversight of the CTO and the AD for Clinical Research. In response to several questions formulated by members of the site visit team, we were left with the impression that it is possible for some cancer clinical trials to be opened and not be under the oversight of the CTO. This has the potential to create unevenness in the management and conduct of studies, and create fragmentation in the oversight processes. The center should strongly consider the value of a mandate to centralize under the CTO all cancer trials.

In summary, there has been a significant improvement in the efficiency of the CPDM in centralizing, managing, and reporting on the cancer clinical trials as well as in performing its quality control functions and training services. Additional strengths include a significant cancer center commitment and support, emphasis on institutional trials accrual and fully-deployed trials management software and training programs for staff. The leadership has been also very responsive to the critiques raised during the prior CCSG visit. Positive new initiatives such as the development of a mentored investigator initiated trial committee and a KUCC-based expansion of clinical trials into the Midwest Cancer Alliance to provide better access to the population of the catchment area are considered a strength. However, how this well-established CTO machinery will deal with the challenge of supporting clinical research in the KUCC's network of community practices and hospitals still remain to be seen.

**Personnel:** The CPDM is led by Dr. Williamson, who is an experienced clinical investigator who also has a strong track-record in clinical trials administration. As such, he is well qualified to lead the CPDM and maintain high standards for quality and integrity of clinical trials conducted at KUCC. Drs. Hobs Apell and Michelle Park assist Dr. Williamson in his leadership role at CPDM. Both are highly qualified and bring significant expertise in data management.

**Assessment:** Outstanding to excellent merit

**Budget:** The budget is recommended as requested.

## Data and Safety Monitoring

**CRITIQUE:** The current Data and Safety Monitoring Plan (DSMP) at KUCC underwent changes in 2015 as a result of the new consortium partnership between KUCC and Children's Mercy. There is now a single DSMP encompassing both institutions. During the site visit the DSMP was reviewed and detailed information was provided regarding how the members are selected or how long they serve in the committee. Similarly, there is information regarding how clinical trials are stratified by risk and how the auditing process takes place, how the audit findings are reported, and how corrective measures are implemented. Concerns that remains are related to the predominance of junior faculty (Assistant Professors) as members of the committee. In addition, because of the higher level of oversight that is required for very high risk studies, DSMP should require that the number of participants audited should be increased from the stated "no less than 10%". The DSMP describes a process for requesting corrective actions that is primarily driven by the auditor. When there are major deficiencies identified through the audit process and corrective actions are required and planned, the DSMC minutes should reflect the resolution of the corrective actions.

**Assessment:** Acceptable

**Budget:** Budget is appropriately justified and recommended for approval.

**Inclusion of Women in Clinical Research:** The proportion of female cancer cases in the catchment area is 48%. The proportion of female treated patients is 55%. Of the 491 patients accrued to interventional treatment studies, the proportion of females was 49%. Of the 2,104 patients accrued to interventional non-treatment, 76% were female and for the 932 patients accrued to observational/ ancillary the proportion of females was 66%. Overall, the accrual of women into clinical research is strong.

**Assessment:** Approval

**Inclusion of Minorities in Clinical Research:** In the previous review, while accrual rates for African Americans to therapeutic clinical trials were higher than the proportion of African Americans in the catchment area, Hispanic accrual was less than the proportion for the catchment area. This was considered to be due to several barriers including access due to travel distance, cultural factors, immigration status, and age and language issues. An additional criticism related to the relatively large number of patients and individuals whose ethnicity and/or race was unknown. As such, cancer center leadership was encouraged to identify the reasons for and also to outline specific action steps to reduce these unknown percentages.

The KUCC catchment area encompasses 105 counties in Kansas and 18 counties in Western Missouri with a diverse population including a rapidly growing Hispanic community, African American urban poor, Native American communities, immigrant Asia populations, and largely elderly rural whites. Accruals of African Americans to interventional clinical trials remain higher than the catchment area demographics (9% and 8% respectively). Similarly, higher percentages of accruals to interventional, non-treatment trials have been achieved among American Indian/Alaska Native, Black, and Hispanic due to the efforts of the Cancer Control and Population Health (CCPH) program conducting community-based trials in tobacco cessation, colorectal cancer prevention, breast cancer screening, and exercise interventions specifically targeted to these minority populations. However, still a significant lower percentage of Hispanics than the catchment area demographic (9%) are treated or enrolled in interventional treatment trials at KUCC. An explanation provided is that the Hispanic population is younger and has a much lower cancer rate than the White population in the KUCC catchment area. Supporting their claim, data from the Kansas Cancer Registry showed that the prevalence of invasive cancers from 2003-2012 was 2.4% among Hispanics compared to Whites at 91.3%. However, the

KUCC should continue to make efforts to improve this lower accrual of Hispanics to clinical trials, in lieu of the rapid growth of this particular population in their catchment area.

Regarding the prior criticism of a relatively large number of patients and individuals whose ethnicity and/or race was unknown, this issue remains in the current application given the high percentage of "Other" in the Racial Categories. An explanation provided by the KUCC leadership is that in some studies with high accrual conducted by CCPH, participants either self-reported "Other" or identified with more than one race (i.e., a breast cancer early detection study aimed at the Hispanic/Latina population with a target enrollment of over 600 participants, many of which self-reported "Other" for race).

Of note, KUCC has launched a comprehensive plan to address disparities in the catchment area and increase accrual of minorities to clinical trials. To address specific population-based needs, the MCA was created in 2007 as a network of 18 state and regional hospitals to ensure the latest clinical discoveries are extended to patients throughout the KUCC catchment area, particularly in rural and low socio-economic communities. Eleven of the 18 MCA centers have been set up as KUCC affiliate sites to accrue to cancer treatment trials. As MCA sites, these 11 hospitals utilize the KUCC CTO Clinical Research Information Service (CRIS) for data management and rely on the IRB of record (KUCC IRB or NCI Central IRB), with the KUCC CTO performing all regulatory submissions. To date, MCA members have referred 198 patients for eligibility screening to KUCC treatment trials with 14 patients enrolled on trials and nine patients being enrolled to early phase trials. KUCC Leadership should be commended for this important initiative that is impacting accruals into clinical trials.

Additional initiatives in advancing outreach and recruitment of minorities have been implemented by the CCPH research program. Examples are the collaboration between CCPH with Community Partnership for Health program, a part of the Clinical and Translational Science Award at KUMC and its extension of clinical research unit activities to a local Federally Qualified Health Center that cares for predominantly underrepresented minority populations. This initiative is facilitating recruitment of African American participants into cancer control studies. Additionally, CCPH members have held numerous community events to address barriers to research participation in minority communities.

Taken together, the KUCC should be commended for their efforts to include minorities in clinical trials. The recruitment of African Americans to clinical research remains high and several outreach initiatives like the MCA network or the use of texting for smoking prevention with Hispanic residents are shown to be of value in improving recruitment of minorities. An additional strength is that all clinical research documents are available in Spanish as well as in English. The hire of a former anthropologist, now physician-researcher with plans to engage Native American populations in Kansas City and southwest Kansas is promising. Involvement of patient advocates is a strength that could improve trust and decrease misconceptions among all minority populations, and rural populations. These accomplishments should be expanded into other minorities in their catchment area, in particular the rapidly growing Hispanic population.

#### **Assessment:** Approval

**Inclusion of Children in Clinical Research:** The inclusion of children is achieved through clinical trials performed by pediatric investigators at the Children's Mercy Hospital, a member of the KUCC consortium. In reviewing the data presented in Data Summary Table 4, there were approximately 41 interventional pediatric oncology trials available for children (30 through COG, 5 external peer reviewed, 1 institutional and 5 industry sponsored). In addition, children have access to a large portfolio of non-interventional trials (~ 21). For the index year CY15, DT4 indicates accruals of 49 enrollments into treatment trials and 163 enrollments into observational/ancillary trials. At the site visit, it was noted that of 187 new pediatric cancer cases, 37 (20%) were enrolled on a clinical trial. Plans to provide greater access to a new biorepository for pediatric specimens at Children's Mercy Hospital is a new initiative. It is important to note that there is representation from pediatric oncology members in the

review and monitoring process of the PRMS ensuring that appropriate research of scientific importance to children is considered and evaluated appropriately as well as in cancer center roles and activities as evidenced by Dr. A. Gamis co-leadership in the Drug Discovery, Delivery, and Experimental Therapeutics research program, and by funding of collaborative pediatric cancer research projects. In conclusion, the KUCC has adequate mechanisms for the inclusion and exclusion of children in clinical trials. Plans to identify barriers and to overcome them to further increase access and enrollments particularly to treatment trials should be developed.

