SITE VISIT REVIEW REPORT

APPLICATION NUMBER:	**2 P30 CA062203-24**
PRINCIPAL INVESTIGATOR:	**DR. RICHARD VAN ETTEN**
APPLICATION TITLE:	**CANCER CENTER SUPPORT GRANT**
APPLICANT INSTITUTION:	**UNIVERSITY OF CALIFORNIA, IRVINE**
REVIEW GROUP:	**CANCER CENTER SUPPORT GRANT (P30) SPECIAL EMPHASIS PANEL**
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RESUME AND SUMMARY OF DISCUSSION: In this renewal application from the Chao Family Comprehensive Cancer Center (CFCCC) of the University of California, Irvine (UCI) the overall goals are to generate and disseminate new knowledge about the causes, prevention, and treatment of cancer, to train of the next generation of cancer providers and caregivers, and to alleviate the overall burden of cancer in the catchment area and beyond. The CFCCC is a matrix center and the only academic cancer center based in Orange County, California, the sixth most populous county in the United States with over 3.2 million residents who embody substantial socioeconomic and racial/ethnic diversity. Support is requested for three research programs; Shared Resource Management and seven shared resources; Cancer Research Training and Education Coordination; Community Outreach and Engagement; Clinical Protocol and Data Management; the Protocol Review and Monitoring System; Developmental Funds; Leadership, Planning and Evaluation; and Cancer Center Administration.

Under the capable leadership of the Center Director, Dr. Richard Van Etten, the CFCCC continues to be highly productive in cancer research relevant to its catchment area and the nation. Major strengths of this center include the superbly qualified Center Director and senior leadership, the highly collaborative and product center members, innovative research producing significant discoveries across the spectrum of cancer research that are being translated into clinical applications, and the strong research environment and institutional support at the UCI. There is substantial breadth, depth, and significance of the cancer-related research within the individual research programs, publications, and peer-reviewed research support. Center members continue to engage in innovative research that capitalizes on UCI's strengths including synthetic chemistry, bioengineering, and physics, with the goal of increasing the translation of these basic science discoveries into the clinic. Dr. Van Etten has the led the recruitment of many talented new faculty and center leaders as well as development of a detailed strategic plan to guide the growth CFCCC. Overall peer reviewed grant support has increased, the research programs have been reorganized and strengthened, and substantial new laboratory and clinical space has been added in the last five years. In addition, the center benefits from the input of eminently qualified internal and external advisors to guide strategic planning, including the Community Advisory Board that is vital to community outreach.

The three research programs are each interactive, collaborative, and productive with highly qualified Program Leaders and members, including many new recruits. The Biotechnology, Imaging and Drug Development Program (BIDD), rated Outstanding merit, is hub for the development of innovative new therapeutics and devices that have high potential for translation into early stage clinical trials in the program. Members have unique areas of expertise in drug discovery, imaging, radiotherapy and bioengineering. Plans for future development of the program are well defined to ensure future growth in translational research. However, integration of clinical activities across the program and the Disease Oriented Teams is not adequately addressed. The Systems, Pathways and Targets Program (SPT), rated Excellent to Outstanding merit, is the driver of innovative basic cancer research at the center, particularly in systems biology and cancer cell metabolism. The program communicates a clear goal of developing multi-investigator teams of clinical and basic science investigators to accelerate preclinical translation, but this process for translation of a promising pipeline of basic discoveries has not yet been fully realized. In addition, the peer reviewed funding base appears relatively low for this size of a program. The Cancer Control Program (CC), rated Excellent to Very Good merit, has benefited from strong recent strategic investments by the CFCCC in member recruitment and pilot project funding. The program has supported multiple successful early career investigators. Although there are promising examples of cancer control and population research in the program, several projects have yet to fully mature and significantly impact cancer burden in the catchment area. In addition, the rates of intra- and inter- programmatic publications and engagement in team science appear relatively modest. However, the program clearly addresses many important cancers of concern within the catchment area and attention to critical caner health disparities are likely to grow with the newly recruited members.

The research programs are supported by seven very cost effective and state-of-the-art shared resources that are highly responsive to member needs. Shared Resource Management, rated Excellent

merit, provides effective administrative oversight of the current and developing shared resources to facilitate high-impact cancer research across the programs. Six of the seven CFCCC Shared Resources are jointly managed with the institution and the CFCCC effectively leverages both informal and formal oversight and management mechanisms to provide services to center members. The shared resources are rated as follows: the Transgenic Mouse Facility (TMF) is rated Outstanding merit ; the Optical Biology Core (OBC) is rated Exceptional merit; the Genomics High Throughput Facility (GHTF) is rated Excellent to Very Good merit; the In Vivo Functional Onco-Imaging (IVFOI) is rated Excellent to Outstanding merit; the Experimental Tissue Resource (ETR) is rated Excellent merit; the Biostatistics Shared Resource (BSR) is rated Excellent to Outstanding merit; and the Biobehavioral Shared Resource (BBSR) is rated Very Good to Excellent merit. These shared resources clearly add substantial value to the research conducted by center members.

Cancer Research Training and Education Coordination (CRTEC), rated Outstanding merit, coordinates several impressive programs that span the continuum of trainees and mentees and add tremendous value to the training, education, and mentoring activities at the CFCCC and UCI. The CRTEC has been particularly successful with an innovative UCI NIH Boot Camp to support new investigators in obtaining peer reviewee funding. A comparable training program is being developed to promote the careers of clinical investigators in developing clinical trials. There are also several successful institutional programs that support cancer research career development of members of under-represented populations.

Community Outreach and Engagement (COE), rated Outstanding to Excellent merit, is well designed and effective in supporting collaborations for outreach and cancer research. The catchment area has been appropriately redefined to focus on OC, California, which encompasses >70% of the highly diverse population of patients presenting for care at the CFCCC. Narrowing the catchment area is well justified and enhances the center’s capacity to have a sustained impact, especially in complex areas of health equity. There are many deep connections with community stakeholders, and service to the catchment area is a well-established priority of the CFCCC. Sustained and meaningful community partnerships continue to inform both the cancer center research as well as numerous outreach initiatives to reduce the cancer burden in the catchment area. While the COE is clearly successful, the metrics used to evaluate the progress of specific outreach activities and plan new initiatives are unclear.

The Clinical Protocol and Data Management (CPDM), rated Outstanding merit, is highly effective and efficient in the management of clinical trial operations through the Stern Center for Cancer Clinical Trials and Research (Stern Center), the CFCCC clinical trials office. Data and Safety Monitoring is rated Acceptable, and the Protocol Review and Monitoring System is rated Satisfactory. The components Inclusion of Women in Clinical Research, Inclusion of Minorities in Clinical Research, and Inclusion of Individuals Across the Lifespan in Clinical Research, are each rated Acceptable. The Stern Center leadership, CFCCC leadership, and UCI Health have clearly put notable effort into supporting the growth of the clinical research enterprise, with several new policies in place to ensure more efficient clinical trial operations. In addition, the current time to trial activation of is admirable.

The administration and organizational components of the CFCCC are very well designed. Leadership, Planning and Evaluation, rated Outstanding merit, has overseen strategic growth in critical areas including research and clinical space, enhanced institutional commitment, and key faculty and leadership recruitments. Several senior leaders are new, and all are well qualified with demonstrated leadership ability. Cancer Center Administration, rated Outstanding merit, effectively supports the mission of the CFCCC through the provision of essential services, management expertise, and program support for the center's research. Developmental Funds, rated Excellent to Outstanding merit, continue to be used effectively to support the recruitment of new faculty, funding of innovative pilot projects aligned with strategic priorities. In addition, the two proposed Staff Investigators are acceptable and will promote translational research at the CFCCC.

All the six Essential Characteristics are all met and rated as follows: Physical Space, Organizational Capabilities, Transdisciplinary Collaboration and Coordination, and the Center Director are each rated Outstanding. Cancer Focus is rated Excellent to Outstanding, and Institutional Commitment is rated Excellent. The status of the CFCCC in the UCI organization has been elevated and the Center Director has appropriate authorities over the cancer service line, philanthropy, and enlarged research space.

Overall, the CFCCC continues to provide robust service to the catchment area with innovative basic, clinical and translational, and population science-based cancer research. The center clearly adds substantial value by fostering collaborative cancer research, education, and community engagement. New recruits to the research programs and senior leadership, and the detailed strategic plans, are likely to enhance the center's impact on the cancer burden in the catchment area and the nation. With the superb leadership of the Center Director, Dr. Van Etten, and robust institutional support, the CFCCC is on a very positive trajectory. Therefore, this application is rated as Excellent and support for five years is appropriate.

TABLE OF CONTENTS

RESUME AND SUMMARY OF DISCUSSION **2**

OVERALL DESCRIPTION **7**

OVERALL CRITIQUE **7**

PROTECTION OF HUMAN SUBJECTS **14**

VERTEBRATE ANIMALS **14**

ADDITIONAL REVIEW CONSIDERATIONS **14**

COMPREHENSIVENESS: **14**

ADDITIONAL REVIEW CRITERIA **14**

RESEARCH PROGRAMS **14**

Biotechnology, Imaging and Drug Development Program (BIDD) 14

Systems, Pathways and Targets Program (SPT) 17

Cancer Control Program (CC) 21

SHARED RESOURCE MANAGEMENT **24**

SHARED RESOURCES **27**

Transgenic Mouse Facility (TMF) 27

Optical Biology Core (OBC) 29

Genomics High-Throughput Facility (GHTF) 30

In Vivo Functional Onco-Imaging (IVFOI) 32

Experimental Tissue Resource (ETR) 33

Biostatistics Shared Resource (BSR) 35

Biobehavioral Shared Resource (BBSR) 36

CANCER RESEARCH TRAINING AND EDUCATION COORDINATION **38**

COMMUNITY OUTREACH AND ENGAGEMENT **40**

CLINICAL PROTOCOL & DATA MANAGEMENT, DSM, and INCLUSIONS **42**

Data and Safety Monitoring 44

Inclusion of Women in Clinical Research 45

Inclusion of Minorities in Clinical Research 45

Inclusion of Individuals Across the Lifespan 45

PROTOCOL REVIEW AND MONITORING SYSTEM **46**

DEVELOPMENTAL FUNDS **47**

LEADERSHIP, PLANNING AND EVALUATION **49**

ADMINISTRATION **53**

ESSENTIAL CHARACTERISTICS **56**

Physical Space 56

Organizational Capabilities 57

Transdisciplinary Collaboration and Coordination 57

Cancer Focus 58

Institutional Commitment 58

Center Director 59

BUDGET RECOMMENDATION **60**

COMMITTEE BUDGET RECOMMENDATIONS/SITE VISIT TEAM'S RECOMMENDATIONS **60**

SUMMARY OF RECOMMENDED BUDGETS/SITE VISIT TEAM'S RECOMMENDATIONS **62**

REVIEW PANEL ROSTER .....

OVERALL DESCRIPTION (provided by applicant): The Chao Family Comprehensive Cancer Center (CFCCC) of the University of California, Irvine (UCI) is the only NCI-designated cancer center based in Orange County, the 6th most populous county in the U.S. that serves as our Catchment Area and is home to ~1% of the nation's people. Now entering its 27th year, the CFCCC will enact its new Strategic Plan to enhance its role as a vital resource for the people of Orange County and surrounding areas in southern California to generate and disseminate new knowledge about the causes, prevention, and treatment of cancer, to train of the next generation of cancer providers and caregivers, and to alleviate the overall burden of cancer on our residents. The CFCCC has 195 members drawn from 32 academic departments across nine Schools at UCI, including the Schools of Medicine, Nursing, Pharmacy & Pharmaceutical Sciences, Population & Public Health, Biological Sciences, Physical Sciences, Information & Computer Science, Engineering, and Business. Our parent institution, UCI, has been consistently ranked in the top 10 of public universities in the U.S., while our CFCCC members are supported by $29.2 million in total annual extramural peer-reviewed cancer research funding, including $9.3 million from the NCI. Our members published 1,792 cancer-focused, peer-reviewed publications from 2015-2020, of which 73% are collaborative and 20% are in high-impact journals. CFCCC research is organized into three Research Programs that provide an interactive and collaborative infrastructure for cancer discovery, clinical investigation including early phase and investigator-initiated trials, and population-based cancer research. These include two Programs spanning basic, translational, and clinical cancer research, Biotechnology, Imaging & Drug Development (BIDD) and Systems, Pathways & Targets (SPT), as well as Cancer Control (CC), our population science Program. The Programs are further linked by seven CFCCC Disease-Oriented Teams that bring together basic, translational, clinical and population investigators to facilitate the movement of CFCCC discoveries through the pipeline into the clinical arena. CFCCC research is supported by seven Shared Resources that provide our members access to specialized services, technology and instrumentation, and expert consultation and collaboration. These Shared Resources include the Transgenic Mouse Facility, Optical Biology Core, Genomic High-Throughput Facility, In Vivo Functional Onco-Imaging, Experimental Tissue Resource, Biostatistics Shared Resource, and the Biobehavioral Shared Resource. Clinical research is supported by the Stern Center for Cancer Clinical Trials & Research, the CFCCC clinical trials office. With this competing renewal application, the CFCCC requests CCSG funding for the next 5 years to support our Administration, Developmental Funds, Program and Senior Leadership, Community Outreach & Engagement, Cancer Research Training & Educational Coordination, Shared Resources, Clinical Protocol & Data Management, and Protocol Review & Monitoring, to allow the CFCCC to continue its mission.

PROJECT NARRATIVE: The Chao Family Comprehensive Cancer Center (CFCCC) of the University of California, Irvine (UCI) is the only academic cancer center based in Orange County, the sixth most populous county in the United States with over 3.2 million residents who embody substantial socioeconomic and racial/ethnic diversity. Designated as a comprehensive cancer center by the National Cancer Institute since 1997 and backed by the research enterprise of UCI, a member of the Association of American Universities, the CFCCC carries out research across the spectrum of cancer including fundamental mechanisms of cancer development, novel modes of detection and imaging, new anti-cancer drugs and devices, and cancer susceptibility, prevention and survivorship. Through its research programs and supporting resources, the CFCCC translates these discoveries through the pipeline into clinical treatments and interventions that are directed specifically towards reducing the burden of cancer on the multi-ethnic population of Orange County and surrounding areas, and advances this new knowledge onto a wider stage to change clinical cancer practice across the country.

CRITIQUE:

OVERALL CRITIQUE:

Criterion Scores:

	Significance	Investigator	Innovation	Approach	Environment
Reviewer 1	2	1	2	3	2
Reviewer 2	1	2	1	3	3
Reviewer 3	3	2	3	3	2

The CFCCC is a matrix cancer center and currently is in its 23rd year as an NCI-designated Cancer Center. In this competing renewal application for a Cancer Center Support Grant, five years of support are requested for three research programs, seven shared resources, a Clinical Trials Office, Protocol Review and Monitoring System, Cancer Research Career Enhancement and Related Activities, Community Outreach and Engagement, as well as Leadership, Planning and Evaluation, Administration, and Developmental Funds.