**Assessment:** Approval

## **PROTOCOL REVIEW AND MONITORING SYSTEM**

**DESCRIPTION** (provided by applicant): The Protocol Review and Monitoring System (PRMS) oversees and ensures the scientific merit, appropriate resourcing and progress of all clinical studies at KUCC. KUCC received conditional approval of PRMS at the 2012 NCI site visit and have made multiple personnel and process changes since that time resulting in full approval in August 2016. The KUCC Clinical Trials Office (CTO) may support the Center's cancer clinical trials that are approved by the PRMS. The PRMS evaluation occurs prior to submission to the institutional review board called the Human Subjects Committee (HSC) and does not overlap with HSC responsibilities. The three components of the PRMS are the Disease Working Groups (DWG; reporting to Associate Director (AD) of Clinical Research; Carol Fabian, MD, 2016), the Executive Resourcing Committee (ERC; Stephen Williamson, MD, Chair, 2013, also reporting to AD of Clinical Research), and the Protocol Review and Monitoring Committee (PRMC; Qamar Khan, MD, Chair 2013, reporting to the Deputy Director). Although each component has a unique role, these are aligned to ensure protocols are efficiently moved through the system, receive high-quality peer-review and monitoring, and that the research portfolio is consistent with KUCC clinical research priorities. The DWGs, which meet monthly, are charged with initial review of clinical trial merit and feasibility, and with prioritizing by disease-site. Highest priority is given to investigator initiated peer-reviewed funded trial proposals. DWG co-chairs are appointed by the AD for Clinical Research. Although the DWG composition is rich in clinicians focused on treatment trials and primarily D3ET members, representatives of CPS and CCPH are also DWG members. DWGs with significant prevention and survivorship components have formal liaisons from CPS and CCPH, and this is likely to extend to CB in the future. To further increase interaction with KUCC programs and translational research, each DWG has one of their meetings per year replaced by a Clinical Translational Research Meeting focused on their area but chaired by the AD of Clinical Research with at least 1 basic or behavioral scientist presenting a relevant proposal or ongoing project along with 1-2 clinical projects. All KUCC members are invited and KUCC program leaders and ADs are expected to attend. DWGs are evaluated yearly by the AD for proportion of trials that are IIT and/or national, quality and translational nature of interventional trials, trial accrual, and national meeting presentations and publications. The ERC reviews protocol resource requirements, available funding, and alignment with KUCC research programs as defined by the Leadership Council (ADs and Program Leaders); CTO sends ERC approved studies to the PRMC for Scientific Review. The PRMC performs independent scientific merit and bio-statistical reviews, including rationale, design, statistical analysis plan, and adequacy of the data safety monitoring. The PRMC also monitors active protocols at least annually for continued scientific merit, clinical appropriateness, progress toward completion of scientific objectives, accrual status, and terminates studies as appropriate.

**CRITIQUE:** The Protocol Review and Monitoring System (PRMS) at KCUU has undergone substantial changes based on prior 'conditional approval' in 2012 and subsequent corrective actions that resulted in approval with comments in August of 2016. The PRMS is implemented through three primary mechanisms: 1) a review by the corresponding Disease Working Group (DWG) for prioritization and identifying competing trials; 2) a review and approval by the Executive Resource Committee (ERC) for resource analysis and feasibility, and 2) the Protocol Review and Monitoring Committee (PRMC) review for scientific merit, scientific progress and accrual monitoring. The PRMC is given authority over all

cancer and cancer-related clinical trials including treatment and prevention trials conducted at the consortium sites that do human subjects cancer research (including Children's Mercy Hospital & Clinics). Involvement of consortium sites conducting clinical trials in the PRMC review processes is evident. Each of these steps is well-defined in the application.

The Disease Working Groups and the Executive Resource Committee are involved in the initial process to prioritize research and disease specific needs, and review for feasibility based on established criteria. It remains unclear how these steps may add value since the center did not clearly articulate the number of proposals that are not progressing to final submission based on these processes. However, the impact of these additional committee reviews prior to PRMC does not appear, at present, to have negatively impacted the activation of studies in a timely manner.

**PRMC/New Study Reviews/Progress Reviews.** The PRMC evaluates prioritization based on established criteria and scientific merit of all cancer related clinical trials conducted at the center, as well as scientific progress and accrual. A multi-step linear process is in place that involves protocol submission and well defined criteria for the steps in the process for review of protocols. A minor concern is the lack of clarity for the involvement of the Chair/Co-Chairs in selecting reviewers with adequate expertise for the review of clinical studies. The review process also includes a biostatistician. Importantly, it is stated that conflicted members appear not involved with study deliberations or in the approval process and assures a transparent process. Studies are submitted directly to the PRMC by administrative staff and reviewers are asked to complete reviewer forms and then present and discuss at the full PRMC meeting. The Chair or Co-Chairs are assigned review of the adequacy of the data and safety monitoring of the study. Cooperative group trials or those previously reviewed by an external scientific council are reviewed by the PRMC Chair or a designee. Studies that are low risk (as defined by 45CFR46 regulations) are exempt from PRMC review. The IRB will not undertake approval of study without prior PRMC review and approvals except cooperative group trials which are reviewed in parallel. A process for resubmission of studies that are not approved is evident by the submission of responses by investigators, and final documentation of the re-assessment of the responses by PRMC reviewers. In the protocols reviewed there was evidence of adequate scientific review in that proposals with study design concerns, adequacy of the statistical plan and other concerns such as resource feasibility were appropriately questioned. Criteria for establishing review of amendments are also well delineated. The quorum requirement for the PRMC is stipulated as 75% including a biostatistician, presently requiring 11 of 15 voting members. Prior to 8/22/2016 the quorum requirement was 8 voting members. At the site visit, it was clarified that the PRMC has operationally two subcommittees allowing meetings every two weeks thus the large membership (n=31) and the newly defined quorum requirements based on voting members. A concern is that the Center Director can apparently overrule PRMC decisions. Although it was stated that this has never been the case at KUCC, this practice is not in alignment with CCSG guidelines and requires immediate correction. PRMC decisions on approval of studies or termination for accrual monitoring are final by the PRMC.

**PRMC Composition and Activity.** The PRMC is a large committee relative to the volume of protocols requiring full committee review. The membership criteria expertise is evident as reflected in the good qualified representation from the spectrum of disease/program groups and clinical trial expertise to provide in depth review of the proposals, including medical oncology, radiation oncology, surgical disciplines, biostatistics, pediatrics, and pharmaceutical sciences. Overall committee composition is diverse but there seems to be a lack of expertise in population sciences/epidemiology. The committee is well-balanced in experience with the majority of members of academic ranking as full/associate professors ensuring depth of knowledge in science and clinical trials, and other junior members contributing unique views on how the science may align to meet clinical needs of the community. There is no overlap of members in the PRMC and the DSMC. The PRMC is chaired by Dr. Qamar Khan, a medical oncologist with expertise in breast cancer, and Co-Chaired by Drs. James Coster, Bruce Kimler and Kevin Ginn. Their roles are well-defined including meeting leadership as well as administrative aspects (overseeing approvals of DSM plan reviews, expedited reviews). Over the previous funding

period, the number of studies reviewed has remained stable with approximately 47% industry trials, 35% National Group/External Peer-Reviewed, and 18% Institutional Investigator-Initiated studies. At the site visit, the center provided metrics indicating that the PRMC submission to PRMC approval is at a median of 13 days, with an overall PRMC approval to IRB approval of 88 days, respectively. Additional rigor is required in addressing the process and documentation when PRMS leaders and reviewers have conflicts of interest with matters before the committee.

**Monitoring of Ongoing Trials.** Criteria are defined for identification of underperforming studies based on an accrual monitoring policy – 50% of the stated accrual goal. During CY16 the PRMC performed continuing view on 85 trials, closed 6 trials, and placed 16 trials on probation for underaccrual. A review of updated DT4 indicates a few additional trials that are underperforming (MERCY01; 673-301; CC-5013-DLC-002). Overall, it appears that the PRMC is fulfilling its role in accrual monitoring and exerting its authority to close underperforming studies.

**Other considerations.** Six protocols from 2014-2015 were reviewed prior to the site visit for alignment with the center's stated PRMS processes. Review of these protocols suggests that the overall PRMS process is working better with improvement in some studies as result of the review process. A number of issues are noted regarding quality control of the documents and processes. The following examples are noted. For Protocol NCT02393794 (Sharma), it is noted that Dr. Q. Khan is listed as Sub PI on the project and also is a member of the PRMC, but there was no documentation of his recusal from initial approval discussion, see 12/11/2014 PRMC minutes; also Dr. Khan declared an amendment as expedited and approved as PRMC Chair, see PRMC minutes dated 7/28/2015 for Amendment version 3.0/7-15-2015. For Protocol NCT01772420 (Yacoub), there was no indication of DWG review and approval. No annual review document by PRMC or DSMC was noted. For protocol NCT02703779 (Ganguly), the study was initially disapproved because of scientific concerns but after PI addressed these concerns, it was approved. However, there was no documentation of DWG review and approval. In general, the PRMC reviewer forms contained abbreviated comments from reviewers. However, an appropriate paper trail and communication between the PRMC and the study PIs was evident. In conclusion, review of these protocols supports that the PRMC is doing an adequate review, and contributions of reviewers are documented. Although it is stated that the PRMC applies prioritization, it is unclear how this is used in practice since the majority of studies reviewed proceeded to a final approval.

The center has an appropriate distinction of the separate roles of the PRMS and the IRB processes. No cancer/cancer-related study is considered by IRB without prior PRMC clearance. Appropriate administrative support for the activities of the PRMC is provided by a dedicated administrative coordinator.

In summary, KUCC has been responsive to past critiques and has successfully implemented a reengineering of their processes although some components are still a work in progress. Positive changes included mechanisms to ensure an appropriate quorum, an increase in the seniority of the members of PRMS, and strict enforcement of accrual progress rules for study continuation or closure. The PRMS review process is fundamentally adequate, and is applied in accordance with the CCSG guidelines assuring high scientific quality of the studies performed at the center and monitoring of their progress. The PRMC has the authority to approve/ disapprove, monitor, and terminate studies and is applying these actions in a consistent way. Concerns that require additional focus include: a need for greater attention to documentation of the checks and balances of the review process including prioritization and DWG approvals, conflicts of interest, greater involvement of the Chairs/Co-Chairs in the selection process for reviewer assignments, and greater attention to content of meeting minutes to be all inclusive and thorough. Attention to these issues will be important for the PRMS as the center continues to grow and solidify a high-quality PRMS.