The overall mission of CFCCC is to discover, teach, and heal within the broad discipline of cancer medicine. This mission is pursued via three broad aims: 1) to discover: to facilitate and promote interdisciplinary and transdisciplinary cancer research across UCI, to develop new knowledge about the causes, prevention, detection, treatment, and survival of cancer that shift scientific paradigms, change public policy and clinical practice, and eliminate health disparities; 2) to teach: to disseminate state-of-the-art cancer knowledge to cancer caregivers, patients and families, and the public, to train the next diverse generation of cancer researchers and care providers; and 3) to heal: to deliver the highest quality multidisciplinary clinical care to cancer patients, and to develop and sustain programs to alleviate the burden of cancer within the catchment area and beyond.

Dr. Richard Van Etten, appointed in 2013, is the highly capable Center Director. Overall, Dr. Van Etten led a strategic planning initiative and orchestrated key improvements in the cancer center since the last competitive renewal. Significant changes in the senior leadership have occurred, including appointments of Dr. David Fruman, Associate Director for Basic Science; Dr. Karen Edwards, Associate Director for Population Science and Cancer Control; Dr. Sora Park Tanjasiri, Associate Director for Cancer Health Disparities & Community Engagement; Dr. Edward Nelson, Associate Director for Cancer Research Training and Education; and Ms. Christine Hui, Associate Director for Administration & Finance/Chief Administrative Officer. Peer-reviewed funding for the CFCCC is approximately $31.1 million (direct costs). NCI funding is approximately $ 10.7 million (direct costs). Some research programs were reorganized and interdisciplinary and transdisciplinary research is evident. The CFCCC has 195 members, increased from 145 members at the time of the last review. During the current funding period, 90 new faculty members were hired, in line with the specific objectives identified in the strategic plan. Regarding collaborative research, there is an overall intra-programmatic publication record of 16%. Twenty percent of the publications are in high impact journals (IF>9.4). There are 19 multi-investigator grants the center participates in with four centered at CHCCC, reflecting considerable intra/inter programmatic/ inter-institutional collaborations. Additionally, investments in cancer physical space, including clinical and research facilities are apparent. An intriguing component of the center is the degree of cutting-edge physical sciences related to cancer that is fostered at the center. Major strengths of the CFCCC continue to be the overall quality of translational research, the strong clinical research, and outreach into the diverse catchment it serves.

The CFCCC defines its catchment area as Orange County (OC) which represents Region 10 of the California Cancer Registry. This definition captures >70% of the patients presenting for care at the CFCCC and included a geographic region of more than four million people. Attention to and research relevant to the catchment area is well-established and addressed in Community Outreach and Engagement. There are many examples where the incidence and/or mortality of certain cancers is higher for specific Orange County racial/ethnic groups in comparison to California or the US at large. This includes cervical cancer among Latina females, hepatobiliary and gastric cancer incidence amongst Latino and Asian/Pacific Islanders, ovarian cancer among non-Hispanic Whites and Asian/PI, melanoma among non-Hispanic White and Latino males, breast cancer mortality in Latina females, and

myeloma in Asian and Pacific island females. Successful training programs and research efforts serving underrepresented groups are also noted, with partnerships evident throughout UC Irvine.

There are three research programs consisting of the Biotechnology, Imaging and Drug Development Program (BIDD), Systems, Pathways and Targets Program (SPT), and the Cancer Control Program (CC). These programs have undergone significant changes in leadership and changes in focus over the current funding period. Since the last review the Molecular Diagnostics & Therapeutics (MDT) program was merged with the Onco-Imaging & Biotechnology (OIB) to become the BIDD. Dr. Van Etten appointed five new program leaders, including Drs. Ganasan and Milner to BIDD, Dr. Becker to SPT, and Drs. Lee and Milam to CC. Four of seven cores have new leadership as well. These decisions were all part of strategic planning for the center as advised by multiple committees including the External Advisory Board.

The BIDD Program, rated Outstanding merit, is one of two translational science programs in the CFCCC and is now co-led by Drs Greg Weis, Anand Ganesan and Thomas Milner. The program includes 78 Members from 24 Departments and six Schools. Productivity is evidenced by $3.5 million funding from NCI out of $11.2 million in total peer reviewed funding. The program has a strong publication record, with 609 publications of which 18% are in high-impact factor journals. The publications reflect a strong science base for the program. Inter-programmatic publications are strong at 20%, and intra-programmatic publications are also at approximately 20%, highlighting a solid integration of members. There are four aims to the program: 1)to engineer bioanalytical and biotechnology devices that use chemical probes, nanoparticles, or engineered cells to improve early detection, detect early recurrence, or develop better treatments for cancer; 2) to develop biophotonic and multi-modality imaging technologies that facilitate the early detection of cancer and aid in its treatment through iterative, machine learning based approaches; 3) to utilize world-class expertise in chemistry and protein engineering to synthesize small molecules, antibodies, and immunotherapeutics for the treatment of cancer; and 4) to translate CFCCC developed drugs and devices from concept to IND enabling studies, to clinical trials. This is a new and quite large program formed by fusing two other previous programs. The major strengths of the program include the impactful work in basic science focused on drug discovery, imaging, and bioengineering. Some of the noted program accomplishments are highly impactful and very novel including the Flash radiotherapy research and virus bio resistor work in bladder carcinoma. The members have considerable expertise in chemistry, engineering, and imaging. Plans for future development of the program are well defined to ensure future growth in translational research. In addition, the program addresses several malignancies of high relevance to the CFCCC catchment area. However, integration of clinical activities across the program and the Disease Oriented Teams is not adequately addressed.

The Systems, Pathways, and Targets Program (SPT), rated Excellent to Outstanding merit, is co-led by Drs. John Lowengrub and Pamela Becker. The program is comprised of 72 members from 16 Departments and five schools across UCI. NCI funding is $3.8 million with a total of $11.5 million in peer-reviewed funding. Program members are productive with a total of 843 publications, 25% in high-impact factor journals. Intra-programmatic and inter-programmatic publications are adequate at 15% and 14%, respectively. There are three aims in the SPT program: 1) identify key targets in signaling networks, developmental pathways, and metabolic programs that are relevant to cancer initiation, progression, and therapeutic resistance; 2) support multidisciplinary teams to study how heterogeneity at the single cell level and cell-cell interactions influence cancer progression and therapeutic resistance; and 3) enable clinical-basic science researcher multidisciplinary teams, via the DOTs, to accelerate the translation of preclinical research with a focus on multi-agent targeted therapy. Several innovations exist in the SPT program and a recently funded U54 systems biology grant is a demonstration of significant member expertise in this program. Significant examples of research results include co-targeting glycolysis and Wnt signaling in colon cancer, and refining models connecting cell cultures to orthotopic systems. For example, the use of statins as chemosensitizers for BCL 2 inhibitors for CLL and projects centering on glutamine starvation and stemness grant are examples of novel concepts in

clinical translation. However, there appears to be modest focus on some of the highly prevalent catchment-area cancers such as melanoma. This will likely change as the pipeline of translation matures moving from basic research to newer DOTs.

The Cancer Control program (CC) Program, rated Excellent to Very Good merit, is led by Drs. Sunmin Lee and Joel Milam. The program has approximately $2.1 million (direct) in peer-reviewed funding from the NCI out of a total of $6.1 million in total peer reviewed funding. The program has a strong publication record, with 647 publications, with 14% in high-impact factor journals. The publications reflect a solid population science base for the program. Inter-programmatic publications are at 15%, and intra-programmatic publications are 14%. The CC specific aims are to identify, understand, and control risk factors to prevent cancer and improve outcomes through diagnosis, treatment and interventions to improve survivorship. The center has demonstrated a strong investment in CC with several recent hires including two well-qualified and experienced co-Leaders. Program impact is highlighted by the maturation of Dr. Tewari's Bevacizumab trial results that led to FDA approval for its use in advanced stage cervical cancer. The showcased scientific examples included multiple early career investigators who utilized CC center pilot funds to generate pilot data to obtain R01 and equivalent grants. Although these are promising examples of research, the projects have yet to fully mature and significantly impact cancer burden in the catchment area. The rates of intra- and inter-programmatic publications suggest that CC researchers may be siloed and evidence of CC member engagement in team science is noticeably lacking. The program addresses many important cancers of concern within the catchment area and attention to critical caner health disparities will grow with the new members. Overall, strengths related to recent progress and promise of this program are balanced by weaknesses of moderate scientific impact during the current funding period and a lack of strong integration of members within the program.

Eight shared resources are proposed by the CFCCC. The shared resources are well designed, cost effective, and responsive to member needs. The shared resources are rated as follows: the Transgenic Mouse Facility (TMF) is rated Outstanding merit ; the Optical Biology Core (OBC) is rated Exceptional merit; the Genomics High Throughput Facility (GHTF) is rated Excellent to Very Good merit; the In Vivo Functional Onco-Imaging (IVFOI) is rated Excellent to Outstanding merit; the Experimental Tissue Resource (ETR) is rated Excellent merit; the Biostatistics Shared Resource (BSR) is rated Excellent to Outstanding merit; and the Biobehavioral Shared Resource (BBSR) is rated Very Good to Excellent merit. In addition, Shared Resource Management, rated Excellent merit, provides effective administrative oversight of these shared resources to facilitate high-impact cancer research by center members. Six of the seven CFCCC shared resources are jointly managed with the institution using a shared governance model. The CFCCC has made considerable investments in new equipment and systems for these resources. The recent implementation of Agilent's iLab will greatly enhance the effectiveness of service delivery to members.

Cancer Research Training and Education Coordination (CRTEC) is rated Outstanding merit. This function is ably overseen by Dr. Edward Nelson with highly competent administrative colleagues. CRTEC has several impressive programs that span the continuum of trainees and mentees. There are several programs to support cancer research careers of under-represented populations – these include the PRIME-LC academy, Black Thriving Initiative, SAGE Scholars Program, and the LEAD-ABC Program that seems to be largely institutionally run and/or with SOM support. These are institution-wide programs for the most part with CRTEC's role not clearly defined in the governance of some programs with respect to cancer. However, outstanding CRTEC activity brings tremendous value to the training, education, and mentoring activities at CFCCC.

Community Outreach and Engagement (COE) is rated Outstanding to Excellent and is led by Dr. Sora Park Tanjasari. The COE component aims to monitor the cancer burden, build partnerships with community stakeholders, and facilitate community engagement in research. COE leadership is superbly qualified, Dr. Tanjasiri is a nationally recognized leader in community-engaged cancer research with

longstanding collaborations with local community stakeholders. There is clear demonstration of sustained and meaningful community partnerships that have informed both the cancer center strategic planning as well as numerous outreach initiatives to reduce the cancer burden in the catchment area. COE has conducted extensive outreach to promote awareness of the COE strategic plan across the research programs, with evidence of increases in catchment area-relevant grant proposals. It is clear that the COE has built strong relationships across the CFCCC and that the needs of the catchment area are communicated effectively to cancer center leadership and members. Evidence of COE infrastructure to support activities at other stages of the research continuum is less robust (for e.g. infrastructure to enhance stakeholder engagement in research design, implementation, and disseminating findings to the community). While the COE is successful, the strategic plan for activities is somewhat unclear including insufficient discussion of associated metrics to measure impact within the catchment area.

The Clinical Protocol and Data Management (CPDM) is rated Outstanding merit. Data and Safety Monitoring per NIH Policy is rated Acceptable. Protocol Review and Monitoring System is rated Satisfactory. The components Inclusion of Women in Clinical Research, Inclusion of Minorities in Clinical Research, and Inclusion of Individuals Across the Lifespan in Clinical Research, are each rated Acceptable. Dr. Susan O'Brien is a dynamic and highly knowledgeable leader of CPDM. Importantly, all the functions are well described and consistent with an efficient QA program in place. Evidence is presented that the Protocol and Review Monitoring System is working well with improved processes for review, activation and closure based on defined metrics. The CFCCC has put a number of new policies in place to ensure more efficient clinical trial operations. Time to trial activation of approximately 100 days is admirable. The center is well equipped to increase prioritization processes for catchment area malignancies in the coming years.

Leadership, Planning and Evaluation is rated Outstanding merit. The leadership structure, internal and external advisory boards, along with various meetings and retreats among programs provide needed support for planning and evaluation in the reorganized. Senior Leaders are well qualified with all possessing demonstrated leadership ability. The leadership team at the CFCCC is relatively new, but it has overseen strategic growth in critical areas including space, institutional commitment, and key faculty and leadership recruitments. Planning and evaluation are done through largely effective meetings with key institutional and community stakeholders where bilateral communications occur. CFCCC has a strong External Advisory Board that has provided critical input and advice to CFCCC and UCI leadership during the current project period. The advice of the EAB and the Cancer Center's response have been critical in obtaining the notable achievements made. The ability and progress made from implementation of the findings of the EAB and IAB are examples of the center and its ability to lead and plan. However, much of the dynamism and major changes appear to have transpired relatively late in the current funding period with modest input from center members outside the senior leadership.

Developmental Funds is rated Excellent to Outstanding merit and the proposed Staff Scientists are clearly acceptable. Developmental Funds have been effectively used to support the recruitment of new faculty, funding of pilot projects, and two staff investigators. During the current funding period the use of these funds was guided by strategic priorities of the center with significant input from both internal and external advisory committees. Overall, these funds have had a very positive impact on center science through faculty recruitment and seeding of new research projects that have led to increased cancer relevant funding. The stated return on investment on pilot projects and faculty recruitment is quite high, but because of admixture with other major funding sources the exact impact of Developmental Funds is somewhat unclear. The future plans for Developmental Funds are clearly driven by the strategic priorities of the CFCCC.

Administration is rated Outstanding merit. The administrative infrastructure effectively supports the mission of the CFCCC through the provision of essential services, management expertise, and program

support for the center's research. Administration supports shared resource management and compliance, coordination of pilot project programs, management of space utilization, organization and staffing of planning and evaluation activities, oversight of budgets and finance, participation with faculty recruitment and onboarding, and management of data, reports and data systems. CFCCC Administration has been strengthened with the recent addition of Ms. Christine Hui, Associate Director for Administration and Finance and Chief Administrative Officer. Notable accomplishments during the current project period, include the development of new space management, cancer-relevance, and membership policies, purchasing and implementation of Agilent's iLab tool and Advarra Forte EVAL, as well as the significant growth in the Clinical Trials Unit, including the substantial decrease in protocol activation time. Appropriate administrative oversight of the CCSG application process is evident throughout the application with some minor data discrepancies noted. There are also opportunities to enhance membership criteria and support for pilot projects.

The Essential Characteristics of the cancer center are fulfilled and are rated as follows:

Physical Space is rated Outstanding merit. The facilities have been improved massively from the time of the last renewal and Dr. Van Etten has increased control of present and future space. Enhanced facilities, including clinical space, provide state-of-the-art facilities for CFCCC activities and adequate space is available for future growth. However, maximizing synergy among investigators located on multiple campuses and clinical locations remains challenging.