**Assessment:** Approval

**Budget:** Requested for efforts for the Chair as well as the administrative coordinator are appropriately justified. Recommend approval of budget as submitted.

### **EARLY PHASE CLINICAL RESEARCH SUPPORT (EPCRS)**

**DESCRIPTION** (provided by applicant): This renewal is the first time that KUCC is requesting Early Phase Clinical Research Support (EPCRS) funds and undergoing formal evaluation as a CCSG component. Although this is the first year to request CCSG support, KUCC has been investing heavily to build the infrastructure, facilities, staffing and capabilities for a successful early phase clinical research program. Stephen Williamson, MD, leads the Early Phase Clinical Research program. Long-range strategic planning is focused on short-term, pilot (pre-phase I) and phase I clinical research studies originating from KUCC scientific investigators. Preliminary data generated from these studies are typically challenged by shortages in funding, yet have great potential to serve as the foundation for later phase studies through competitive grants or industry. The Investigator-Initiated Trial Steering Committee will score and prioritize proposed studies for EPCRS funding based on whether the new compound was invented by a KUCC member, a repurposed drug with KUCC pre-clinical data and highly likely to provide preliminary data for further clinical development. In order to be considered, the proposals requesting EPCRS funds must be: 1) high priority, innovative, pilot and phase 0 or I institutional clinical studies focusing on initial testing of a candidate agent or device for the diagnosis, prevention, detection or treatment of cancer; 2) conceptualized/designed by KUCC members; and 3) of short duration (e.g., 1-2 years). If the proposal is selected for EPCR support, the Protocol Review and Monitoring System must approve the study before funding will be released.

**CRITIQUE:** This is the first request by KUCC for CCSG funding for Early Phase Clinical Research Support (EPCRS). A mechanism to identify and prioritize studies potentially eligible for EPCRS is present through the Investigator Initiated Trials Steering Committee with well-defined criteria based on new compound invented by KU, repurposed drug with KU preclinical data, preliminary data to support clinical development, and the strength of the rationale/hypothesis. Additional criteria included in the CCSG guidelines need to also be incorporated into the prioritization elements. Although KUCC previously did not request funding from CCSG for their early phase program, the applicant has provided a historical summary of their past performance in phase I trials including the notable commitment efforts of KUCC leadership to the success of an early phase program including a new 82,400 sq. ft. facility and a clear trajectory in the past 2 years of increasing enrollments into their current phase I portfolio. In addition, the availability of a GLP compliant bioanalytical laboratory is seen as a strength but the lack of a robust trajectory of the pharmacology core in IITs may significantly limit the scope of future EPCRS trials. Importantly, past concerns related to the plateauing of enrollments in the years 2013 and 2014, and long accrual timelines resulted in a restructuring of the efforts in 2015 with new leadership, more focused attention, and targeted institutional funding. New leadership in phase I efforts are seen as a positive change, but additional presence and contributions to inform the national phase I agenda portfolio will be important for the center's imprint and recognition.

The applicant now proposes CCSG support for 4 KUCC investigator-initiated phase I trials, and one trial (phase I-II) co-sponsored with the ETCTN. Two of the studies (CPX-POM and pyrimethamine) involve drugs that have been developed (CPX-POM) or repurposed (pyrimethamine) by KUCC investigators, and represent first steps in the cancer drug development process for these agents. The proposed clinical trial using mesenchymal cells represents an innovative treatment approach with high regulatory demands (IND trial) for which EPCRS seems highly appropriate and important to meet the compliance regulatory demands. However, the proposed trial involving HIPEC is less innovative as this technique is well-established in similar settings, and it remains unclear as to how this study is aligned with the goals of the Discovery, Delivery and Experimental Therapeutics research program. Overall, only 4 of the studies proposed for future support are linked to science within the programs. Enthusiasm is thus tempered by concerns on the lack of innovation in some of the proposed studies, and the



inclusion of a trial that is not aligned with CCSG guidelines since it is otherwise receiving partial NCI funding from other mechanisms (i.e., NCI-ETCTN – nivolumab/afatinib pilot study).

In conclusion, it appears that the KUCC is planning to leverage the support of the CCSG to enhance their overall plans for early phase clinical research program and to bring new ideas to the phase I activities at the center, but with concerns as noted above.

**Personnel:** The center has strong leadership for the EPCR provided by Dr. Stephen Williamson.

**Assessment:** Excellent to very good to outstanding merit

**Budget:** Support is requested for 4.2 calendar months for a TBN research nurse. The role and responsibilities of this research nurse are well articulated and aligned in support of the position. This is adequately justified and recommended for approval.

## SENIOR LEADERSHIP

**DESCRIPTION** (provided by applicant): The KUCC Senior Leadership team is made up of the Director, Deputy Director, Associate Directors and the Chief Operating Officer. This group meets every other week to evaluate cross-programmatic and multi-campus activities including pilot project programs, research symposia, seminars and conferences; review the progress of the research programs and shared resources; and discuss and make decisions related to the budget, resource allocation, membership, space, leadership appointments and strategic initiatives. This group aims to advance the cancer focus of KUCC by fostering collaborative initiatives, defining areas of strength, addressing areas of weakness and integrating basic scientists and clinicians for both the advancement of basic discoveries and training and educational efforts.

**CRITIQUE:** Dr. Roy Jensen has served as cancer center director for the past 13 years and, under his leadership, the center achieved NCI-designated status during the previous review. He is responsible for all programmatic and fiscal aspects of the KUCC across the consortium and has final decision-making power in this regard. He reports directly to the Executive Vice Chancellor of the University of Kansas Health System and the Provost and Executive Vice Chancellor of the University of Kansas-Lawrence. He also keeps the CEOs of the Stowers Institute for Medical Research and Children's Mercy abreast of cancer center activities and accomplishments. In addition to his activities across the consortium, Dr. Jensen directs a breast cancer research laboratory that is focused on the regulation and function of BRCA1/2. In 2013, Dr. Godwin was appointed Deputy Director of the KUCC. He is a well-respected translational researcher who is internationally recognized for his numerous accomplishments towards elucidating the genetic basis of GIST and ovarian and breast cancer. His active roles in SWOG, TCGA, EDNRN, and CIMBA provide strong evidence of his leadership qualities. Because of his long-standing track record in cancer genetics, predictive biomarkers, early detection, and biobanking, he also heads the Personalized Cancer Medicine Initiative at KUCC and the Biospecimen Shared Resource. It was readily apparent from the site visit that Dr. Godwin has a solid understanding of all aspects of the KUCC and is thus highly qualified to serve as Deputy Director.

Dr. Jensen has been highly successful in assembling a strong leadership team to assist him in carrying out the mission of the center. Despite the prior recommendation to reconsider the number of Associate Directors (ADs) at KUCC, all six have been retained and a seventh AD has been added. Dr. Shrikant Anant, PhD, who serves as AD for Cancer Prevention and Control, is an expert in gastrointestinal cancer, drug resistance and late stage events in tumorigenesis. His work on elucidating the mechanistic basis for the antitumor activity of natural compounds is highly respected. He has been well-funded throughout his career for his work in bladder/colon cancer, dietary chemoprevention and cancer stem cell biology. While his expertise is better aligned with the CPS research program, his ability to foster collaborations in the CCPH research program as well was evident at the site visit.

Carol Fabian, MD, transitioned from leader of the CPS research program to Associate Director of Clinical Research in 2016, following the departure of Dr. Kumar. Dr. Fabian has led numerous clinical trials at the cancer center over the years, integrated biomarkers into clinical studies, and trained many prevention researchers and clinical fellows, including the physicians in the Midwest Cancer Alliance. She will ensure that the clinical activities meet the needs of the catchment area with respect to cancer prevention, treatment and survivorship. Her clinical expertise is critical to the success of the clinical prevention efforts at KUCC; a situation that requires forward thinking. However, because the Center's focus on novel agents and phase I trials is anticipated to grow extensively, it will be important to revisit the need to extend the expertise of this Associate Director beyond the area of prevention.

Sally Maliski, PhD, RN, FAAN, now Dean of the School of Nursing at KUMS, was recruited in 2016 to fill the newly created position of Associate Director of Health Equity. By building on her experience addressing the needs of underserved Latino men with prostate cancer, she has begun to establish a comprehensive program to identify health disparities in the catchment area and develop the resources and expertise needed to address these inequities. Close collaboration with the members and leaders of the CCPH and CPS research programs and the ADs of Clinical and Translational Research will be essential to attain this goal. The delineation of responsibilities among these leaders in that regard has not been articulated clearly.

Matthew Mayo, PhD, MBA, FASA, a biostatistician, is highly qualified to serve as Associate Director of Shared Resources. He formed the Biostatistics Department at KUMC and has over 20 years of experience managing resources, establishing successful new facilities (the Biostatistics and Informatics Shared Resource) and mentoring trainees. This extensive experience is invaluable to the oversight and growth of the shared resources at KUCC. A thorough approach is being taken to gain insight from the advisory boards, shared resource directors and program members to aid in ensuring that the facilities are state-of-the-art and meeting the needs of its customers.