Organizational Capabilities is rated Outstanding, given the effective structure and processes that have allowed the center to make significant progress in reorganizing programmatic structures. This has been a major focus over the last five years in response to input from advisory boards. The Center Director , Dr. Van Etten, occupies key leadership positions within the institution that enhance integration of the center, the result of which is to facilitate a stronger impact of the center priorities on the catchment area. Many of the center's senior leaders are recently recruited and possess the skill sets necessary to implement the mission and vision of the center. In the most recent period, the CFCCC has reorganized and strengthened the programmatic structure and linkages to leadership committees, as well as the senior leadership teams, with overall reporting and direction from the center leadership. The EAC is appropriate, has been indispensable as a team of advisors and advocates, and has a strong group to assess and contribute to Dr. Van Etten's leadership and decision-making process. Dr. Van Etten has led a new round of strategic planning with implementation which began in 2017. Future strategic planning is exceptionally well described, allowing for an actionable blueprint for the center. The center also has taken advantage of institutional capabilities in fostering scientific interactions and joint initiatives among the various research programs. Membership criteria are somewhat broad but allow for a diverse multidisciplinary team membership. Training activities are well-described and effective, including CME activities of the center offered to healthcare practitioners.

Transdisciplinary Coordination and Collaboration is rated Outstanding merit. There has been a strong effort at the CFCCC to improve collaboration and coordination across the center from the time of the last review. Institutional pilot funds have supported new team science projects that have resulted in new investigator-initiated trials and intra-programmatic NCI funding. Inter- and intra-programmatic publications have shown improvements with intra-programmatic publications ranging from 11%-20% and inter-programmatic publications ranging from 13%-20%. Inter-institutional publications range from 48%-68% across the three programs. Importantly, there are a number of new collaborative grants and initiatives at the center, and these awards are a testament that work performed to foster additional collaboration across the programs and center is effective. For example, the systems biology U54 grant will undoubtably influence translation over the next period. When increasing the integration of peripheral sites like the VAMC and the Children's Hospital, attention has been paid to strategically integrating the translational science and population-specific issues into the center's research portfolio. In addition, there is an improving clinical trial pipeline through the Disease Oriented Teams and key recruits into clinical oncology disciplines (e.g. medical oncology and urology).

Cancer Focus is rated Excellent merit. There is an overall movement towards increased scientific focus on cancer research as defined by the objectives of each research program. There is better attribution of cancer focus to grants throughout the center as compared to the last review. The collaborations between laboratory investigators and the clinical enterprise has been facilitated by the development of Disease Oriented Teams. This is still a work in progress, as relatively few therapeutics are presently in clinical trials from these new Disease Oriented Teams. There is very substantial breadth, depth, and significance of the cancer-related research within the individual research programs, publications, and peer-reviewed research support. Strengths lie in unique cancer research in areas like engineering, and there are incentive plans including seed grants to improve clinical translation of novel concepts.

Institutional Commitment is rated Excellent merit. Institutional commitment of 25,000 sf of laboratory space as well as accommodations for translational research in both the new clinic buildings and the EMR infrastructure will occur in the next five years. There is a clear succession plan in place to replace the director. There has been a consistent increase in financial support for the programmatic expansion of the CFCCC in terms of research space, funding and personnel. Support for the center could be significantly greater given the dramatic increase in patients treated. While institutional support for the Stern Center is very solid, additional support may be needed, as cancer referrals and clinical trial accruals are on a positive trajectory.

The Center Director is rated Outstanding merit. Dr. Van Etten is highly qualified to serve as director. During the current funding period he has gained additional institutional authority through his position as Associate Vice Chancellor for Cancer with a direct report to the Vice Chancellor for Health Affairs. This gives him additional oversight of both clinical and scientific activities relating to cancer at UC Irvine, thus ensuring alignment of these critical areas to serve the needs of the CFCCC. He has appropriate authority over considerable resources at the center including improvements in the amount and control over research space. He has directed significant and strategic leadership over center leadership and faculty. Inpatient and outpatient clinical facilities and center revenue are improved and considerable expansion of cancer clinics into the catchment has occurred and will expand over the next five years. Dr. Van Etten’s control and authority ensure the successful accomplishment of the mission and vision of the center. He has successfully led efforts to recruit a large number of new members, including multiple new leaders, increase cancer relevant funding, and increase the center’s educational and community outreach and engagement.

In summary, the CFCCC demonstrates strong productivity in cancer research. The unique innovations and consolidation of the research programs are highly strategic and new leaders foster increased collaborative team science. In addition, the Shared Resources are well matched to the translational goals of the center. The next five years will likely reveal important therapeutic outcomes from member developed devices and therapeutics that are already in advanced preclinical stages. The growth in number of patients seen by the center and accrual to clinical trials are on an impressive positive trajectory. However, implementation and support for the new Disease Oriented Teams is a work in progress. The CFCCC has clearly been moving in a positive trajectory from the time of Dr. Van Etten’s appointment. The Center Director’s strategic vision is a strength and places the CFCCC in a position to reach its full potential. Under the capable leadership of the Center Director and with the continued commitment of the institution, this center is well-positioned to move to the next level. Overall, this application is rated Excellent and support for the requested five years is recommended.

THE FOLLOWING 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: ACCEPTABLE (Also, see the heading, Data and Safety Monitoring)

DATA AND SAFETY MONITORING PLAN: ACCEPTABLE

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

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

INCLUSION OF INDIVIDUALS ACROSS THE LIFESPAN PLAN: (Also, see the heading, Inclusion of Individuals Across the Lifespan in Clinical Research.)

VERTEBRATE ANIMALS: ACCEPTABLE

ADDITIONAL REVIEW CONSIDERATIONS

COMPREHENSIVENESS: The CFCCC has significant strengths in the full spectrum of basic, clinical and translational, and population sciences-based cancer research. There are many active collaborations between the research programs. Clinical and translational research has expanded. There are increased numbers of patients enrolled on therapeutic and non-therapeutic clinical trials, along with an increased number of investigator-initiated, institutional clinical trials. The level of transdisciplinary research and collaborative interactions has substantially expanded, as evidenced by a high level of intra- and inter-programmatic collaborative publications and a growing number of multi-investigator, team-based grants. The center effectively serves its well defined catchment area and provides effective education, training, and outreach activities. Overall, the CFCCC clearly fulfills the requirements of comprehensive designation.

Assessment: [to be determined at the CANCER CENTER SUPPORT GRANT (P30) SPECIAL EMPHASIS PANEL]

RESOURCES SHARING PLANS

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

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

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

ADDITIONAL REVIEW CRITERIA

RESEARCH PROGRAMS

Biotechnology, Imaging and Drug Development Program (BIDD)

DESCRIPTION (provided by applicant): The overarching goal of the reorganized Biotechnology, Imaging, and Drug Development (BIDD) Program is to utilize novel computational, chemical, and engineering-based approaches to detect, diagnose, and treat cancer. The BIDD Program evolved in response to the increasingly interdisciplinary nature of cancer research, spanning chemistry, physics,

mathematics, optics, engineering, biology, and medicine. The Program initiates concepts through cross-disciplinary meetings at the pre-design phases; progresses through technology development involving advanced chemistry, physics, and engineering; and proceeds through preclinical validation in model systems and tissues before testing in clinical trials. The BIDD Program fuses two prior complementary programs and provides leadership and structure to translate basic discoveries to the clinic. The formation of the Program synergistically combines UCI's strengths in synthetic chemistry, bioengineering, and physics to maximize translation of basic research. As the de facto technology development hub for the Cancer Center, BIDD reaches out to other Cancer Center programs, Catchment Area stakeholders, and the investment community to build interdisciplinary teams able to steer new technologies into cancer-relevant directions. The BIDD leadership facilitates this process by establishing interdisciplinary teams of clinicians, physical scientists, and biologists to guide each project from its earliest stages; assist in the design of validation experiments using appropriate models (animal models with the Transgenic Mouse Facility, TMF), human tissues through the Experimental Tissue Resource (ETR), and ex vivo tissue models); implement deep learning approaches for drug and diagnostics development; provide infrastructure to complete IND-enabling studies; and design clinical trials to test drug candidates and devices

Membership: 78 Members from 24 Departments and 6 Schools
Funding: $3,003,969 NCI (Directs); $7,540,410 Other Peer-Reviewed (Directs)
Accruals: Interventional: 272; Treatment: 169; Institutional/Investigator-Initiated: 166
Publications: Total: 542; High Impact Journal: 101 (19%); Intra-programmatic: 107 (20%); Inter-programmatic: 109 (20%); Inter-Institutional: 262 (48%)

CRITIQUE: The Biotechnology, Imaging, and Drug Development (BIDD) Program is a new program formed recently (in 2020) by fusing two previously programs, Molecular Diagnostics & Therapeutics and Onco-imaging & Biotechnology into one. This reorganization has allowed improved integration of research in chemistry, physics, engineering, and biology to deliver improved diagnostic and cancer technologies to detect and treat cancer. The BIDD is rather large, including 78 Members from 24 Departments and 6 Schools. Productivity is evidenced by $3 million funding from NCI, out of over $10 million total funding and 542 publications (609 updated number at site visit), including 20% intra-programmatic collaborations, 20% inter-programmatic collaboration and close to 50% inter-institutional collaborations. A significant number of publications (20%) are considered high impact. There are 8 grants funded by NCI with the remaining large funding agencies being NSF, NIGMS, NIBIB and NINDS.

Program members engage in research that capitalizes on UCI's strengths in synthetic chemistry, bioengineering, and physics with the goal of translating these basic science discoveries into clinical applications. Cancer applications include both cancer prevention/early detection as well as therapeutics. The research activities of the members of the program span the gamut from very basic to clinical applications. The objectives of the program are: 1) to develop chemical probes, nanoparticles, or engineered cells to improve early detection, detect early recurrence, or develop cancer treatments; 2) to develop biophotonic and multi-modality imaging technologies that facilitate the early detection of cancer; 3) to use chemistry and protein engineering to synthesize small molecules, antibodies, and immune-therapeutics for the treatment of cancer; and 4) to take drugs and devices from concept to IND enabling studies to clinical trials. The strengths reside in the highly novel technologies being developed and the unique bioengineering expertise of the group rendering BIDD the technology development hub for CFCCC. The program's vision is somewhat broad and unfocused.

Program members engage in cutting edge chemistry, molecular imaging and bioengineering research with cancer focus. The technology development focus represents a strength of this BIDD Program. During the current funding period, 8 start-up companies with technologies entering the clinical space were formed around drugs and devices developed by BIDD members. The development of novel drugs and devices, some close to IND and clinical testing represents a major strength of this program.

The BIDD membership is primarily concentrated in the fields of chemistry and molecular biology /biologic chemistry (approx. 21 members), Engineering (approx. 13 members), radiologic sciences (approx. 7 members) as well as physics and the Beckman Institute (approx. 5 members each). Other members include 5 from surgical fields, 3 from neurology, 1 from radiation oncology, 2 from OB/GYN, 5 from hematology/oncology, 2 from dermatology and 1 each from GI and psychiatry. It is not clear how membership of clinical investigators is allocated to BIDD. Membership has been strengthened by new hires for the Convergence Optical Sciences Initiative (COSI) inclusive of Dr. Shawn Xiang (R37 in photoacoustics) and Dr. Zhuoli Zhang (COSI and Radiologic Sciences; 2 R01s in tracking immune and stem cells via novel MRI approaches) Intra- and Inter- programmatic activities have included 18 seminars at DOT meetings, greater than 20 seminars at the Beckman Institute, greater than 30 seminars at UCI institutes and centers and one large retreat in August of 2020. Attendance at these meetings is unclear. Program members are active in clinical cooperative groups (ECOG, NCCN) and IITs. The program emphasizes basic science research over clinical investigation.

Members of this program have diverse expertise and focus of research in imaging, biotechnology, chemistry/structural biology, clinical science (broad focus, not restricted to oncology), and immunology/immunotherapeutics. Some of the highlighted contributions of members are the work of Dr. Zhao's group who used engineered mechanoresponsive mesenchymal stem cells to specifically deliver prodrugs to tumors and avoid neighboring normal cells in a model of breast cancer; development of tumor on a chip for therapeutic drug screening and matrix analysis (Dr. Hughes), engineering orthogonal luminescent probes for dissection of tumor heterogeneity Dr. Prescher); breast imaging to detect and predict response to cancer treatment (Drs. Su and Mehta), use of AI to develop radiomic and improve cancer imaging, etc. On the therapeutic side, members have developed new drugs such as EG5 kinesin inhibitors; development of new antibodies for cancer therapy; development of RHOJ inhibitors for melanoma and new immunotherapy approaches including strategies to target tumor associated carbohydrate antigens (TACAs), using glycan dependent T cell recruiter. Overall, the contributions are highly impactful, but the breadth of research activities is somewhat unfocussed. The creation of the BIDD was in part due to recommendations by the EAB and to improve collaborative interactions between scientists, engineers, physician/scientists and DOT members.

The clinical trial accrual to institutional treatment trials within the BIDD team is limited and includes few patient accruals to catchment areas of importance in melanoma and breast cancer. Clinical trial accrual includes 25 patients to an important pilot study in glioblastoma patients. Accrual to diagnostic studies evaluating AI assisted polyp detection and novel skin imaging and oral pathology detection was robust with multiple hundred patient accrual. Aside from these, the clinical activities in the program are not well described and the pipeline channeling basic science discoveries to the clinic is unclear. Though the current BIDD program has increased cancer relevance and reasonable NCI funding with significant progress in potential translational projects there appears to be limited progress from prior projects. Despite a number of novel devices and drugs having been developed by members of this program, it is not clear when the first IND will be awarded and when human trials will start.

Major strengths of the program are the technological focus, BIDD being the hub for new drugs and devices being developed for translation to clinic in CFCCC. Additionally, BIDD includes all CFCCC early stage (Phase I) clinical trials. However, this aspect is not sufficiently described, and the capacity and activities of the Phase I Unit remain unclear. CFCCC support aided the program to recruit at least 8 established investigators in the past 3 years. The CFCCC is developing a new shared resource for Mass Spectrometry (MS) and UCI has invested significantly in developing the cryogenic electron microscopy (CryoEM) shared resource facility, used by many of the BIDD members. BIDD members effectively use the shared resources, including IVFOI, TMF and OBC. CFCCC has also allocated space and funds to support pilot projects.

The catchment area of CFCCC is Orange County and diseases of special interest are breast cancer, melanoma, liver cancer and prostate cancer. BIDD members conduct research for early detection of

bladder/prostate cancer and has a long tradition of research focused on early detection of breast cancer through new imaging technologies (DOSI). Program co-leader Dr. Ganesan leads a strong program in melanoma, including development of new drugs (RHOJ inhibitors) and of imaging technologies for studying melanocytes in the skin (FLAME microscopy by Drs. Balu and Ganesan). Overall efforts to address catchment area are appropriate.

Future plans for the program align with the CFCCC and UCI strategy for development, including growing operational capacity in early clinical trials, recruitment of a seasoned phase I trialist, development of PK/PD capabilities to serve the Phase I Program, building a cGMP facility for cellular therapy and development of biological agents to increase immunotherapy capacity, increasing Precision Oncology efforts, expanding imaging technology capabilities (university wide effort). Among emerging imaging developments are the laser compton X-rays (TMXS technology) being developed through a new recruit, Dr. Barty; X-ray-induced Acoustic Computed Tomography (XACT) and FLASH Radiotherapy (FLASH-RT) using TMXS. Of significance is the possibility that three drug development programs (Siege, Alyra, GlyTR) developed in BIDD are nearing the IND stage leading to potential first-in-human clinical trials run. The plans for future growth in the program are impressive.

In summary, this is a new and quite productive program formed by fusing two previous programs. The strengths of the program are the impactful work in basic science focused on drug discovery, imaging and bioengineering. Some of the accomplishments are highly impactful and very novel. The program builds on the strengths in chemistry, engineering and imaging at the UCI. Plans for future development are well delineating and predict future growth and success and include first in human trials. The program addresses several malignancies of relevance to the CFCCC catchment area. However, the clinical activities of the program are not well described, representing a minor weakness.

Program Leader(s): The new BIDD program is now run by co-directors Drs. Greg Weis and Anand Ganesan who previously led the CDB/MDT program with the addition of Dr. Tom Milner who replaces Dr. Bruce Tromberg as the head of the Beckman Institute. As a testament to the science produced from the Beckman Institute and former OIB program, Dr. Tromberg has been tapped as the leader of the NIBIB at NIH. Dr. Milner is a Professor of Surgery and Biomedical Engineering and the Director Beckman Laser Institute at UCI and was newly recruited to UCI. His expertise is in optical physics and has developed multiple imaging technologies including optical coherence tomography and mass spectroscopy, which are relevant to cancer detection and laser surgery for cancer. Dr. Ganesan is Professor of Dermatology with expertise in melanocyte biology and oncogenic signaling in melanoma. He is multi-R01 funded to study new targets in melanoma and develop new imaging technologies for skin imaging. Dr. Weiss is a Professor of Chemistry at UCI with expertise in development of biosensors for cancer detection, protein engineering, bioelectronic for assessing enzyme activity. He is co-PI of NSF and R01 projects.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

Systems, Pathways and Targets Program (SPT)

DESCRIPTION (provided by applicant): The overarching goal of the Systems, Pathways & Targets (SPT) Program is to discover new critical mechanisms of cancer proliferation, survival and drug resistance that can be exploited for the development of novel treatments and diagnostics. SPT members include cell biologists, immunologists, geneticists, systems biologists, computational scientists, and clinicians who leverage diverse perspectives to build collaborative teams that tackle long-standing problems in cancer using bold and innovative approaches. SPT members work at different scales, from molecules and cells to tissues and organs, to study the fundamental biology of individual cancer cells and the interactions among cells in the tumor environment and metastatic sites.

Several SPT members are physician-scientists with independent research programs and are well-positioned to translate discoveries from bench to bedside. Moreover, SPT leadership actively connects basic scientists with clinicians through Disease- Oriented Teams (DOTs) and the annual CFCCC Scientific Retreat. These interactions lead to new clinical trials and facilitate access to patient samples for research projects. A unique aspect of SPT is the integration of systems biology approaches to the study of cancer. This emerging emphasis has resulted in productive intraand inter-programmatic collaborations and extramural funding including a NCI-U54 grant to support a Center in Cancer Systems Biology. SPT maximizes progress toward the identification of targets for cancer therapeutics and diagnostics by devoting resources to recruiting new faculty members, nurturing development of early career faculty, and supporting mid-career faculty members with cutting-edge research programs focused on cancer cell biology and therapeutic targeting. To promote collaboration, SPT supports working groups with shared interests and sponsors conferences and workshops. The Specific Aims of SPT are: to identify key targets in signaling networks, developmental pathways, and metabolic programs that are relevant to cancer initiation, progression, and therapeutic resistance; to support multidisciplinary teams that study how heterogeneity at the single cell level and cell-cell interactions can influence cancer progression and therapeutic resistance; and to enable clinical-basic science multidisciplinary research via DOTs to accelerate the translation of preclinical research. These efforts to discover critical pathways and survival mechanisms will reveal novel therapeutic targets for testing and validation in preclinical models, and eventually in clinical trials.

Membership: 72 Members from 16 Departments and 5 Schools
Funding: $3,467,881 NCI (Directs); $7,256,055 Other Peer-Reviewed (Directs)
Accruals: Interventional: 133; Treatment: 130; Institutional/Investigator-Initiated: 98
Publications: Total: 793; High Impact Journal: 199 (25%); Intra-programmatic: 113 (14%); Inter-Programmatic: 106 (13%); Inter-Institutional: 504 (64%)

CRITIQUE: The Systems, Pathways, and Targets (SPT) program was formed in 2011. The overarching goal of the SPT is to identify critical proteins or interactions between oncogenic signaling pathways for therapeutic intervention. The program leaders propose accomplishing this goal through three specific aims: 1) To identify key targets in signaling networks, developmental pathways, and metabolic programs that are relevant to cancer initiation, progression, and therapeutic resistance; 2) To support multidisciplinary teams to study how heterogeneity at the single cell level and cell-cell interactions influence cancer progression and therapeutic resistance; and 3) To enable clinical-basic science researcher multidisciplinary teams, via the DOTs, to accelerate the translation of preclinical research with a focus on multi-agent targeted therapy.

The program is comprised of 72 members across 16 departments and 5 schools. NCI funding is $3.5 million and other peer-reviewed funding is $7.3 million. The CPT is the largest program of the CFCCC. Of the 793 total publications, 15% involved intra-programmatic collaborations and 14% were inter-programmatic. 25% of the publications were in high impact journals (IF>9.4). At the 2015 review, the SPT program had 57 members and an NCI funding base of $3.1 million and other peer-reviewed funding of $12.3 million. The membership of the SPT program has grown by 26%, but NCI funding has increased by only 13% and other peer-reviewed funding has declined. Of the 19 Multi-PI grants listed in Data Table 2A, 4 involve multiple PIs from the CFCCC. This includes a U01 (Drs. Dai, Nie, Plikus), an R61 (Drs. Hughes, Thompson), a U54 (Drs. Lowengrub, Lander, Waterman) and an NSF grant (Drs. Komarova, Wodarz). Program funding reflects strong cancer relevance. A Skin Biology Center led by Dr. Andersen is mentioned but is not included in Data Table 2A. The NSF Multiscale Cell Fate grant led by Dr. Qing Nie is included in the data table but is not listed as a multi-PI effort. Program efforts to translate basic science discoveries to the clinic have involved engagement of disease-oriented teams (DOTs). Interactions with the Heme DOT resulted in the transition of a concept developed in the laboratory of Dr. Fruman to a DoD-funded clinical trial concept in late 2020. A goal of the SPT is to take basic science discoveries and translate them to clinical utility. This may involve member transitions as the projects mature to preclinical drug development, the members may transition to the Biotechnology,

Imaging, and Drug Development (BIDD) program where three former SPT members have moved. The15% intra-programmatic, and 14% inter-programmatic publications represents an improvement and additional collaborative projects are expected.

Several innovative, team efforts are supported by the SPT program, CFCCC pilot grants, and shared resources. A collaborative inter- and intra-programmatic study directed by Drs. Lowengrub, Waterman, and Hughes demonstrated heterogeneity in Wnt signaling in colon cancer models that is associated with differences in tumor cell metabolism and cellular composition. The team developed a computational model that predicted the cellular heterogeneity and that co-targeting glycolysis and Wnt signaling should provide an effective therapeutic approach for this disease. They further developed a mathematical model predicting tumor/stromal interactions and ongoing studies are assessing the impact of the orthotopic microenvironment on tumor cell composition and growth. Moreover, they are refining the models as they transition from cell cultures to orthotopic systems. This project led to the funded U54 grant supporting the CaSBC and was supported by the GHTF, ETR, BSR, and OBC shared resources.

Early career investigators Drs. Lawson and Kessenbrock are conducting single cell transcriptomics studies examining normal breast tissue organization, premalignant changes in the microenvironment, immune suppression and metastasis. This team is now funded by the Chan-Zuckerberg Human Cell Atlas Initiative. This led to the discovery that basal cells of the breast form two types of luminal cells and resulted in a Nature Communications publication. Both Drs. Lawson and Kessenbrock are collaborating with other members of the CFCCC to identify epigenetic changes that may contribute to differences in OXPHOS in breast cancer metastasis, and characterization of MDSCs in breast tumors. These studies have been supported by the GHTF, OBC, ETR, and BSR shared resources. Both Drs. Lawson and Kessnebrock participated in the NIH boot camp grant writing program offered by the CFCCC to support early career investigators and earned major funding as a result of this activity.

Dr. Fruman discovered that statins can potentiate the efficacy of Bcl-2 inhibitors such as ventoclax in CLL and multiple myeloma. Dr. Fruman has now partnered with Dr. Brem to translate this finding for clinical utility. They are identifying predictive biomarkers of statin response in MM patients. In addition, an intra-programmatic collaboration has been developed with the Heme DOT to conduce a phase I dose escalation study in patients with CLL and AML and this work is funded by a DoD grant. This project was supported by a two pilot grants from the CFCCC and discussions with the Heme DOT. This is an important example of translation of basic science to clinical trials.

A collaboration between Dr. Kong and Waterman revealed that glutamine starvation promotes stemness in APC mutant intestinal organoids and PDX models. This work was published in Nature Cancer. Dr. Kong is further collaborating with Dr. Fruman to assess the impact of glutamine modulation on melanoma growth. This work was supported by a CFCCC pilot grant and OBC and ETR shared resources.

Clinical trials in ovarian, GI, and heme cancers are described but the initial leaders of two of these trials have moved. Dr. Jeyakumar is leading several Phase I/II trials in blood cancers. It is not clear if these activities involve collaborations within the program or are supported by the program. They appear to be independent efforts and, although a major goal of the SPT program, there is limited translation of basic science findings to clinical trials. Clinical trial accrual for the CFCCC is modest overall, involving 62 trials with 130 patients. An example provided that launched from the discovery of synergies between venotclax and statins entered into a Phase I trial in collaboration with the Heme DOT has only accrued 1 patient in 5 months. Additional translation of SPT discoveries to clinical trials should be facilitated by the DOTs.

Five cancers are identified as being catchment foci for the program: melanoma, gastric and liver cancers, and breast and ovarian cancers. Research in melanoma is focused primarily on basic

mechanisms that may ultimately lead to clinical intervention. In gastic and liver cancers, the members of the program are developing PDX models from diverse patients within the catchment. This may ultimately reveal novel pathways that control cancer outcomes in Asian-Pacific Islander groups within the catchment. A clinical trial in ovarian cancer using HIPEC was conducted by a former member of the center, having direct impact on catchment patients. In addition, the work using normal human breast and breast cancer specimens by Drs. Lawsen and Kassenbrock should reveal important insights regarding breast cancer risk in general. While studies are being conducted on catchment-related diseases, questions specifically addressing the unique features of the catchment are limited.

The program has been advantaged by the recruitment of new investigators and seed funding by the CFCCC. The CFCCC also provided support for retreats for the CaSBC, the T32, UCI symposia, and SPT members used all of the shared resources. The CaSBC and the Center for Complexity, Cooperation, and Community in Cancer were also developed from efforts by co-leader Dr. Lowengrub and others and are integral components of the SPT. A metabolism working group was also developed by the SPT and has been a major advance for the program. This group has regular meetings, has been supported by focused multi-faculty recruitment effort in metabolism. It also successfully advocated for an expansion of capabilities in the shared resources and has been awarded seed funding. The CaSBC and the metabolism group are major strengths.

In summary, the SPT program is a driver of innovation in basic sciences, particularly in systems biology. Notable accomplishments include the acquisition of a multi-PI U54 in Cancer Systems Biology, transition of a novel concept from Dr. Lowengrub's group to a clinical trial, albeit with limited accrual to date, the development of a strong metabolism working group, recruitment of exceptional early career faculty, and excellent training and education. These major strengths are offset by unclear engagement of the DOTs. The program communicates a clear goal of developing multi-investigator teams of clinical and basic science investigators to accelerate preclinical translation, but this has not yet been realized. In addition, the funding base is relatively low for this size of a program. Lastly, the extent of interactions with the COE and catchment related research are unclear.

Program Leader(s): The SPT program is led by Drs. John Lowengrub and Pamela Becker. Dr. Lowengrub has led the program since its inception and Dr. Becker recently joined as a new leader in the past six months. Program leadership is well qualified for this task and their respective roles are well described in the application and during the site visit.

Dr. Lowengrub is Chancellor's Professor of Mathematics, Biomedical Engineering and Chemical Engineering & Materials Science. His research program focuses on the use of mathematical modeling to understand feedback signaling, metabolic programming and interactions of tumor cells with the microenvironment. Dr. Lowengrub is also the founding Director of the interdisciplinary MS/PhD program in Mathematical, Computational and Systems Biology, is the co-Director of the NCI-funded UCI Cancer Systems Biology Center and is an Associate Director of the NSF-Simons Foundation Center for Multiscale Cell Fate Research. Dr. Lowengrub co-organizes a 3-week-long NCI R25 Short Course on Cancer Systems Biology. He is also involved in mentoring early career faculty.

Dr. Becker was recruited from the University of Washington/Fred Hutchinson Cancer Research Center in 2020 to be a Professor of Clinical Medicine in the Division of Hematology/Oncology at UC Irvine. Dr. Becker also assumed the role of co-PL of the SPT in 2020. Dr. Becker recently led an industry-sponsored trial (Novartis/SecuraBio) in multiple myeloma and was a co-I on a P01 on molecular determinants of cancer therapeutic response overseeing the experimental hematology core. Dr. Becker has published extensively on the treatment of hematologic malignancies. Dr. Becker has developed a CLIA approved in vitro high throughput cancer drug sensitivity assay for which she is the Medical Director. Dr. Becker serves as the interface between the basic scientists and the DOTs. She is also involved in systems biology collaborations associating mutations with drug sensitivity. Dr. Becker's

presentation at the site visit was strong and her leadership can help strengthen the translational basis of this program.

Assessment: Excellent to Outstanding merit

Budget: The budget is appropriate as requested.