The Associate Director for Translational Research, Scott Weir, PharmD, PhD, is tasked with bridging the disciplines to foster inter- and intra-programmatic interactions, as well as new partnerships with industry and philanthropic groups. Based on his expertise in clinical pharmacology and drug development, it is unclear how he fosters collaborations among members of the population-based programs. It is difficult to determine the extent to which this effort has contributed to the high percentage of transdisciplinary publications within and among the four programs. He is also responsible for developing inventions with commercial entities through the Institute for Advancing Medical Innovation.

Danny Welch, PhD, Associate Director for Basic Research, is founder of the Department of Cancer Biology at KUCC. He is an accomplished investigator who has made many seminal discoveries in the area of tumor progression and metastasis. Dr. Welch continues to be highly effective in initiating and monitoring basic research activities at KUCC and identifying opportunities for the integration of basic biology across the research programs. Evidence of success is the proposed establishment of a Center for Tumor Microenvironment (COBRE funding pending) by Drs. Welch and Anant that relies on collaborative efforts from all four programs. Dr. Welch's input will be instrumental in shaping the growth and research direction of the KUCC going forward.

Accomplishments of Senior Leadership since the last review include: 1) the development of new Strategic Plans in 2013 and 2016, 2) solicitation of interdisciplinary early phase I IITs, with four awarded; 3) establishment of an IIT Steering Committee to foster hypothesis-driven IITs and increase patient accruals; 4) recruitment of an Associate Director for Health Equities; and 5) creation of the "Grant Rounds". In addition, Senior Leadership has recruited 37 investigators during the last cycle.

In summary, the Senior Leadership team has been strengthened since the last review and products of its collaborative efforts are beginning to emerge. However, the concerns noted previously regarding the high number of Associate Directors and potential overlap in their roles still remains. The impact these directors have on shaping the direction of programmatic research was not readily apparent. Future plans for growth are generic and strategies for further addressing the needs of the catchment area remain under development. A coordination of effort to identify priorities and direction to integrate the four programs was not well articulated either in the grant or at the site visit. The Senior Leadership Team will also need to focus on optimizing the interprogrammatic collaborations amongst the four research programs, on developing strategies to optimize transdisciplinary collaborations, and to ensure consistently high quality services provided by the five shared resources.

**Assessment:** Excellent merit

**Budget:** The budget is recommended as requested.

## PLANNING AND EVALUATION

**DESCRIPTION** (provided by applicant): Planning and evaluation activities play a key role in the growth and continuous improvement of The University of Kansas Cancer Center (KUCC). Multiple internal committees and the External Advisory Board (EAB) guide the planning and evaluation process under the leadership of the Director, Jensen. The EAB serves a critical role in providing external oversight of KUCC's vision, direction, leadership, research programs and supporting infrastructure. The EAB was selected by KUCC leadership to complement the basic laboratory, prevention, cancer control and population science and clinical expertise represented within KUCC research programs, shared resources and administrative components. The EAB has made numerous major recommendations such as carefully defining the roles and responsibilities of Associate Directors and Program Leaders, recruiting strong physician scientist leaders, creating a replacement plan for senior leaders, increasing multidisciplinary science initiatives, defining the KUCC catchment area and relevant research initiatives, strengthening connections with consortium partners and leveraging KUCC's drug discovery and development capabilities. Internally, KUCC utilizes many groups to regularly assess KUCC goals and activities. KUCC Leadership Council promotes scientific interactions between the basic, translational, and clinical elements of KUCC, plans the development of the research programs, leverages KUCC resources for maximum benefit, and oversees activities of KUCC programs. The Associate Directors meet to evaluate cross-programmatic and multi-campus activities including research symposia, seminars and conferences. The Associate Directors Council also endeavors to increase cancer focus for the center and oversee allocation of KUCC pilot grants. Each year the Associate Directors Council reviews the progress of the research programs, shared resources and administrative functions of KUCC. The Associate Directors Council makes final recommendations to the Director on practically all issues including budget, resource allocation, membership, space, leadership appointments and strategic direction. The Midwest Cancer Alliance, the outreach division of KUCC, helps promote collaboration of key hospitals and research institutions regarding research and educational activities and advises the Director on the impact of KUCC regionally. Planning and evaluation activities are an essential component of KUCCs continued and steady improvement over the past grant period and will continue to play an essential role in the future. KUCC's EAB and key internal advisory groups have played critical roles in this process. Overall, KUCC has effectively utilized the Planning and Evaluation component of the CCSG to put in place a vigorous and robust process of vision setting, evaluation of progress, implementation of improvements and planning for the future.

**CRITIQUE:** Under the direction of Center Director, Roy Jensen, MD, all Planning and Evaluation (P&E) activities are focused on the comprehensive strategic review of the KUCC and its scientific platform, consortium partners, research programs, shared resources, clinical research, and associated operations. This coordination involves all of the University of Kansas campuses (Kansas City, Lawrence, Wichita and Salina), the University of Kansas Health System, the Stowers Institute for

Medical Research and Children's Mercy. Furthermore, KUCC assimilates activities of the Midwest Cancer Alliance, state and local government agencies, civic leaders, nationally-recognized cancer center experts and most importantly KUCC patients in development and growth of the cancer center.

The center effectively employs external and internal advisory strategies to advance their goals and has assembled a strong External Advisory Board (EAB) with exceptional leaders in basic and population sciences, clinical and translational research, and cancer center leadership and administration. As noted in the application, the P&E component is conducted in a multi-faceted approach that includes the review and assessment by the EAB and several key internal advisory committees including the KUCC Associate Directors Council (KUCC-ADC), Leadership Council (KUCC-LC), Program Leaders Meeting, Membership Committee, Recruitment Committee, Catchment Area Committee, Shared Resource Director's Committee, Clinical/Translation Research Leadership Committee, Target Acceleration Group and Investigator-Initiated Trial Steering Committee, Internal Advisory Board, and a philanthropic Cancer Funding Partners council.

In response to the previous critique, the EAB was a strong advocate to resolve considerable issues related to inconsistent and weak planning and evaluation efforts. Throughout this project period, Dr. Jensen and the senior leadership have been receptive to the EAB's recommendations to reorganizing responsibilities related to the number of Associate Directors relative to the size of the center; alignment of resources to support multidisciplinary science initiatives with newly established program project development grants, and to strengthen clinical investigation activities, senior leadership targeted investments in early phase clinical trials and convened an early phase summit to develop solutions to low accruals. To resolve questions on the definition of the KUCC catchment area, a Catchment Area Committee was convened to meet quarterly to discuss strategies around definition, understanding the demographics, cancer incidence and mortality rates, and how to relate current research to the population. This committee is novel, yet it is not entirely clear how it operates and impacts outcomes. The center is lauded for initiating and implementing the PIVOT Committee to engage cancer patient stakeholders and interact with researchers, and given that it is new and under development, its goals and implementation are still evolving.

In response to the recommendation to lead drug development and participate in each phase of the preclinical and clinical evaluation of drugs, the senior leadership organized the Target Acceleration Group and Investigator-Initiated Steering Committee to provide a platform for basic scientists and clinicians to present IIT concepts. Although 15 IIT concepts have been presented, they are only just moving forward with no progress to date at the time of the grant submission and site visit.

Dr. Jensen has created an organizational framework around internal planning and evaluation to develop new and support ongoing key successes. The Associate Director's Council, with rotating membership evaluates inter and intra-programmatic activities such as the annual research symposium and pilot projects, seminar series and shared resources. The Leadership Council is charged to lead vision and goals, develop synergistic interactions and leverage resources at the county, state and national level. Research program leaders meet every other month to discuss strategies around engagement activities, understanding needs of research programs and shared resources, and increasing the depth of science. Although these committees meet on a regular basis, the rigor to align vision and goals and implement new initiatives is too new to measure real outcomes.

As a consortium center, KUCC has created an Internal Advisory Board to govern and advise its members on progress to date around strategic initiatives, coordinate recruitment efforts and exchange research and clinical priorities. At the time of the grant submission, this was just formalizing, and the next project period will be key to fully realize the impact of these efforts.

Strategic planning activities are evident, and various committees have been assembled to implement and evaluate the strategic plan. Since the last site visit, strategic planning has occurred in three distinct

phases providing evidence of an engaged and committed leadership. However, the written application falls short of delineating and evaluating the benchmarks of success, and whether such metrics were achieved and although strategic initiatives were discussed extensively at the site visit, the plan seems to lack a clear vision or roadmap for guiding interconnected, high priority scientific themes across research programs.

**Assessment:** Excellent merit

**Budget:** The budget is recommended as requested.

**DEVELOPMENTAL FUNDS** (including staff investigators, where appropriate)

**DESCRIPTION** (provided by applicant): The University of Kansas Cancer Center requests CCSG developmental funds to support pilot research projects, develop additional shared resources to strengthen research initiatives, support new faculty recruits and promote basic, translational and clinical science research activities. Funding pilot projects, developing shared resources, recruiting new faculty and supporting staff investigators will collectively enhance the ability of KUCC to serve the catchment area and mitigate the impact of cancer in the region. KUCC believes that these activities will enable the Cancer Center to provide the optimal environment to focus the power of precision medicine, basic science inquiry, drug discovery and development, and behavioral interventions to decrease cancer incidence, morbidity, and mortality. Furthermore, these activities will promote a cancer center culture whose highest priority is to leverage the collective state-of-the-art basic, clinical, translational and population research programs to understand cancer at a fundamental level and catalyze a comprehensive, multidisciplinary approach to defeating cancer. KUCC has demonstrated a successful track record in its investment of CCSG developmental funds and other KUCC-directed funding mechanisms and will continue to grow a strong return on investment from these funds.