Cancer Control Program (CC)

DESCRIPTION (provided by applicant): The scientific goals of the Chao Family Comprehensive Cancer Center (CFCCC) Cancer Control (CC) Program are to foster and facilitate research that identifies and reduces cancer risk and improves cancer outcomes and quality of life for patients and survivors in the CFCCC Catchment Area and beyond. The CC Program contributes to the overall mission of the CFCCC by strengthening the knowledge base for developing, implementing, evaluating, and disseminating strategies to our community to prevent and reduce cancer incidence, mortality, and morbidity. CC members work closely with the Office of Community Outreach and Engagement (COE) and provide leadership and guidance in conducting population-based studies and clinical trials. CC members play an important role in translating discoveries to the population. The CC Program Specific Aims are to identify, understand, and control risk factors to prevent cancer and improve outcomes through diagnosis, treatment and interventions to improve survivorship. CC members conduct research that spans the cancer control continuum. Researchers examine genomic and environmental influences on cancer; design, implement, and evaluate clinical trials to increase cancer screening; develop and assess innovative approaches to improve quality of life in children, adolescents, and young adults with cancer; test novel biobehavioral interventions in cancer survivors; conduct clinical trials to improve outcomes and prevent recurrence; and work to reduce disparities that impact those living within our community and beyond.

Membership: 45 Members from 19 Departments and 5 Schools
Funding: $1,528,757 NCI (Directs); $3,988,348 Other Peer-Reviewed (Directs)
Accruals: Interventional: 1,015; Treatment: 0; Institutional/Investigator-Initiated: 1,132
Publications: Total: 607; High Impact Journal: 84 (14%); Intra-programmatic: 68 (11%); Inter-programmatic: 92 (15%); Inter-Institutional: 410 (68%)

CRITIQUE: The Cancer Control (CC) Program brings together 45 members across 19 departments and 5 schools for the broad mission of fostering research to identify and reduce cancer risk and improve cancer outcomes for patients and survivors. CC program research is situated within two aims that span the cancer control continuum: Aim 1) Discover etiological factors for cancer occurrence and advanced disease to mitigate health disparities and Aim 2) Evaluate determinants and interventions to improve cancer outcomes and inform evidence-based practices. The CC program is led by recent hires Drs. Sunmin Lee and Joel Milam, both experience leaders with well-funded cancer prevention and control research agendas that are strongly aligned with relevant catchment area populations.

The CC research program is supported by $6.1 million in annual peer-review direct funding, a nearly 70% increase from the prior funding period ($3.8 million). Current NCI funding ($2.2 million) is similar to the last funding period ($2.3 million). The CC grant portfolio lists 9 fully cancer relevant R01s or equivalents across 7 different PIs. It is notable that this funding portfolio is reliant on multiple R01s brought to CC by investigators hired in the 6 months rather than emerged from CC research during the current funding period. The designation of funding from an addition 5 R01/equivalents across 5 PIs as partially cancer relevant is mostly appropriate with their focus on neuropathic pain, e-cigarettes, weight control. Although overall cancer focus is strong, the number of NCI-funded R01s is relatively low for a program of this size.

A total of 647 publications are reported, a commendable increase from 516 at the last review. CC members are highly collaborative with other centers (72% inter-institutional publications) with several involved in nationally- and internationally- visible research collaborations. The CC publications list contains an impressive number of publications related to therapeutics, genetics, and cancer outcomes in the highest impact medical journals (e.g., J Clin Oncol, Lancet Oncol, N Eng J Med, Lancet, Nat Genet) and many other examples of publications in upper tier journals for their respective fields.

Rates of intra- (11%) and inter- (15%) programmatic publications are relatively low and the examples of collaborative CFCCC publications are concentrated within a few investigative teams. Examples of collaboration of CC with other programs are noticeably absent from scientific highlights and there is a lack of involvement in team science grants. These issues raise concerns about a lack of integration of members within CC and across the center. Attention to the specific barriers to collaboration and strategies to address were noted as lacking by the EAB and the critique remains largely unaddressed. Newly formed momentum groups described at the site visit by the new co-Leaders are intended to facilitate collaborative research. This is a promising strategy, but there has not been sufficient time to demonstrate success.

For a program with a focus on cancer treatment, the clinical trial activity is low with 2 active treatment trials and limited accrual to them. There were 12 active intervention trials with 1,015 accruals although most of those are from two screening studies. Non-intervention trial accrual is 414. This represents a low level of activity for a cancer control program. Additional strengths include the progression of the chemoprevention research into a national Phase III trial and the presence of multiple IITs and early stage behavioral intervention trials.

CC Aim 1 is to prevent cancer by identifying and controlling risk factors with research highlights presented within the cancer control continuum space spanning etiology, prevention, and detection. Aim 1 research highlighted at the site visit included early-stage genetic studies seeking to identify biomarkers of aggressive prostate cancer in African American men and a large-scale trial of a pilot smoking cessation program delivered via social media. Both are examples are intra-programmatic collaborations supported by center pilot awards that led to Ro1 funding. The translation of the smoking research into policy-relevant studies of online nicotine advertising is exciting. Other notable CA-relevant Aim 1 research includes genetic analysis in ovarian cancer and Dr. Park’s R01-funded research to identify markers of pesticide exposure. The genomic research led by Drs. Edwards and Wenzel has produced several papers with multiple citations and is a strength in the prevention space. Cancer detection is a notable gap with research highlights reliant on research conducted by new faculty at prior institutions and non-published preliminary research.

CC Aim 2 is to improve outcomes by identifying factors that influence diagnosis, treatment, and survivorship. Dr. Tewari’s trial of Bevacizumab for advanced cervical cancer produced multiple publications in top journals (Lancet, N Eng J Med, and J Clin Oncol) demonstrating efficacy, safety, and cost-effectiveness. This work has direct impact on treatment with regulatory approval of bevacizumab by the FDA and other regulatory agencies across the world. The research of Dr. Bristow, Dr. Viera, and colleagues within CC and across CFCCC in the space of ovarian cancer treatment, survival, and geographical disparities, is a strong example of team science and global reach.

Aim 2 survivorship research is highlighted by Dr. Michelle Fortier's e-health intervention research for children's cancer pain management. Dr. Fortier’s formative work was supported by cancer center pilot that led to a funded R01 application. However, findings during this period are limited to preliminary studies. The intervention work of Wenzel and Nelson has strong potential for impact if efforts related to implementation and dissemination are continued. Dr. Hoyt has promising pilot data for a CA-relevant testicular intervention.

The CA has unique considerations including a large proportion of Latino and Asian American residents. Cancers accounting for the highest mortality in the catchment area mirrored the U.S. making lung and breast cancer high priorities. Latino residents have higher rates of cervix cancer incidence and mortality compared to Non-Hispanic Whites. Liver/Bile duct and gastric cancers are also concerning with elevated incidence and mortality among both Latinos and Asian Americans. Health behavior concerns include obesity, diet, and physical activity levels of Latino residents. Non-adherence to breast cancer screening among Latino residents and low colorectal cancer screening among Asian American residents were also present. The research highlights were generally well-aligned with cancer needs of the CA. Several newly recruited program members (e.g., Drs. Lee, Tanjasiri) have expertise in community engaged research methods which are likely to enhance translation of these scientific findings to the CA in the future. CA-relevant projects underway including Dr. Lee's studies of colorectal cancer disparities and colonoscopy decision support programs among Asian Americans, Dr. Timberlake's studies of e-cigarette advertising, and Dr. Park's environmental risk factor study. Additionally, 15 of 22 CC seed grants focus on specific issued relevant to the CFCCC catchment area, highlighted by Dr. Hoyt's pilot trial of an intervention to reduce distress among young adult Hispanic men with testicular cancer and two studies relevant to prevention of liver cancer. Moving forward, it will be important to address lung cancer and behavioral prevention research related to lifestyle, nutrition, and obesity as well as demonstrate use of COE infrastructure by CC members to disseminate evidence-based interventions, scientific findings, or policy recommendations to impact the catchment area.

Examples of impact can be found in the quite mature streams of research that were published early in the current funding period. Efforts to translate such findings into future studies that will sustain these long-standing areas of programmatic strength into the future will be important moving forward. There is some unevenness in the program aims and problematic gaps in behavioral science and risk behaviors for a program intended to address the cancer control continuum. There are however promising examples of emerging research that is expected to produce impactful findings in the near future and the new hires and pilot funding investments should help to close these gaps. This is a program with talented members, highly capable leadership, and a promising future.

CFCCC's investment in multiple faculty lines, start-up and recruitment packages, and pilot funding with discretionary and CCSG funding is substantial. There is solid utilization of CFCCC's shared resources by CC members. The described seminar series likely provides some value but there appears to be a lack of robust programmatic meetings and efforts to engage CC members. Value added is clear with resources but less convincing with catalyzing team science.

Future directions focus on several strategic areas. The first centers around melanoma and builds upon an area of high catchment area relevance and program strength. This represents a potentially high-impact opportunity for enhanced inter-and intra-programmatic collaborations. A SPORE grant is already in development including members from CC, BIDD, and COE. A minor weakness is a lack of expertise in melanoma prevention within the CC program. A second area of planned future growth is around AYA survivorship and builds upon strengths of Dr. Milam. Other plans are not as specific and may reflect the need for more faculty in these areas.

Program Leader(s): The CC program is led by Drs. Lee and Milam, who have both been recently recruited to CFCCC. Dr. Lee is a social epidemiologist with expertise in community-based participatory research and RCTs to intervene to reduce health disparities. Dr. Milam is a behavioral scientist with expertise in survivorship and cancer outcomes research. The co-leaders both have research programs that focus on health disparities, with specific focus on Asian American and Latino communities. These are directly relevant to COE areas of focus and add considerable value to the ability of the CFCCC to address the catchment area. The co-leaders have complimentary expertise and collaborate to oversee program aims, recruitment, mentoring, student training, and Program pilot projects. The new leadership hires have engaged members with needs assessment surveys and worked to coordinate multiple virtual

retreats in the last year and are encouraged to continue efforts to increase the frequency and relevance of programmatic meetings. AD Dr. Edward has served as a bridge in the leadership transitions but her role moving forward in CC is not well addressed.

Assessment: Excellent to Very Good merit

Budget: The budget is appropriate as requested.

SHARED RESOURCE MANAGEMENT

DESCRIPTION (provided by applicant): The central goal of Shared Resource Management (SRM) is to ensure that the seven Shared Resources (SRs) supported by the Chao Family Comprehensive Cancer Center (CFCCC) provide cutting-edge, cost-effective, easily-accessible services that facilitate high-impact cancer research. CFCCC SR services span the spectrum from patient-focused behavioral science to cellular and molecular aspects of cancer, providing high quality services that operate at the leading edge of their respective disciplines. In support of these services, the CFCCC provides financial support, management and oversight, ensuring that SRs offer state-of-the-art technologies, services and consultation. In the current funding period, the CFCCC has provided $1.12M for equipment costs alone. The overall total CFCCC contribution to support the SRs ($6.2M) was matched by institutional support from UC Irvine (UCI; $4.30M). The CFCCC directly manages one SR and jointly governs the other six with UCI academic units. Governance mechanisms and ongoing monitoring are in place to ensure that SRs are adequately supported and that they follow NCI guidelines for Cancer Center member accessibility, cost-effectiveness, and quality. The SRs are led by CFCCC Deputy Director (DD) Marian Waterman, PhD, with leadership assistance from the Associate Director (AD) for Administration & Finance Christine Hui, MPH. Together the DD and AD oversee and monitor the development and effectiveness of technologies and services offered to CFCCC members. Waterman and Hui are assisted by the ADs for Basic Science, Clinical Science, and Population Science & Cancer Control. The SRM team works on behalf of CFCCC membership to ensure priority access to technologies, services, and expertise that enhance scientific interaction and productivity; to monitor the stability, reliability, costeffectiveness, and quality of research resources; and to evaluate the scientific needs of cancer center members and facilitate the development and/or purchase of new technologies, services and methodologies. During the next funding period, the CFCCC plans to develop a new SR in Mass Spectrometry.

CRITIQUE: The CFCCC) provides financial and administrative management of seven Shared Resources to facilitate high-impact cancer research. These Shared Resources (SR) include the Transgenic Mouse Facility, Optical Biology Core, Genomics High Throughput Facility, In Vivo Functional Onco-Imaging, Experimental Tissue Resource, Biostatistics Shared Resource, and Biobehavioral Shared Resource. which provide cutting-edge, cost-effective, and easily accessible services. These SRs provide a broad spectrum of expertise and technologies to support the cancer research of CFCCC members as evident by the percent of users that are Cancer Center members (all but one has >40% of users CFCCC members). In addition, 75% of CFCCC members use at least one SR and 53% use more than one annually. Data supplied in the application shows steady increase in the use of SRs with stabilization in 2020 which can be explained by the impact of COVID-19.

CFCCC has added several mechanisms for the SRs to add value and cost-effectiveness for members including market comparisons, a newly established User Subsidy Program (7% subsidy for CFCCC members), Publication Rebate Program, and grant assistance for facility descriptions. Data on the effectiveness and outcomes of the first two of these programs will be useful for evaluating their effectiveness once the programs are fully implemented. SRs are located on two campuses, Orange and Main, which are located 12 miles apart. CFCCC has policies in place to enhance member access and utilization of institutionally managed SRs with priority access if a resource is nearing service capacity.

As six of the seven CFCCC Shared Resources are jointly managed with the institution, CFCCC Leadership and Administration and campus academic units share governance. All seven SRs receive direct oversight from the Deputy Director, Dr. Marian Waterman, in partnership with the Associate Directors of Basic, Clinical, and Population Sciences, and Associate Director for Administration and Finance, Ms. Christine Hui. The Associate Directors for Basic, Clinical and Population Sciences oversee specific SRs and along with a representative from Administration, are members of the Internal Advisory Councils (IAC) for each SR, which also include CFCCC members and non-member users. Each Associate Director reports back to Dr. Waterman on their assigned Shared Resources. There is no clear representation from the UCI Office of Research (OOR) in these meetings; however, SRs are responsible for providing budgetary information on an annual basis to a centralized UCI OOR recharge committee that oversees annual budget analyses and determination of rates.

In addition to the IAC, Shared Resource oversight is woven into multiple internal and external meeting platforms including the Associate Directors Committee, Program Leader and Shared Resource (SR) Directors (quarterly includes SR Directors and Managers), Internal and External Advisory Boards. CFCCC leadership appear responsive to recommendations from the advisory boards and committees on the SR. The narrative describes ad hoc meetings between the Associate Directors and SR Directors and Managers that happen regularly for immediate feedback. There are newly established SR Operations meetings that incorporate roundtable discussions of best practices by SR Directors and Managers and were specifically initiated to address issues with iLab implementation; however, plans are in place for these meetings to continue. Notably, the CFCCC engages strongly with all of these Shared Resources even those not directly managed by the center.

In 2020, the CFCCC spearheaded the purchasing and implementation of two new information management systems, iLab and EVAL. The use of iLab Solutions Software across these Shared Resources will greatly enhance oversight and management, as well as provide real-time data on usage and expenditures. With these new tools and initiatives for Shared Resource Management, CFCCC, on advice from the External Advisory Board, developed and hired a new staff position in January 2021. This position will greatly enhance the capabilities of Shared Resource management and oversight for the center.