**CRITIQUE:** In the current project period, the KUCC successfully invested \$2,390,189 of KUCC funds and CCSG Developmental Funds to support 73 pilot projects, with a total Return on Investment (ROI) of \$15,077,183. Use of these funds across the various mechanisms resulted in 121 peer-reviewed articles, twenty-five externally awarded grants, thirteen clinical trials, eight accruals, nine patents and one copyright. Sixteen pilot projects totaling \$478,389 from CCSG Developmental Funds were awarded to 15 cancer center members across four research programs, 62 peer-reviewed articles were published and seven external peer-reviewed grants totaling \$6.3 million were funded. Two Developing Shared Resources: Transgenic & Gene-Targeting Shared Resource (TGTSR) and Health Communications Research Shared Resource (HCRSR) were funded. In addition, KUCC supported 36 other faculty recruits.

In response to the previous review, Senior Leadership created targeted RFA's for pilot funding, utilized the Leadership Council (with ad hoc additions) as the review committee and began tracking metrics. The KUCC has demonstrated effective use of the various funding mechanisms, utilizing institutional commitment with CCSG funds to invest in strategic scientific priorities. Pilot programs include the Pilot Project Program, ACS-IRT, Program Project Development Grants, Philanthropy, Early Phase Clinical Research and Research Program Development Funds. Administration has detailed processes to support these pilot projects and there are guidelines on review criteria, collaborative outcomes and reporting expectations. The KUCC External Advisory Board recommended focusing on multi-team initiatives and three teams were funded, although the precise funding source was not clearly identified. It is also unclear whether these teams have been successful in submitting grants and/or obtaining funding. It should be noted that there are a number of published articles that are missing PMID #'s. With the improvements noted above, there remains a lack of clarity as to how these funding mechanisms align to specific scientific priorities within and across programs. Further, the current application does not address several of the concerns raised on the prior review. The Pilot Program, while important, did not appear to be guided by a strategic vision; this was a concern raised in the prior

review and remains a concern in this current application. The Pilot Program would be significantly strengthened if the applicants could highlight specific programs in need of improvement and identify future emphasis. A more strategic use of these funds to facilitate programmatic emphasis going forward would be useful. Increased input from Associate Directors and program leaders would increase the strategic vision and while input is currently on a rotating basis, dedicated leadership will result in a more sustained and collaborative vision.

Dr. Jensen has requested support for two investigators. Dr. James Calvet, PhD, is a Professor in the Department of Biochemistry and Molecular Biology at KUMC with a joint appointment in the Department of Cancer Biology, and he is a member of the Cancer Biology research program. Dr. Calvet has a long-standing interest in kidney development and signal transduction, acute and chronic kidney disease, genetic kidney disease, cancer genetics, and genomics. His early research showed the abnormal expression of proto-oncogenes in polycystic kidneys, which paved the way for further research in his lab that has uncovered many of the cellular and molecular mechanisms of renal cyst formation. While the applicants cite that renal cysts are benign tumors, the rate of neoplastic transformation is very low. Dr. Calvet is clearly a world's expert in polycystic kidney disease, with extensive funding from NIDDK, but his specific focus on cancer research is unclear. While Dr. Calvet is clearly a welcomed and valued member of KUMC, leadership was not able to clearly articulate the definable and unique role Dr. Calvet would play in helping the center achieve scientific objectives above and beyond his own research.

Dr. Joseph McGuirk, DO, is the Schutte-Speas Professor in Hematology-Oncology, the Division Director of Hematologic Malignancies and Cellular Therapeutics, and a member of the Drug Discovery, Delivery and Experimental Therapeutics research program. Dr. McGuirk has worked in the field of hematologic malignancies for over 25 years and has performed over 3000 transplant procedures. He actively serves on numerous editorial review boards, has authored/co-authored over 150 peer-reviewed publications, and serves on several committee assignments, including co-chair of the ASBMT Reimbursement Committee (2011-present), as well as acting as the ASBMT liaison for the ASCO Clinical Practice Committee. Dr. McGuirk contributes to the clinical mission of KUCC. Dr. McGuirk is instrumental in the development and implementation of the center's clinical activity, including authorship of clinical trials, accrual of patients on interventional trials, and leadership role in NCI National Clinical Trials Network studies. At the site visit, the investigators, while clearly elucidating the contribution of Dr. McGuirk to the transplant program, the strategic vision for selecting Dr. McGuirk as a staff investigator was not well articulated.

Future use of Developmental Funds. The applicant requests CCSG Developmental Funds for pilot awards, two developing shared resources: Nutrition Shared Resource and Cell Authentication and Pathogen Screening Shared Resource; faculty startup in areas such as radiation oncology, bioinformatics, phase I clinical scholar, GI/pancreas, molecular pathology, tumor micro-environment, cell cycle regulation and tumor immunology; and two staff investigators. It should be noted that the requested funds represent a small percentage of those obtained from the Kansas Bioscience Authority for new recruitments. Authority for decision-making is under the direction of the KUCC Deputy Director, with a rotating membership of leaders on the Advisory Committee, with final approval given by the KUCC Director. Enthusiasm is diminished given that the process for setting a strategic vision is not well described and a dedicated leadership committee to sustain this vision has not been realized.

In summary, the request for Developmental Funds for pilot projects, shared resources and faculty recruitment is appropriate and justified; however Developmental Funds, as cited in the prior review, would be enhanced by greater strategic planning and vision, with increased and consistent input from the Associate Directors.

The justification for support of the two staff investigators is not well described in the written document and the special role staff investigators will play to enhance the strategic vision for the cancer center was not well articulated at the site visit. Specifically, program leaders were not able to clearly describe the

definable and special role Dr. Calvet would play as a Research Staff Investigator in helping the center achieve scientific objectives above and beyond his own research and therefore is not recommended for approval.

**Assessment:** Very good merit.

**Budget:** Remove requested support for Dr. Calvet as a Research Staff Investigator (\$24,433); the remainder of the budget is recommended as requested.

## ADMINISTRATION

**DESCRIPTION** (provided by applicant): The University of Kansas Cancer Center (KUCC) administration office is the principal organizational component through which the Associate Directors, Research Program Leaders and Shared Resource Directors execute their responsibilities to Cancer Center members. The administrative office provides administrative and fiscal oversight of Cancer Center functions. These functions include grant development; human resources; communications; Cancer Center Support Grant management; Cancer Center, Clinical Trial Office and shared resource financial administration; outreach and information dissemination; and information technology. The aims of the administrative office are to:

1. Provide direction, leadership and cost effective management to allow efficient use of resources for KUCC members across campuses and throughout its consortium partners;
2. Establish and maintain consistent information organization and dissemination among research programs and shared resources to ensure aims are met;
3. Enhance research and education opportunities for KUCC members, students and post-doctoral fellows by providing strategies that encourage and facilitate collaborative, cross-disciplinary investigations across campuses and consortium partners; and
4. Impact cancer in KUCC's catchment area by leveraging consortium partners, key stakeholders, community advocates and regional leaders to develop and promote research collaboration and implementation of evidence-based cancer prevention, diagnosis, treatment and survivorship practices through community partnerships directed toward urban underserved and rural communities.

**CRITIQUE:** The University of Kansas Cancer Center (KUCC) administration office is the principal organizational component through which the Associate Directors, research program leaders, and shared resource directors execute their responsibilities to cancer center members. The administrative office provides administrative and fiscal oversight of cancer center functions which includes grant development; human resources; communications; Cancer Center Support Grant (CCSG) management; Clinical Trial Office and shared resource financial administration; outreach and information dissemination; and information technology.

The KUCC administrative office is led by the Associate Director for Administration, Teresa J. Christenson, who reports directly to the Center Director, Roy Jensen. Ms. Christenson has organized the administrative office to efficiently facilitate and implement the Director's vision and support a cancer-focused culture that fosters collaboration and productivity among cancer center members. In response to the previous review, accomplishments of the office include the establishment of a central database for KUCC membership and associated metrics of productivity; implementation of the iLabs software for managing shared resources across the center; the recruitment of 37 new faculty members; and the establishment of a Grants Development Office. The Assistant Director for Administration, Susan Harp, oversees this portfolio, which includes pilot project management such as solicitation, review, post-award support to faculty and tracking of outcomes/successes; and pre-award grant submissions across the consortium, which has been highly successful in submitting over 400 grants since its inception in 2012. Anna Nguyen, Assistant Director of Finance, manages budgeting,

accounting and financial management of all funds, including philanthropic gifts, clinical trials, and shared resources.

KUCC provides financial support for five shared resources (Biospecimen, Biostatistics & Informatics, Transgenic & Gene-Targeting, Clinical Pharmacology and Lead Development & Optimization) and the three remaining facilities are institutionally run with partial financial support from KUCC. The Associate Director for Shared Resources and Assistant Director for Administration, Lisa Harlan-Williams, meet with shared resource directors and assistant directors quarterly to identify appropriate utilization metrics and tracking mechanisms, prevent duplication of aims and services and conduct an annual survey to measure satisfaction, needs for new services, and relevance related to science.

The administrative staff supported 37 faculty recruitments in collaboration with departments and consortium centers over the course of the project period. The Recruitment Committee manages and makes recommendations for appointments and promotions. Dr. Jensen collaborates with the requisite consortium partner to co-recruit and invest in recruits. It appears that all recruitment and retention policies are appropriate, although there is no definitive information regarding policies at all sites.

A unique aspect of the KUCC Administration is the Midwest Cancer Alliance (MCA), a membership fee-based network of hospitals and physician groups located in KUCC's catchment area with the primary purpose of leveraging unique regional resources to promote and translate the latest evidence-based clinical and community health practices for patients close to their homes. The MCA, led by Executive Director and Assistant Director for Community Outreach, Dr. Hope Krebill, collaborates with local organizations to enhance their research infrastructure and to proactively execute cancer prevention and control strategies to decrease the burden of cancer in the catchment area. Technologies such as tele-video are used to connect researchers with communities. Another tool to increase patient engagement with research, MCA has launched PIVOT (Patient and Investigator Voices Organizing Together), an evolving community of patient advocates learning and working with academic research stakeholders to enhance research to more effectively address patients' needs and desired outcomes. Finally, MCA members and Kansas Patients and Providers Engaged in Prevention Research (KPPEPR) identify, enroll and/or refer participants to clinical trials. KUCC leverages in-kind research support from MCA members who provide 12 FTEs in research staffing as well as in-kind site-investigator support. Critical to understanding its overall impact, specific metrics aligned with needs to serve the catchment area requires further development as this has not yet been fully defined nor reported.

An appropriate communication framework has been established with the geographically distinct partners within the consortium. A strong relationship with KUSM continues to be fostered by the integral role of many cancer center members at the university. Recruitment of KUCC members at Stowers and Children's Mercy is accomplished as a collaborative effort. The strategies to promote KUCC and the value it brings to the area have been well-delineated, and it is recommended in the next project period to tailor communications to the underserved and minority populations in the catchment area – those who are in most need of the services.

Overall, the administration team continues to make progress with effective oversight and management of an extensive research infrastructure to run the KUCC, including members across the consortium. There is sufficient fiscal and programmatic oversight for finances, shared resources, consortium partners, faculty recruitment, informatics, technology transfer, compliance, contracting and support to research programs and shared resource directors. Staff rely on and represent the center at the institutional level, including the research institutes for each of the consortium members. The Associate Director of Administration and her assistant provide support to the Associate Directors and Program Leaders to aid them in achieving their goals, including grant submissions, budgets, and the organization of various meetings. While the support is appropriate, the programs are expected to only meet twice a year with smaller group meets at least once a quarter. In addition, each program is expected to host three guest speakers per year. The schedule could be further expanded to help guide



and foster meaningful collaborative interactions, particularly at a center that is in an important phase of early growth. Enthusiasm is somewhat diminished, however, through a lack of rigor around communications and visualization of strategic planning efforts, and it was difficult to follow the thread of research program and leadership activities given the inadequate documentation in meeting minutes.

Future plans are limited to continuing to enhance data integration across the consortium and facilitating patient engagement through the interaction of patient advocates with research investigators (PIVOT).

**Personnel:** Administrative staff are well qualified to oversee, manage and support all aspects of an NCI-designated cancer center.

**Assessment:** Excellent merit

**Budget:** The budget is recommended as requested.

## ESSENTIAL CHARACTERISTICS

**Physical Space:** (Outstanding merit) The KUCC facilities were rated highly at the time of their previous CCSG review, and during this funding period, there has been continued growth in terms of dedicated research space, clinical space, clinical research space, and total overall space. The KUCC has 170,000 sq. ft. in the Kansas Masonic Cancer Research Institute (KMCRI) on the University of Kansas Medical Center (KUMC) main campus. The final phase of renovation of this space was completed in 2012, and this building contains wet lab bench space, an administrative area for offices, and selected shared resources. The KMCRI allowed the KUCC to more effectively cluster investigators working in related scientific areas and significantly enhanced intra- and inter-programmatic collaborations. In addition to the space in the KMCRI, there is an additional 50,000 sq. ft. of laboratory and office space on the KUMC main campus. An additional 33,000 sq. ft. of space is provided to the four KUCC shared resources, divided between the KUMC, KUH and KU Lawrence campuses, and the KU Clinical Research Center. Administrative space, now totaling 6000 sq. ft., is located in the Kansas Masonic Cancer Research Institute (KMCRI) on the main KUMC campus. This space provides administrative and fiscal oversight of all cancer center functions. Other shared resources are available to KUCC investigators at the KUMC including DNA sequencing, RNA arrays, confocal and electron microscopy, laboratory animal resources, flow cytometry, mass spectrometry, proteomics, and bioinformatics.

A total of 38 KUCC members are located at KU-Lawrence, and they are housed in one of three different buildings that are in close proximity to one another. In the spring of 2016, construction of a new, state-of-the-art biomedical research facility was begun, and this facility will significantly expand the core of basic cancer investigators located on the KU-Lawrence campus. The University of Kansas School of Pharmacy is located on the KU-Lawrence West campus and a 5-minute drive from the main KU-Lawrence campus and is housed in a 110,000 sq. ft. facility of which approximately half (55,000 sq. ft.) is dedicated to cancer-relevant research. This School of Pharmacy facility is home to the High Throughput Screening and Biotechnology Innovation and Optimization Center, which forms part of the KUCC Lead Development Optimization Shared Resource. Approximately 1,500 sq. ft. is dedicated to cancer research on the Wichita campus in the Kansas Health Foundation for Primary Care building, and the focus in this facility is on clinical trials as well as prevention and survivorship research.

The Stowers Institute for Medical Research includes 880,000 sq. ft. of laboratory and office space, and houses 24 independent research programs with a total of 500 scientists and staff. Eleven KUCC members are housed at Stowers Institute, which also has 13 shared resources, including bioinformatics, proteomics, and imaging, to which KUCC members have access.

Substantial clinical facilities are available for clinical care and clinical cancer research although there is no single site on the KUMC campus that houses these clinically oriented services. Inpatient cancer

services include 55 newly renovated beds located in 26,334 sq. ft. on the KUMC main campus. Radiation oncology occupies 21,000 sq. ft., and this is also located on the KUMC main campus. All of the center's outpatient cancer services are housed in the 62,500 sq. ft. Richard and Annette Bloch Cancer Care Pavilion, which is in Westwood, about 5 min from the KUMC main campus. KUCC clinicians occupy an additional 8,300 sq. ft. of office space in the east wing of the Westwood facility, and research nurses and data managers of the Clinical Trials Office occupy 1,340 sq. ft. of space in the Bloch Cancer Care Pavilion. Geographically separate buildings are dedicated to breast prevention (4,230 sq. ft.), breast cancer survivorship (1,425 sq. ft.), and stem cell transplantation (7,500 sq. ft.). In 2015, the building of a 12-story 550,000 sq. ft. bed tower for the hospital was initiated. This facility will house 12 new operating rooms and 132 patient beds, and this space will be mainly focused on surgical oncology and ENT. At the site visit, it was stated that about 2/3'rds of this new facility will be cancer-focused.

The KUCC Clinical Research Center is housed in a 82,000 sq. ft. building, and this facility houses many of the center's clinical and translational research activities. This building is located 5 min from the main outpatient clinical facility in Westwood and 10 min from the main KUMC campus. The Clinical Pharmacology Shared Resource, the administrative operations of the Midwest Cancer Alliance, and the KUCC Clinical Trials Office are housed in this facility. Of note, the KUCC Clinical Research Center is supported by \$5 million each year from the county sales tax. The Pediatric Clinical Research Unit is located in Children's Mercy Hall Tower, which is a 5,000 sq. ft. state-of-the-art facility dedicated to the support of clinical and translational research. This unit supports the clinical research activities of the Experimental Therapeutics in Pediatric Cancer Program.

One concern expressed by the site visit team related to the fact that the KUCC research, clinical, shared resources, and administrative facilities are geographically fragmented and dispersed among at least five different campuses. It will be particularly important for the Center Director and Senior Leadership to continue to focus on developing effective strategies to address the ongoing communication and transportation challenges to facilitate collaborative interactions. This is a critically important and relevant issue given the expressed priority of the center on developing investigator-initiated clinical trials that directly arise from KUCC science and/or discoveries as the ideal situation would be for the basic and translational investigators to be in close proximity with their clinical investigator counterparts.

**Organizational Capabilities:** (Excellent merit) Four research programs and five shared resources have been created and are proposed by the KUCC. Membership criteria have been well defined; both full and associate members participate actively in cancer research and participate in KUCC activities. Full members have effort listed on peer-reviewed grants, whereas associate members do not. Applications for full or associate membership are reviewed annually with the Center Director having final decision making authority regarding membership and program assignment.

Center Leadership includes one Deputy Director, seven Associate Directors, eight Program Leaders, and Shared Resource Directors. While each Associate Director is accomplished in their own respective fields of research, concerns as had been previously discussed at the previous CCSG review, still exist to the relatively high number of Associate Directors and the potential overlap of their roles and responsibilities. There was limited evidence for their effective coordination of efforts across/amongst the Associate Directors and their interconnectivity was limited. Two of the Associate Directors are new to the center and the Deputy Director, Dr. Godwin, while not new to the center, is new to his leadership role, so continuous reassessment and monitoring of how these leaders will add to the team and interact with the Center Director is warranted. In the executive session with the Director, it was also not well-articulated as to the specific criteria used in the selection of the Associate Directors.