In partnership with the School of Medicine, the CFCCC surveyed members in 2019 (42% responded) to evaluate each Shared Resource and obtain feedback on access, availability of training opportunities, responsiveness and staff professionalism, turnaround time, quality of data and services, and costs of services offered. In addition, this survey offered an opportunity for members to provided recommendations for improvements and suggestions for new technologies and/or services. It is hard to compare across cancer centers, but the overall results of the survey appear acceptable with about 50% rating the services as excellent and 30-50% more rating the services as good. Demonstrating the strength of this data, the CFCCC and the Optical Biology Core were able to utilize this feedback and support the purchase of a new super-resolution microscope and multiphoton system with CARS and FLIM imaging for deep-tissue imaging. Additional mechanisms have been effectively utilized by CFCCC for the continuous evaluation of the Shared Resources, including Shared Resource participation in the CFCCC Annual Scientific Meeting with town hall-based breakout sessions focused on emerging research trends and strategic directions. An emphasis on metabolism at this Annual Scientific Meeting led to the creation of a Mass Spectrometry Shared Resource in development. This is an excellent example of the cancer center delivering value to its membership and enhancing the research mission of the CFCCC. While plans are in place for this user survey to be issued annually moving forward, annual feedback over the last five years would have greatly benefitted the CFCCC Leadership in the formal evaluation of these Shared Resources. Mechanisms for addressing changes in satisfaction with individual shared resources will be substantially enhanced with this approach.

CFCCC leadership works with the Shared Resources to ensure that there is corresponding education and direct training on services and expertise, with each Shared Resources taking advantage of different avenues. Additional information on the quantity of training available for all of the Shared Resources, not just a select few, would be beneficial in assessing the full extent of their contributions to training and education at the Cancer Center and institution.

The center has planned for future Shared Resource needs using the 2020-2025 CFCCC Strategic Plan as a roadmap, that will provide enhanced and new technologies to CFCCC members and the community. Several important objectives over the next project period include enhancement of reporting and management capabilities with the implementation of EVAL and iLabs, expansion of user survey frequency, incorporation and expansion of training and education into existing education forums, further integration of Shared Resources into team science, growth into new technologies and service areas, and development of a Mass Spectrometry Shared Resource.

In the current funding period, the CFCCC provided $480K from the CCSG and over $780K from other CFCCC sources for new equipment and systems for these resources. However, details on the financial support for the SRs outside the CFCCC are difficult to assess. This is in part due to the more distributed model of administration and management of the SRs. It becomes difficult to assess the extent of institutional support to the shared resource effort in this respect. In some ways, the effectiveness of SRs is best shown in the quality of the science that they support and in this setting that appears to be robust.

In summary, the CFCCC demonstrates effective management and oversight of the seven Shared Resources. The CFCCC has made investments in new equipment and systems for these resources, including ~$1.13 million for equipment costs. In addition, the recent purchase and implementation of iLab will greatly enhance the effectiveness of center oversight and provide critical analytics to CFCCC leadership and IACs on the state of the Shared Resources. Concerns about the frequency and effectiveness of the user feedback survey have been addressed with plans to annualize this survey of Shared Resource users. Overall, the CFCCC effectively leverages both informal and formal oversight and management mechanisms to provide access to Shared Resources which support high-impact cancer research.

PERSONNEL: Dr. Grant MacGregor is the Shared Resource Director for the Transgenic Mouse Facility and has 32 years of experience in the design, production and analysis of genetically modified mice. He is well qualified to direct this Shared Resource. In addition, an experienced facility manager and staff oversee day-to-day operations.

Dr. Rahul Warrior is the Shared Resource Director for the Optical Biology Core and has a long-standing track record of utilizing microscopy technologies to image whole organisms, organs and tissues. He is well qualified to direct this Shared Resource. In addition, experienced facilities managers oversee operations at two locations.

Dr. Suzanne Sandmeyer is the Shared Resource Director for the Genomics High-Throughput Facility. She is the founding director of the facility and is highly qualified as Director. In addition, an experienced facility manager oversees operations.

Drs. Gultekin Gulsen and Zhuoli Zhang are Shared Resource co-Directors for the In Vivo Functional Onco-Imaging Facility. Dr. Gulsen has extensive experience, working on molecular optical and multi-modality imaging techniques for more than 20 years. He has served as Shared Resource Director for nearly 14 years. Dr. Zhang was recently recruited to UCI and for the last 20 years has been actively involved in CT/MRI/PET imaging modalities, cancer immunology and cancer metabolism. Both are well-qualified to direct this Shared Resource. In addition, an experienced facility manager oversees operations.

Drs. Robert Edwards and Wendy Cozen are the Shared Resource co-Directors for the Experimental Tissue Resource. Dr. Edwards is a board-certified surgical pathologist and has been the Director since 2012, prior to which he served for ten years as the Associate Director for the LCM facility. Dr. Cozen was recruited to UCI in 2020 from USC Norris Comprehensive Cancer Center where she served as co-Director for the Pathology Core and Director of the Tissue Modeling Core for a U54. Both are well-qualified to direct this Shared Resource. In addition, an experienced facility manager oversees operations.

Dr. Christine McLaren is the interim Shared Resource Director for the Biostatistics Shared Resource. She has over 36 years of experience in the design, conduct, and statistical analysis of clinical research. She is highly qualified to direct this Shared Resource. In addition, several experienced senior statisticians provide biostatistical support to CFCCC members.

Dr. Lari Wenzel is the Director for the Biobehavioral Shared Resource and has been in this role since 2003. Her breadth of experience in cancer survivorship, clinical trials research, and various leadership roles in the field, including as Associate Director of Population Science and Cancer Control for four years, and as Program Leader of the Cancer Prevention, Outcomes and Survivorship Program for three years, make her highly-qualified in this role. In addition, an experienced facility manager oversees operations.

Assessment: Excellent merit

Budget: The budget is appropriate as requested.

SHARED RESOURCES

Transgenic Mouse Facility (TMF)

DESCRIPTION (provided by applicant): The Transgenic Mouse Facility (TMF) Shared Resource provides expertise and raises awareness about existing and emerging methods and resources for the production and use of genetically engineered mouse models (GEMMs) to CFCCC members and help them incorporate these tools into their research. The TMF provides services on a recharge basis that require specialized and lengthy training, are technically difficult to perform, or use expensive equipment. The services cover design, development, re-derivation, cryopreservation, and reanimation of GEMMs in an efficient and cost-effective manner. The TMF provides information about new resources from the literature and available services include: a) consultation on strategies to engineer the mouse genome, b) targeted engineering of loci in mice via CRISPR/Cas-9 (94 projects completed as of September 2020), c) targeted transgenesis at the ROSA26 and Hipp11 loci, d) targeted engineering of endogenous loci in mouse embryonic stem (mES) cells, e) southern blot analysis of targeted loci in ES cells and animals, f) insertion of conventional multi-copy transgenes and bacterial artificial chromosomes (BAC) at random loci via pronuclear injection of DNA, g) cryopreservation, importation, export, rederivation or reanimation of GEMMs via IVF or embryo transfer, h) breeding and genotyping of GEMMs, and i) production of large cohorts of genetically defined mice for studies, by IVF and embryo transfer. The TMF collaborates and cost-shares with CFCCC members to develop or import new methods involving GEMMs. Consultation regarding projects for CFCCC members, including help writing grants and manuscripts, and providing letters of support, continues to be provided at no cost. In addition to CFCCC members, the TMF supports investigators at many different universities and corporations. These include academic institutions including five other NCI-designated CCCs (UCLA, UCSD, UCSF, Stanford, Indiana University) and several corporations (e.g., Irvine Scientific, Ionis Pharmaceuticals). The TMF also services investigators at institutions in eight additional states and the District of Columbia. A link on the TMF home page invites CFCCC members to contact the TMF Manager and Scientific Director to request a personal consult and training about resources for their

use, including advice on mouse models of cancer, identifying and importing strains of mice with cancer susceptibility, and mouse genetics resources of use in studying the cancer problem. TMF personnel identify resources tailored to meet researcher needs and provide these at the lowest possible cost in a timely manner.

CRITIQUE: The CFCCC TMF has been in existence since 1996 and provides superb services for generating, breeding, genotyping, importing, and preserving genetically engineered mouse models (GEMMs) on a recharge basis. The TMF is primarily an institutional core that provides a state-of-the-art service to a relatively limited number of CFCCC members. The shared resource is staffed by a highly competent team and is very effective at providing low cost, high value service for these members. This has led to a set of high impact publications. Oversight is provided by an IAC and the staff of the TMF actively updates skills and technologies. However, there appears to be limited prioritization for CFCCC members that occurs with cancelations by other users. Members will receive a subsidy for services with the new funding period. Since 2015, 78 CRISPR-based projects have been completed.

The TMF is directed by Dr. Grant MacGregor, who has impressive experience in the production and analysis of GEMM, including 21 years of experience overseeing Transgenic Facilities at Emory University and UCI. He is joined by a TMF Manager, a Project Scientist/Project Manager, and Staff Research Associates. TMF oversight includes interactions with CFCCC leadership during Shared Resource Director/Program Leader meetings, an annual Internal Advisory Committee meeting that includes two CFCCC members, and other administrative meetings at the university-level. TMF surveys have demonstrated feedback of high-quality of services.

The TMF receives an average institutional subsidy of ~43% from the Office of Research. In addition to CFCCC members, the TMF supports investigators at many different universities and corporations. These include academic institutions including five other NCI-designated CCCs (UCLA, UCSD, UCSF, Stanford, and Indiana University), several corporations, and institutions in multiple other states. Approximately 40% of services are provided to investigators at other academic institutions. Non-UC academic and commercial users pay higher rates for equivalent services subsidizing CFCCC activities. The Shared Resource Director provides advice and support (~35% effort), without re-charge. Relevant to the CFCCC, the TMF has appeared to help 6 investigators develop grants and/or publications. 18 publications were listed as being supported by the TMF, 5 of which were published since 2019. 72% of the publications were from four members of the CFCCC: Drs.Cahalan, Ganesan, Fruman, and Esser-Kahn. Services are provided on a first-come, first-served basis. This appears to include outside entities and CFCCC members are only provided priority for cancelled slots.

In the upcoming grant period, The TMF will continue its services and communications. Under development are technologies for humanization of mouse genetic loci (50 -> 200kb) via CRISPR-mediated genomic replacement and targeted transgenesis of BAC genomic clones to the Hipp11 locus. The CFCCC has plans to initiate a subsidy program to provide a 7% subsidy on SR services, including TMF, to CFCCC users. The TMF educates and trains CFCCC members predominantly on a one-on-one basis in person or via e-mail, phone, or Zoom. Additionally, the TMF Director and Manager present seminars to CFCCC members on general capabilities of the TMF (“Tech Talks”). Workshops and lectures by external companies are also offered by TMF to CFCCC members, however their frequency and structure remains unclear.

Overall, the TMF is an important resource for the CFCCC that is well-managed. There appears to be limited prioritization for CFCCC members that occurs with cancelations by other users. However, members will receive a subsidy for services with the new funding period. In all, this is an outstanding core facility for the CFCCC.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

Optical Biology Core (OBC)

DESCRIPTION (provided by applicant): The CFCCC Optical Biology Core (OBC) Shared Resource is a matrix SR on the UCI main campus, consisting of a self-use microscopy facility (SUF) in McGaugh Hall, the Non-Linear Optical Microscopy (NLOM) Laboratory in the Beckman Laser Institute, and the self-use Flow Cytometry Facility (FCF) in Hewitt and Gross Halls. The overall goals of OBC are to provide Cancer Center members access to cutting-edge optical technology and to develop new applications to further their research programs. The OBC is overseen by Director Rahul Warrior, PhD. Cancer Center members from all three programs utilize the OBC for state-of-the-art applications, including preparation for single cell RNA sequencing services provided by the Genomics High Throughput Facility (GHTF). To educate and train users, OBC organizes monthly workshops, Tech Talks, and training sessions. The Self- Use Facility (SUF) has three confocal microscopes, a Zeiss Elyra 7 lattice structured illumination microscope capable of super resolution imaging and a Zeiss Z1 Light Sheet microscope. A 2-photon laser for deep tissue imaging and single photon lasers for imaging all fluorophores from DAPI (405nm) to far red (633nm). A fluorescence lifetime microscopy (FLIM) detector for studying molecules based on their fluorescence lifetime provides a way of both studying metabolic states and more sensitive measurements of FRET. Adeela Syed, PhD manages this facility and provides training, on-site troubleshooting and experimental advice. Training is provided for Image Analysis software packages available on high end workstations or from individual office computers. The NLOM laboratory focuses on collaborative use and protocol development using a number of microscopes and technologies developed in-house. These include multi-dimensional microscopy platforms that allow researchers to non-invasively screen for skin and breast carcinomas using visible light (diffuse optical spectroscopy and imaging, DOSI), rather than X-rays. Mihaela Balu, PhD directs the NLOM, and specialist Amanda Durkin provides consultation and protocol development for investigators seeking new imaging applications. NLOM support includes shop facilities that allow construction and modification of imaging platforms. The FCF operates four flow cytometers for fluorescence-activated cell sorting (FACS) for analysis, emerging flow cytometry assays and preparation for single cell analysis and sequencing. The available instruments include an Amnis ImageStreamx Mark II Imaging Flow Cytometer which combines flow cytometry capability with the detailed imagery of microscopy. Data is analyzed using IDEAS® software; an ACEA NovoCyte Flow Cytometer; two cell sorters (BD FACSAria Fusion and BD FACSAria II SORP) and the Aria II Temperature Control system. The FACSAria Fusion is housed in a biosafety cabinet for sorting cells that are exposed to BSL2 viruses. A new Helios Cytometry Time of Flight system (CyTOF) enables single cell analysis of 40+ parameters. Jennifer Atwood, PhD manages this facility and provides instrumentation training as well as advice on experimental design and data analysis.

CRITIQUE: The OBC at CFCCC is a matrixed shared resource situated on the UCI main campus and has been in operation for 34 years. The OBC comprises a self-use microscopy facility (SUF), the Non-Linear Optical Microscopy (NLOM) Laboratory, and the self-use Flow Cytometry Facility (FCF). The overall goals of OBC are to provide center members access to cutting-edge optical technology and to develop new applications to further their research programs. The staff supporting the resource are well trained and experts in their respectively fields. There is a large user base and the shared resource is highly cost-effective. Appropriate prioritization is in place and the shared resource provides exceptional training and education opportunities. The core clearly supports ongoing innovation.

The OBC is directed by Dr. Warrior since 2018. Dr. Warrior is an Associate Professor in Developmental and Cell Biology. He oversees the managers of each of the three facilities. Cancer Center members from all three programs utilize the OBC. The staff are well qualified to provide innovative microscopy and flow sorting capabilities to the CFCCC membership. The OBC has oversight by an internal advisory committee that considers feedback from the user community – this has resulted in the purchase of a Zeiss Elyra 7 system and a Leica SP8 multiphoton system.