Internal and External Advisory Boards are in place. A strong External Advisory Board meets annually; its several members are highly experienced and knowledgeable regarding the CCSG application and

P30 review process, having served as current or former directors of established NCI-designated centers. Their input and advice has played an important role in the continued success of the center. Advice to the KUCC Director also comes from four internal advisory groups that meet regularly and these groups include a leadership council, Associate Directors group, Program Leaders group, and the Shared Resource Directors.

KUCC's catchment area includes the entire state of Kansas and 18 counties in Western Missouri. Of the 123 counties, 96 are either rural or frontier counties, and they include a significant underserved population. The KUCC has established a Catchment Area Committee to discuss strategies to refine the KUCC catchment area, understand the patient demographics, and identify unmet needs of the population. The center has done an impressive job in characterizing its catchment area, made effective use of stakeholder engagement strategies to guide research, and has been investigating solutions that specifically address catchment area cancer issues.

The KUCC sponsors a wide range of cancer education seminars and conferences. Of note, the center recently established two new cancer focused graduate programs in Cancer Biology and Biostatistics. KUCC is also a member of the Cancer Biology Training Consortium (CABTRAC), which is dedicated to the mission of training the next generation of cancer researchers, and Dr. Welch, the KUCC Associate Director of Basic Science, currently serves as president of this group. Drs. Welch and Jensen worked with CABTRAC and other NCI-designated cancer centers to publish the essential components of cancer education and in so doing, they played an instrumental role in codifying the cancer education standards for NCI-designated cancer centers. In 2012, Drs. Welch and Anant established "Grant Rounds" to facilitate the development of grant ideas from cancer center faculty, but with a specific focus on junior faculty and post-doctoral fellows. This group meets on a weekly basis to discuss and provide feedback on a specific grant proposal under development. This program has been successful in helping faculty members to have their grants be awarded by NIH/NCI, ACS, and DOD, as well as by several prestigious foundations, including Komen and V Foundation. At the site visit, the Director presented data that the funding of training awards has doubled from \$1.3 million to \$3 million. However, it was not clear from this discussion as to the number of cancer-focused T32 training grants that have been obtained through their training and education initiatives. In addition, there was no mention of center activities focused on training/education of high school students and undergraduate students.

KUCC has a consortium agreement with the Stowers Institute for Medical Research, which was renewed in 2015, and most recently signed an agreement with Children's Mercy. The consortium arrangement is clearly described in the application and states that investigators at Stowers and Children's Mercy engaged in cancer research are eligible to be KUCC members, have access to KUCC shared resources, and serve in leadership roles. In addition, KUCC members who are collaborating with Stowers investigators have access to Stowers core technology centers and facilities. Communication between these two consortium sites is facilitated by e-mail, teleconferencing, and videoconferencing. Mechanisms to resolve differences, although mentioned as existing in the agreements, were not included in the application nor discussed at the site visit. Partnership with the UK-Lawrence campus provides access to medicinal chemistry and drug development at the School of Pharmacy. A consortium agreement with the KU Hospital provides \$5 million of annual support and a partnership with the Midwest Cancer Alliance that supports a network of medical oncologists throughout eastern Kansas and western Missouri. As a Consortium Center, KUCC has created an Internal Advisory Board that includes all of the key players of the consortium to govern and advise its members on progress around strategic initiatives, coordinate recruitment efforts, and exchange research and clinical priorities. At the time of the site visit, this internal committee was just being formalized, and the next funding period will be key to fully realize the impact of these planning efforts.

Overall, the organizational capabilities of the center have facilitated and added value to the cancer mission as well as fostered scientific interactions and joint initiatives among external partners. However, despite the numerous internal committees, the rigor to directly align vision and goals and implement

new initiatives is too new to measure. In fact, the individual research programs may need to consistently meet monthly at the very least to collaboratively work together to fully realize the center's scientific vision and operationalize the strategic plan.

Strategic planning activities are evident, and various committees have been assembled to implement and evaluate the strategic plan. Since the last site visit, strategic planning has occurred in three distinct phases providing evidence of an engaged and committed leadership. However, the written application falls short of clearly delineating and evaluating the benchmarks of success, and whether such metrics were achieved. Although strategic initiatives were discussed extensively at the site visit, the overall strategic plan seems to lack a clear roadmap and sharp vision for guiding interconnected, high priority scientific themes across research programs and for providing the critical research infrastructure that effectively supports center-wide themes.

**Transdisciplinary Collaboration and Coordination:** (Excellent merit) The KUCC has developed several different approaches to promote interactions among center members and to foster transdisciplinary collaborations including the Pilot Projects Program, Program Project Development Grants, Research Program Meetings and Developmental Funds, Disease Working Groups, Molecular Tumor Board, the Target Acceleration Group, and the Investigator-Initiated Trial Steering Committee. In addition, multiple symposia, roundtables conferences, speakers' series, and clinical working groups have been established to encourage transdisciplinary collaboration. At the time of the previous CCSG review, the relative percentage of inter-programmatic collaborations was felt to be modest with room for improvement. As updated at the site visit, the overall inter-programmatic publications have increased from 10% in CY 2011 to 14% in CY 2016. Perhaps more importantly was the significant increase in the intensity of the interactome figures from 2011 to 2016, which nicely highlighted the growth and maturation of the programmatic interactions.

At the time of the site visit, 24 pilot projects totaling \$758,389 obtained 14 peer-reviewed grant awards of \$9.7 million (an ROI of 12.9-fold). KUCC developed a Program Project Development Grants Program to foster and facilitate collaborative projects that are focused on P01 grants, COBREs, SPOREs, or other team science grants. In 2014, three teams were selected to receive funding of \$50,000 for each project for year one and then received an additional \$50,000 for a second year. Each of these teams were multi-investigator teams with members coming from at least two of the KUCC Research Programs. The American Cancer Society provides IRG Awards with matching funds for the KUCC. The Institute for Advancing Medical Innovation (IAMI) has provided \$1.3 million in awards to KUCC investigators. However, it is not clear that specific requests for applications have encouraged multiple investigators from multiple programs and disciplines to apply for somewhat larger awards working toward a P01 or other multi-investigator award.

As updated at the site visit, in 2016, there were 30 active multi-PI grants, which represents a significant increase from the 23 multi-PI grants in 2012. Although not presented in the written application, Dr. Jensen showed data at the site visit that highlighted several team science grants, including four P30 grants, four P20 grants, 4 PCORIs, one P01, two U01s, one U10, 1 U54, and one U58. While progress has been made over the past five years, there is a need to take greater advantage of the opportunities afforded for successful collaborative interactions between the multidisciplinary clinical teams and the various KUCC research programs.

One concern was that there was limited discussion in the application and at the site visit regarding the specific roles of medical oncology, surgical oncology and radiation oncology in multidisciplinary patient care and in the clinical and translational research mission. Greater emphasis needs to be placed on enhanced multidisciplinary clinical care and the integration of these multidisciplinary disease teams with the various KUCC research programs with the goal of developing investigator-initiated clinical trials.

Another minor concern that has been raised previously in this report on research program evaluations relates to the missed opportunities for the two population science programs to interact with each other as well as with the other two KUCC research programs.

**Cancer Focus:** (Outstanding merit) Over the past 5-year funding period, the center has experienced an increase in membership from 146 in CY 2011 to 183 in CY 2016, and as updated at the site visit, this has translated to an increase in NCI funding, going from \$11.61 million in CY 2011 to \$12.85 million in CY 2016, and total cancer-related peer-reviewed funding has increased from \$46.45 million in CY 2011 to \$54 million in CY 2016. Patient accrual to treatment clinical studies at the center has increased from 242 in 2012 to 390 in 2016. The number of cancer-focused manuscripts has increased over the 5-year funding period where KUCC members published 1,741 publications (435/yr.), which is increased from the period of 2006-2011 where KUCC members published 1,311 cancer-related manuscripts (218/yr.). Over the 5-year funding period, there has been recruitment of 37 faculty members, all of whom are cancer-focused, and these recruits include several high profile senior basic and clinical cancer investigators as well as investigators focused on health disparities and diversity. In summary, there has been an increase in the breadth, depth and significance of the cancer-focused research. However, there are missed opportunities for cancer-focused research in the catchment area, especially as it relates to the African American and Native American populations, missed opportunities for the Cancer Biology research program to work with the Drug Discovery, Delivery, and Experimental Therapeutics research program to translate their scientific discoveries to investigator-initiated clinical trials, and for continued focus on enhancing inter-programmatic collaborative interactions across the 4 KUCC research programs.

**Institutional Commitment:** (Exceptional merit) Institutional commitment for the KUCC is truly exceptional. Support by the KUMC in 2010 was \$38.7 million and over \$140.5 million has been provided since FY2005. The KUH has recently committed \$3.6 million annually to the KUCC and since 2003 has provided more than \$76 million, if construction and renovation costs are included. Since Dr. Jensen assumed the role of KUCC Director in 2004, over \$200 million in philanthropy has been raised. There has also been a focused effort to increase the endowed funds available to KUCC. In 2004, KUCC had an endowment of less than \$11 million, and the current endowment is \$36.2 million with an additional \$32.5 million that has been endowed to 24 cancer-focused professorships. As presented at the site visit, a total of \$453 million has been provided to the center through institutional, state, and regional commitment. In addition, Children's Mercy has recently committed 4 endowed chairs in pediatric cancer to KUCC.