The Self-Use Facility (SUF) has three confocal microscopes, a Zeiss Elyra 7 lattice structured illumination microscope capable of super resolution imaging and a Zeiss Z1 Light Sheet microscope. There is also a 2-photon laser for deep tissue imaging) and a fluorescence lifetime microscopy (FLIM) detector for studying FRET. Notably, FLIM has been developed in the Laboratory for Fluorescence Dynamics at UCI. The NLOM laboratory includes multi-dimensional microscopy platforms for non-invasively screening skin and breast carcinomas. The FCF houses four flow cytometers for FACS and preparation for single cell analysis and sequencing. There also is a Helios Cytometry Time of Flight system (CyTOF) for single cell analysis of 40+ parameters.

Each of these facilities is administered by a Manager who oversees daily operations and also provides assistance and free training. The OBC organizes workshops, Tech Talks, and training sessions to train users. The NLOM facility provides consultation and protocol development for investigators seeking new imaging applications. Approximately 60 new users from CFCCC laboratory groups are trained annually.

The OBC facility is used by >200 unique users, with >50% of its usage by CFCCC members. 33% (44 members) of its users are funded CFCCC members and an additional 13% are unfunded members. The OBC lists 60 member publications supported by the shared resource over the prior funding period. Many of these were published in high tier journals (Cancer Discovery, Nature Communications, PNAS, JCI, Developmental Cell, Nature Cell Biology, etc.). While there are many cancer relevant manuscripts, there were also several that appeared to be strictly focused on developmental biology or non-cancer topics. Cancer Center members can request priority to reserve instruments and receive an instrument time credit (although the details of this remain unclear) as well as a $250 subsidy towards publication costs when acknowledging CFCCC and OBC support. The costs of all the facilities are very reasonable as evidenced by costs relative to other UC locations.

Overall, the OBC is an exceptional core and of great value to the CFCCC. The OBC holds 6–8 formal workshops each year. Facility Managers lecture in the graduate Cell Biology course every fall, give presentations to Disease-Oriented Teams, and speak at Tech Talks sponsored by CFCCC and the School of Medicine. The training aspects of the OBC are superb. Moving forward, the OBC will continue to educate its users in various applications, expand their workshop schedule, and employ new technologies for imaging.

Assessment: Exceptional merit

Budget: The budget is appropriate as requested.

Genomics High-Throughput Facility (GHTF)

DESCRIPTION (provided by applicant): Since its inception more than twenty years ago, the UCI Genomics High-Throughput Facility (GHTF) has introduced and supported emerging technologies for CFCCC members. The Aims of the GHTF are: 1) to provide analysis and cutting-edge technologies to enable breakthroughs in cancer research; 2) to provide analytical support for interpretation of high throughput genomics and transcriptomic data; and 3) to provide an environment that encourages awareness and adoption of new technologies for basic and translational research. Featured technical and analytic services currently address long range genome mapping, gene expression including epigenetic, chromatin, and splicing levels of regulation, and effects of tissue and tumor cellular heterogeneity on carcinogenesis and development. Library preparation to enable these findings includes, but is not limited to, DNA libraries for whole genome sequencing, ATAC-seq including for single-cells, and Me-Seq and RNA libraries for long (Iso-seq) and bulk and single-cell transcript analysis. The GHTF brings special value to each of the CFCCC programs. In the case of the Systems, Pathways & Targets (SPT) Program, the GHTF provides insight into potential therapeutic targets in breast cancer, melanoma, colon cancer, and metabolic pathways. For the Biotechnology, Imaging and

Drug Development (BIDD) Program, single-cell sequencing performed in the GHTF is increasing understanding of the extent to which a three dimensional, vascularized culture system reflects physiological changes associated with cancer and personalized patient tumor drug sensitivity. In the Cancer Control (CC) Program, the GHTF works with newly recruited faculty experts in the population variation of cancer susceptibility by providing economical bead array genetic diversity screening for dissection of genetic contributions to ethnic differences in cancer susceptibility. In one of the most critical developments, the GHTF has synergized with the CFCCC and researchers in the U54 Cancer Communities program to develop a single cell sequencing core that has supported funding of the U54 grant itself, and also enabled discoveries related to tumor development, heterogeneity and metastasis. Finally, the GHTF provides bioinformatics support for individual analysis, workshops and making available current approaches in analysis via readily accessible containerized pipelines and providing portals through which internal and external data sharing is enabled. In the next funding period, the GHTF will continue its high level of service to CFCCC members. In addition, there will be 1) introduction of genetic screening using bead array technology; 2) investments in spatial omics collaboratively with the Stem Cell Research Center; 3) emphasis on translational outreach through expanded interactions with the disease-oriented teams; and 4) expansion of analytical support through additional bioinformatics staff and self-sustaining workshop programs.

CRITIQUE: The Genomics High-Throughput Facility (GHTF) has been in place for more than 20 years and is an integral resource for many members of the CFCCC. Members from all three programs utilize the shared resource. The GHTF supports library preparation and a broad array of sequencing protocols including single cell RNA, ATAC, and Iso-seq and bulk RNA, DNA, ChIP, Me, miRNA, and CLIP-seq. In the past two years it is also expanded to include single cell genomic analysis. The GHTF provides both sequencing and analytics services to the CFCC. This shared resource has invested substantially in new technology during the period of the last funding period and appropriate equipment is available to obtain rigorous data. These include MiSeq, NovaSeq, HiSeq4000, 10X Chromium, NanoString nCounter Max, Sequel II and BioNano Saphyr II that can be used to detect rearrangements and chromosome variants. The shared resource also provides some bioinformatics support in the form of experimental consultation and computational pipelines. In addition, the GHTF facilitates data sharing through engagement of the high-performance computing cluster at UC Irvine.

The GHTF is led by Dr. Suzanne Sandmeyer, the founding director of the GHTF. She has considerable expertise in single cell sequencing technologies and management of shared resources. Dr. Melanie Oakes provides direct support for sequencing and Dr. Jenny Wu is the Bioinformatics Director of the shared resource. Dr. Wu supervises 1 support personnel (unnamed) to provide bioinformatics support. The bioinformatics support is shared across the UCI and there does not appear to be an individual that is solely committed to supporting cancer center member needs.

The GHTF is guided by Internal Advisory Committee (IAC) comprised of ~20 members that meets annually and as needed. In addition, annual surveys as well as meetings with program leaders are used to inform the GHTF of emerging needs. These guide capital expenditures for genomics instrumentation to meet user demand. Overall, it appears that the use of the GHTF has shifted slightly more toward non-Cancer Center users in terms of costs given the rise of single cell sequencing.

The GHTF supports a large number of workshops (~10/year) that are primarily focused on technologies. Dr. Wu also leads quarterly workshops in bioinformatics and individual consultation upon demand. Drs. Sandmeyer and Wu consult with users to facilitate experimental design. The workshops are widely attended by graduate students and post-doctoral fellows. Specific training in bioinformatics for CFCCC membership is not specified and the degree to which bioinformatics needs of the membership are being met is unclear. Future plans included engaging in population-based genetic and epigenetic studies, to expand spatial ‘omics, translate basic science discoveries to the clinic, and expanding bioinformatics support. It is notable that increasing training in bioinformatics was a goal of

the prior funding period and this continues to be a need. It is anticipated that the new leader of the BDR will bring bioinformatics expertise and focus to the center.

The GHTF has expanded its suite of services and a large number of CFCCC members have used the resource. Of the 129 users of the GHTF in the last year, 33 (26%) were funded CFCCC members. An additional 17 (13%) unfunded members also used the GHTF. Currently, CFCCC members receive priority access. Members also benefit from free consultation and workshops as well as discounted access to Ingenuity Pathways analytics software. The chargeback structure for the GHTF is comparable to other University of California schools (UCSD and UCLA). Thus, the facility is cost-effective. Beginning in 2021, the GHTF anticipates providing a 7% subsidy to CFCCC members. The GHTF lists 62 publications from the prior funding period. Many of these were in high tier journals (Cell, Nature Communications, PNAS, etc.), however, many of the cited publications had questionable cancer relevance.

Overall, the GHTF supports the research programs of many of the CFCCC members and this has led to numerous high impact publications. While many of these are cancer relevant, there were also a number of publications listed with questionable cancer relevance. In addition, while the facility provides clear support for the mechanics of the sequencing projects, there appears to relatively limited bioinformatics support for the large amounts of data generated with these methodologies. Access to pipelines and commercial software appear to be the primary approach. The educational methods for resolving some of these data analysis issues is not entirely clear. In addition, it is unclear whether the resource is providing innovation in tool development or data analytics.

Assessment: Excellent to Very Good merit

Budget: The budget is appropriate as requested.

In Vivo Functional Onco-Imaging (IVFOI)

DESCRIPTION (provided by applicant): The In Vivo Functional Onco-Imaging (IVFOI) Shared Resource provides CFCCC members with ready access to state-of-the-art imaging technologies, consultation for design of experiments and imaging protocols, and image acquisition and data analysis, as well as coordination among individual projects. IVFOI provides numerous imaging modalities for preclinical and clinical studies and supports researchers by contributing to their study design, helping with IACUC and IRB protocol preparation, and with data analysis after imaging sessions. IVFOI team members continuously support researchers during imaging studies through acquiring the imaging data and coordinating the clinical study or handling the animals. Furthermore, the IVFOI team provides support by analyzing and interpreting the results. The value provided by the IVFOI Shared Resource is enhanced by IVFOI's ability to customize imaging techniques for any specific research project and availability of novel molecular multi-modality imaging techniques that exist in only a handful of institutions worldwide. Some examples of these capabilities are two new patented imaging technologies: i) Temperature-modulated Fluorescence Tomography and Photo-magnetic Imaging, where optical and nuclear molecular imaging techniques are integrated on a commercial preclinical irradiator; and ii) integration of a custom-built X-ray CT system with a Laser Compton Source to investigate K-edge subtraction imaging with a tunable monochromatic X-ray beam. These capabilities allow IVFOI to not only provide service to the CFCCC members but also attract users from other academic institutions such as Children's Hospital of Orange County, UCLA, UC Davis, UC Riverside, and City of Hope, in addition to many local, national and international companies with commercial imaging and contrast agent/drug development programs. The IVFOI continuously explores ways to expand its systems and services. In addition to having new imaging systems for Cancer Center members and efforts in data analysis, adding Artificial Intelligence (AI) data analysis to the portfolio of services is a future plan for IVFOI. Although most of the novel imaging techniques are oriented towards preclinical imaging, IVFOI team is already upgrading those systems to translate them into clinical

arena. MRI-compatible nuclear imaging and photo-magnetic imaging of breast cancer are two examples. Besides instrumentation development, IVFOI also work towards facilitating clinical trials. One IVFOI highlight is the successful clinical trial of a folate-targeting ovarian cancer fluorescent imaging agent developed by On Target Laboratories. If the Phase III clinical trial of these ovarian cancer targeting agents with an intraoperative fluorescent camera is successful, this will be the first commercially available optical molecular smart probe in clinical use.

CRITIQUE: The overall goal of the In Vivo Functional Onco-Imaging (IVFOI) Shared Resource is to provide CFCCC researchers with expertise in imaging instrumentation and data analysis. This shared resource has the capacity to integrate molecular and structural imaging modalities and to develop new contrast agents and molecular pathway-specific imaging probes .The shared resource aims to: 1) enhance molecular imaging capabilities by leveraging cutting-edge optical and nuclear imaging technologies for preclinical studies; 2) to translate new imaging modalities to the clinical arena; and 3) to support translational clinical studies, with precise protocol execution and high-standard quality control. The IVFOI has 2 new patented technologies (1)Temperature-modulated Fluorescence Tomography and Photo-magnetic Imaging, where optical and nuclear molecular imaging techniques are integrated on a commercial preclinical irradiator; and (2) integration of a custom-built X-ray CT system with a Laser Compton Source to investigate K-edge subtraction imaging with a tunable monochromatic X-ray beam. The shared resource activities use several imaging systems including MRI, MRI-sodium imaging, hybrid MRI and nuclear imaging, PET/CT, SPECT/CT for human use and combined MRI and DOT, hybrid MRI-SPECT; micro PET/CT for animal use.

The IVFOI Director is Dr Gultekin Gulsen, an Associate Professor of Radiology, who served as Director or Co-Director since 2002. He has expertise in in vivo optical imaging and multi-modality imaging; is well published and funded. He is well qualified to lead the IVFOI. Dr. Farouk Nouizi is the IVFOI manager and one animal technician aids with core activities.

Imaging technology and expertise for data analysis are state of the art. The IVFOI is supported by the CCSG (35%), charge backs (28%) and other sources (36%). 70% of core utilization is from CFCCC members. The core has provided services to members resulting in >45 publications. Several high impact contributions are highlighted. The IVFOI team successfully completed a study in collaboration with Purdue University using image guided surgery for ovarian cancer with use of a folate targeting fluorescent imaging agent and collaborated with City of Hope and UC Davis on an R01 evaluating optical tomography and PET in a multi-modal imaging system for guided and targeted (theranostic) radiation treatment. An internal advisory committee reviews the activities of the IVFOI annually and a survey of users in 2019 documents satisfaction of the members with the services. Costs are comparable to other centers.

Overall, the IVFOI is clearly essential for translational research and clinical trials and provides added value to the CFCCC members. However, the description of core activities relative to clinical trials is not well described. Future plans include expansion of services and acquisition of several new systems for animal research, with additional services related to use of AI for data analyses.

Assessment: Excellent to Outstanding merit

Budget: The budget is appropriate as requested.

Experimental Tissue Resource (ETR)

DESCRIPTION (provided by applicant): With facilities on the UCI main campus and at UCI Medical Center in Orange, the Experimental Tissue Resource (ETR) is a Shared Resource in its 20th year of service to members of the Chao Family Comprehensive Cancer Center (CFCCC). The overarching

goal of the ETR is to provide access and analysis of human and animal tissues for basic, translational, clinical and population research. Due to high demand, the ETR has expanded personnel and services to include a user-searchable Pathology Database of Archival Tissue and is currently developing a service for custom tissue microarrays with stains that can be analyzed via digital pathology software. ETR services include tissue procurement from patients treated at UCI Medical Center as well as liquid samples (blood, saliva, urine, fecal) and remnant diagnostic formalin-fixed, paraffin-embedded (FFPE) specimens. The new user-searchable Pathology Database of Archival Tissue is a virtual biorepository portal that allows investigators to search by final diagnosis for (de-identified) human tissue specimens. This service is linked to standard histological services that include tissue embedding, FFPE and frozen tissue block sectioning, and histology services. Histology services include cytochemical stains, immunohistochemical staining of targets (IHC), and interpretive histopathology consultation. Additional services include preparation of re-cut slides or tissue shavings for nucleic acid extraction. Equipment systems are provided for automated IHC staining, optimization of non-standard IHC protocols and high-resolution slide scanning, and electron microscopy via the Department of Pathology and Laboratory Medicine's histology division. Mouse pathology services include necropsy and histopathology consultations, as well as consultations on tumor models and xenografting (subcutaneous and orthotopic). The ETR is led by Co-Directors Robert Edwards, MD, PhD (SPT), and Wendy Cozen, DO, MPH (CC). Edwards is a board-certified surgical pathologist and has more than 20 years of expertise in mouse pathology. Cozen is a cancer epidemiologist with 15 years of experience in pathology services. ETR manager Delia Tifrea, PhD, MBA has 16 years of animal tumor model experience and is available for consultations of mouse necropsy and one-on-one instruction for xenograft and orthotopic tumor modeling. Embedded within the Specific Aims of the ETR are plans for CAP certification of the laboratory, introduction of automated tissue microarray capabilities with digital pathology analysis (VisioPharm, Inc.), and outreach activities to train Cancer Center members in the utilization of new ETR technologies and databases. ETR Specific Aims for the next funding period are to i) provide human and animal tissue procurement, high-quality histology services and interpretive consultations; ii) facilitate outcomes research by developing query tools that link tissue data in the CoPath database with demographic, therapeutic and outcomes-based data in the electronic medical record (Epic); and iii) obtain full College of American Pathologists accreditation.