The community has been exceptionally supportive of the KUCC with the local Johnson County adopting a 1/8<sup>th</sup> cent sales tax, producing a perpetual income of >\$5 million each year to support the new Clinical Research Center and clinical trials research. Of note, this sales tax has a "no sunset" clause. Since 2007, the state of Kansas has provided nearly \$49 million to KUCC, and the Kansas State Legislature contributes \$5 million each year to KUCC. KUCC has received \$1.24 million from the Kansas Breast Cancer Research & Outreach License Plate that was signed into law in 2007, and the center has also received \$675,242 from the Breast Cancer Income Tax Check-off since 2008 to support pilot programs in breast cancer research. Since 2004, philanthropic funds over \$194 million were raised, and these funds are matched 1:1 by the Kansas Bioscience Authority.

A well-defined succession plan is in place in the event that the Center Director is unable to fulfill his responsibilities. The Deputy Director would serve as interim Director and principal investigator of the CCSG, until a permanent Director is named following a national search.

The presence of high-ranking dignitaries of the institution, including the KU Chancellor, the Executive Dean of the KUMC School of Medicine, Executive Vice-Chancellor KUMC, President and CEO of Stower's Institute, and the Executive Director of the Children's Institute of Children's Mercy, and the

continued presence of these leaders during the entire site visit were further evidence of the exceptionally strong institutional support for the KUCC.

**Center Director:** (Outstanding merit) Dr. Jensen is an outstanding physician-scientist who is well qualified to serve as Director. He is a leading expert in the molecular and cellular biology of breast cancer, with particular focus on the role of BRCA1 and its critical role as a tumor suppressor in the repair of damaged DNA and other important cellular functions. He is an active member of the KUCC Cancer Prevention and Survivorship Program and the Breast Disease Working Group. His research has been funded by the NIH/NCI, ACS, Susan Komen Foundation, and the Department of Defense. In 2004, he was recruited from the Vanderbilt-Ingram Comprehensive Cancer Center to be the founding Director of KUCC. Prior to that time, he had worked closely with Dr. Harold Moses, the founding Director of the Vanderbilt-Ingram Cancer Center, on helping that center achieve NCI-designation, and for 10 years, he served as Director of the Human Tissue Acquisition and Pathology Shared Resources and was a key member of the Breast Cancer Research Program. He presently serves on NCI Subcommittee A, the committee overseeing the review of NCI Cancer Centers; is an advisory board member of two non-NCI cancer centers, University of Oklahoma Stephenson Cancer Center, which he chairs, and the Georgia Cancer Center; and was elected in the summer of 2016 as the Vice-President/President-Elect of the Association of American Cancer Institute, which is made up of nearly 100 leading cancer research centers in the U.S. He also serves on the editorial boards of various cancer-related journals.

Organizationally, the cancer center is recognized as a formal center of the Kansas University Medical Center (KUMC), with the requisite space, positions and resources to enable its stability and success, and the Director functions in the role equivalent to Department Chair. In this regard, he attends the monthly Basic Science Chair/Center and Institute Directors meeting organized by the KUMC Executive Dean. The Director controls more than 400,000 sq. ft. of space for research, shared resources, administration, and clinical operations. He allocates an annual budget of \$15 million and has direct control over all cancer-related philanthropic funds and fundraising activities. Working closely with the department chairs, the Center Director recruits faculty members. He has full authority to appoint new KUCC members, approves their program assignments, and can discontinue existing members. He controls operation of all of the KUCC shared resources. The KUCC Director has direct reporting lines to KUMC Executive Vice Chancellor/Medical School Executive Dean, the KU Provost, and a "dotted line" relationship with the KU Hospital CEO. The KUCC Physician-in-Chief has oversight of all clinical inpatient and outpatient facilities, reporting directly to the KUCC Director and the KU Hospital CEO. This position, along with the Oncology Service Line Committee, ensures access to clinical inpatient and outpatient facilities needed for the conduct of clinical trials.

Dr. Jensen's in-depth knowledge of the cancer center was evident throughout the site visit. He is an extremely strong advocate for the center and for the critical importance of cancer research at the University of Kansas. Dr. Jensen is exceptionally well-qualified to be cancer center Director and the center's chief advocate. It is clear that he has the energy and commitment to continue to succeed in this role, and he has the appropriate resources and authority to serve in this position. He has made a 50% commitment of time and is also committing time for his own research program in BRCA regulation for breast chemoprevention, which is entirely appropriate to maintain his skills and credibility as a physician-scientist. However, there remain concerns relating to the overall scientific quality of the center, the interaction of population science with the other KUCC research programs, the integration of multidisciplinary-based clinical oncology with the clinical research efforts, the unevenness of the shared resources, and his strategic plans for the future. While he has succeeded in recruiting highly qualified senior leaders, it is not yet clear whether the senior leadership team is optimally configured and their full potential has yet to be realized.

In summary, Dr. Jensen is extremely well-qualified to be cancer center Director, and he is to be credited with being the main driving force for the significant achievements and progress made by this

center. His knowledge, understanding, and leadership skills are a great advantage to the KUCC as it continues to evolve in an upward trajectory as an NCI-designated cancer center.

## BUDGET RECOMMENDATION

The site visit team recommended a total reduction of \$ 24,433 from the total direct costs of the CCSG. In total direct costs, the current budget is \$ 1,400, 000 (from Data Table 5); requested budget is \$ 1, 551,221 (from Categories Budget Summaries); and the recommended budget is \$ 1,526,788. The site visit team recommends that the budget be evaluated by the NCI Special Emphasis Panel, as needed.

The budget tables that follow are provided as informational item only. The official recommendation for support is provided under the heading, RECOMMENDED BUDGET/NCI SPECIAL EMPHASIS PANEL, after the NCI Special Emphasis Panel (parent committee) meeting.

## COMMITTEE BUDGET RECOMMENDATIONS/SITE VISIT TEAM'S RECOMMENDATIONS

The table below summarizes the estimated effects on the original amounts requested by the applicant of implementing the budgetary changes recommended by the reviewers and summarized in the Budget section(s) of the Summary Statement above. The table below does not take into account either additional information that may be provided by the applicants in response to administrative requests for updates or additional administrative changes that may be required to meet Institute funding policies, either or both of which may result in a significantly different final recommended budget figure. Consequently, applicants should make no inferences from these figures about what the final budget might be should an award be possible.

	First Year Requested Direct Costs \$	First Year Recommended Direct Costs \$
SENIOR LEADERSHIP	347,489	347,489
PROGRAM LEADERSHIP (including other budget categories, where appropriate)	159,650	159,650
PLANNING AND EVALUATION	15,000	15,000
DEVELOPMENTAL FUNDS (including staff investigators)	324,880	300,447
ADMINISTRATION	29,971	29,971
Biospecimen Shared Resource	99,601	99,601
Biostatistics & Informatics Shared Resource	179,090	179,090
Clinical Pharmacology Shared Resource	75,908	75,908
Lead Development & Optimization Shared Resource	84,436	84,436
Transgenic & Gene-Targeting Shared Resource	60,496	60,496
CLINICAL PROTOCOL & DATA MANAGEMENT (CPDM)/ CLINICAL TRIALS OFFICE & DATA AND SAFETY MONITORING		
Clinical Protocol and Data Management	99,879	99,879
Data and Safety Monitoring		

PROTOCOL REVIEW AND MONITORING SYSTEM	37,122	37,122
EARLY PHASE CLINICAL RESEARCH SUPPORT (EPCRS)	37,699	37,699



**SUMMARY OF RECOMMENDED BUDGETS/SITE VISIT TEAM'S RECOMMENDATIONS**

Budget Categories	YEAR 06 \$	YEAR 07 \$	YEAR 08 \$	YEAR 09 \$	YEAR 10 \$
Salary, Wages and Fringe Benefits	1,202,109	1,202,109	1,202,109	1,202,109	1,202,109
Equipment	0	0	0	0	0
Travel	6,000	6,000	6,000	6,000	6,000
Participant/Trainee Support Costs	0	0	0	0	0
Other Direct Costs (excluding Consortium)	285,014	285,014	285,014	285,014	285,014
Consortium Costs	33,665	33,665	33,665	33,665	33,665
Direct Costs	1,526,788	1,526,788	1,526,788	1,526,788	1,526,788
Indirect Costs	803,102	803,102	803,102	803,102	803,102
Total Costs	2,329,890	2,329,890	2,329,890	2,329,890	2,329,890

## MEETING ROSTER

National Cancer Institute Special Emphasis Panel  
NATIONAL CANCER INSTITUTE  
ZCA1 RTRB-C (E1)  
Dr. Roy Jensen (2 P30 CA168524-06)  
Agenda Seq Num - 00316599  
02/08/2017 - 02/10/2017

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## MEETING ROSTER

National Cancer Institute Special Emphasis Panel  
NATIONAL CANCER INSTITUTE  
ZCA1 RTRB-C (E1)  
Dr. Roy Jensen (2 P30 CA168524-06)  
Agenda Seq Num - 00316599  
02/08/2017 - 02/10/2017

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Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.