CRITIQUE: The primary objectives of the Experimental Tissue Resource (ETR) are to provide basic, translational, and clinical researchers within and outside of the CFCCC access to, and analysis of, human and animal tissues. This resource leverages the expertise of the Department of Pathology and Laboratory Medicine. Three primary services are offered: 1) Tissue and Correlative Clinical Data Procurement and Distribution, 2) Tissue Histology, IHC and Digital Pathology services, 3) Interpretive Histopathology and Mouse Pathology services.

The leadership of the ETR has been strengthened with the addition of Dr. Wendy Cozen, a medical epidemiologist, who has joined from the USC Norris Cancer Center as the Co-Director. Dr Cozen has a strong track record of NIH/R01 funding in hematologic malignancies and has prior experience in solid and liquid tumor banking with linked outcomes data. She joins Dr. Robert Edwards from the Department of Pathology who has led the ETR since 2012. A key highlight from the CFCCC leadership has been the retention of the ETR Manager, Dr Delia Tifrea who has been an important resource in both basic tissue banking as well as the development of patient derived xenograft models.
The ETR core uses a virtual portal Pathology Database of Archival Tissue (Sunquest CoPathPlusTM) to search and access resources. Over 50% of core utilization is from CFCCC members, and the usage has increased by 33% compared with the previous funding period (111 users during the past year). Within the CFCCC; utilization is reported by 35% of BIDD members, 51% of SPT members and 38% of Cancer Control members. Funding is provided from the Cancer Center (41%), Recharge (49%) and other sources (10%). A total of 47 publications are reported which is a slight decrease from 2015. The ETR leadership however notes several high impact publications resulted from significant ETR resources and expertise including one in Nature Communications. A critical success of this shared resource is the support for the Cancer Systems Biology grant as well as the Minority PDXNet project.

In response to EAB reviews, the ETR has developed a HIPPA compliant searchable tissue database utilizing coPath from which a request can be made to have the ETR staff link the associated outcomes from the EPIC EMR as an honest broker. This is a step in the right direction for annotated specimens but appears to be labor intensive and it is not clear if these are linked to the cancer registry. The histology component provides high-quality service at below-market recharge rates in comparison to other NCI biorepositories. Going forward, priorities for growing the service include a new “opt-in” consent for remnant tissue, development of tissue microarrays and digital pathology platforms as well as CAP accreditation for the biorepository.

In summary, this is well managed and increasingly utilized shared resource for the CFCCC. Data generated by the IVFOI contributed to over 45 publications. Services provided are appropriate and cost efficient. Within the application, the number of specimens banked are not clear nor are the quality assurances processes adequately described. Improvement in data annotation has been achieved during the current funding period. Leadership of the IVFOI is strong and plans for growth are well described. This CFCCC shared resource is on an appropriate trajectory and provides an important service to members.

Assessment: Excellent merit

Budget: The budget is appropriate as requested.

Biostatistics Shared Resource (BSR)

DESCRIPTION (provided by applicant): The Biostatistics Shared Resource (BSR) provides statistical support to CFCCC investigators at all phases of scientific projects, from conception and design through data analysis and reporting. The BSR is staffed by three PhD-level statisticians and one MS-level statistician with specific expertise in clinical trial design and sequential monitoring, optimal experimental design and dose-response models, epidemiologic methods including survival and longitudinal data analysis, evaluation of diagnostic tests, and statistical genetics. BSR services include study design, power/sample size determinations, assistance with database design and maintenance, full data analysis and interpretation of statistical and scientific results, as well as abstract generation and manuscript drafting. BSR faculty and staff maintain offices on the both main UCI campus in Irvine and at UCI Medical Center in Orange. A presence at both locations provides CFCCC investigators with easy access to BSR consultations at all times. The overarching goal of the BSR is to integrate solid statistical methods and study design, efficient use of resources, and analysis of data in all CFCCC research projects. To achieve this, BSR faculty and staff partner with CFCCC members for close involvement in the conception, design, implementation, analysis, and reporting of research projects. While significant effort is devoted to collaboration and consultation with CFCCC investigators, the BSR also develops new statistical methodologies that relate to the scientific needs of CFCCC investigators. The aims of the BSR are to consult and collaborate with CFCCC members and Shared Resources in all aspects of basic, translational, and population research, to consult and collaborate with CFCCC in carrying out clinical research, and to provide biostatistical and methodological review of all cancer protocols submitted to the CFCCC Protocol Review and Monitoring Committee (PRMC) and Data and Safety Monitoring Board (DSMB).

CRITIQUE: The Biostatistics Shared Resource (BSR) provides statistical support to CFCCC investigators at all phases of research projects, from conception and design through data analysis and reporting. It also provides statistical reviews of all cancer protocols submitted to PRMC, supports DSMB activities, and provides educational opportunities through formal seminars, lectures, and individual consultations. The majority of the BSR operating budget comes from CCSG, 7% (or 4%) from chargebacks, and other sources.

The BSR has been productive in the current funding period. A total of 78 publications used BSR support, 58% co-authored by BSR members. Between 2/1/2019 and 1/31/2020, there are a total of 68 users, 34% as members with peer-reviewed funding and 51% as members without peer-reviewed funding, and 10 users were non-members. The application highlights 3 examples of high-impact studies one from each program. It is evident BSR has been providing high-quality and cost-effective statistical support. The user survey conducted in 2019 reported 80% of responders gave excellent (50%) or good (30%) ratings. Since the last review, the IAB had met twice (2018 and 2020) with a plan to meet annually moving forward.

In the current funding period, the involvement with the basic science programs (BIDD, SPT) appears to remain limited with the majority of the publications from the CC program even though the overall usage seems to be comparable between the three programs according to the site visit presentation.

Dr. Christine McLaren, Professor in the Department of Medicine, is serving as interim Director for BSR since 2016. Dr. McLaren has more than 34 years of experience in clinical research and is well qualified for this position. She is also a member of the CC program and serves as Co-Chair of the CFCCC Protocol Review and Monitoring Committee (PRMC). The faculty and staff of the BSR have expertise in several areas of statistical methodology and cancer applications. Drs. Dr. McLaren, Taylor, and Ziogas are all well-qualified for their roles in the BSR and have been actively engaged with CFCCC collaborations. During the virtual site visit, it was noted that the recruiting of the permanent Director is in the final stage.

Currently, the BSR is lacking bioinformatics expertise but it was explained during the virtual site visit that Dr. Jenny Wu from the Genomics High Throughput Facility (GHTF) is leading that efforts at the moment and they are in the process of expanding her team. The concern is that Dr. Wu's group provides support to the whole campus, not specifically to cancer center members, and interactions between the BSR and Dr. Wu are unclear, which may be a missed opportunity. The ongoing recruitment of the permanent Director position also has been focusing on expanding bioinformatics expertise. The hiring of the new Director has the potential for additional expansion in the BSR memberships to cover emerging areas such as machine learning, statistical methods for next-gen sequencing or single-cell sequencing data analysis, and early phased clinical trial design. In the short term, lacking expertise in those areas may continue to hinder BSR's interaction with the BIDD, SPT programs. One of the stated functions for the BSR is to assist in database design and data linkage of clinical, epidemiologic, and laboratory data but specific BSR efforts on this are unclear.

The funding model for BSR is appropriate and has been productive (~ 48 grant applications/year have resulted from the free-of-charge proposal development assistance). The coordination plan with the two other biostatistics units on campus for non-biomedical and/or non-cancer-related biomedical projects is in place and also appropriate.

In summary, the BSR provides necessary and critical services to a large number of cancer center members. The BSR has been productive in the current funding period but the lack of expertise in areas such as bioinformatics and other state-of-the-art statistical methods have limited their interactions with the BIDD and SPT programs. Successful recruitment of the permanent Director in a near future will be critical to address this concern and enable growth in the services offered.

Assessment: Excellent to Outstanding merit

Budget: The budget is appropriate as requested.

Biobehavioral Shared Resource (BBSR)

DESCRIPTION (provided by applicant): The Biobehavioral Shared Resource (BBSR) was established to assist cancer researchers to measure, collect, and integrate patient-reported outcomes (PRO) into their respective Cancer Center research programs. The aims of the BBSR are to support cancer researchers by providing the necessary expertise and assistance to incorporate patient/participant-reported outcomes into research projects, to assist cancer investigators with focus group design and patient counseling interventions, and to expand services to include the latest technologies in biobehavioral measurement science to meet scientific needs. Specific services include behavioral and quality-of-life self-report measurement recommendations, research design considerations including focus group development and conduct, patient counseling intervention development, PRO data collection strategies, interpretation of self-report data, and grant and manuscript preparation. The BBSR supports a primary Aim of the Cancer Control (CC) Program to foster and facilitate research that identifies and reduces cancer risk and improves cancer outcomes throughout the disease continuum. In addition, the BBSR engages in collaborations with the Biotechnology, Imaging and Drug Development (BIDD) and Systems, Pathways & Targets (SPT) Research Programs and with outreach projects in cancer health disparities and community engagement. Lari Wenzel, PhD has served as the BBSR Director since its inception in 2003. She is a Professor of Medicine and Public Health at UCI and has expertise in quality-of-life assessment and clinical trial development in cancer. The BBSR is managed by Chelsea McKinney, PhD, MPH who specializes in behavioral health, clinical medicine, and health disparities with a strong background in research design and project management. Future plans include expanding upon these services to extend state-of-the-science health-status screening via an electronic platform. Further, an innovative collaborative expansion is being considered to include salivary biomarker collection which would augment certain biobehavioral studies. These expanded services are likely to increase the user base across all Programs. In this manner, the BBSR will continue to be a valuable and cost-effective shared resource that contributes to the research efforts of CFCCC members and UCI faculty addressing the broader Catchment Area.

CRITIQUE: The aims of the Biobehavioral Shared Resource (BBSR) are to: 1) support cancer researchers to incorporate patient-reported outcomes into research projects; 2) to assist with focus group design and conduct, and patient counseling interventions; 3) to expand services to include the latest technologies in biobehavioral measurement sciences. To achieve these aims, the BBSR offers researchers a variety of services for qualitative research design, data collection and interpretation. Additional expertise in patient reported outcome instrument selection and development, along with integration of these measures into other research projects is described. This focus makes it distinct from the services offer by the BSR. The BBSR receives 13% of its support from the CCSG, 58% from UC Irvine (Other), and 29% from charge backs.

The majority of the users of the BBSR are from the CFCCC, and the vast majority of use comes from the CC program. Usage has remained relative stable over the 2015-2020 period. The BBSR contributed to 13 funded grants (7 NCI) and 32 publications during this period. Dr. Wenzel is a co-Investigator on nearly all of the studies that use the BSSR, leading to the question of the reource in terms of value added to the broader center membership. Examples of collaborations with all CFCCC Programs are described, although it is noted that some of the references (4, 8, 13) do not appear to relate to the services offered by this Shared Resource.
Of the total utilization, it appears there were 26 total users (12 of 195 members, ~6% of members use this service), although it is not clear how many unique consultations occurred over the period, nor are metrics clearly included about user satisfaction. There is notable usage beyond the CFCCC, across the country and with other NCI Cancer Centers.

The integration of the PROMIS into the Epic modules and workflow is a great achievement, but still in pilot stages. Collaborations will be critical to utilize and grow this resource but resources or plans to promote the collection and usage of these data by CFCCC members are not adequately discussed.

This, along with the process for identifying, prioritizing and integrating other technologies in Biobehavioral Sciences (Aim 3) are not well described.

The BBSR remains under the excellent leadership of Dr. Lari Wenzel, an expert in QOL assessment and developing interventions for cancer survivors. She is joined by Dr. McKinney, who serves as Facility Manager. She has managed studies that include patient reported outcomes for over a decade.

In summary, the BBSR provides a niche service to a small number of CFCCC members and usage has remained relatively stable. Notably, the BBSR serves as a resource for collaborators across the country. While the integration of PROMIS into the electronic medical records is laudable, there does not appear to be a robust process to encourage and facilitate the integration of this or other technologies into CFCCC research.

Assessment: Very Good to Excellent merit

Budget: The budget is appropriate as requested.

CANCER RESEARCH TRAINING AND EDUCATION COORDINATION

DESCRIPTION (provided by applicant): Cancer Research Training and Education Coordination (CRTEC) is overseen by Edward Nelson, MD, Associate Director for Cancer Research Training & Education, who coordinates and supports research education and training activities within the Chao Family Comprehensive Cancer Center (CFCCC) and throughout the University of California, Irvine (UCI) in keeping with the matrixed structure of the Cancer Center. The mission of the CFCCC is to Discover, Teach, and Heal within the broad discipline of cancer medicine and to reduce the burden of cancer through research, education, patient care and community outreach within our Catchment Area. The activities of the CRTEC support cancer research exposure, education and career development across the spectrum of high school students, undergraduate students, graduate students, postdoctoral associates, medical students, clinical fellows, faculty, clinicians, and community healthcare professionals. The goal of CRTEC is to strengthen CFCCC and UCI as the preeminent resource: i) to provide rigorous training in, and conduct of, cancer research; ii) to provide career enhancement activities that prepare all trainees for productive careers as cancer researchers and/or healthcare professionals; and iii) to support a community of cancer care professionals in providing quality care as partners in alleviating the burden of cancer in our Catchment Area. The CRTEC component leverages and coordinates CFCCC, UCI, and extramurally-supported activities for these purposes. Specific activities reside within discrete elements of the CFCCC such as Community Outreach and Engagement, the three CFCCC Research programs, the Stern Center for Cancer Clinical Trials & Research, and CRTEC itself. CRTEC cultivates the pipeline of potential cancer researchers, promotes the advancement of junior and established researchers in basic, translational, clinical, and population cancer science, and specifically seeks to utilize the ethnic and socioeconomic diversity of UCI and our Catchment Area to support the cancer research career development of under-represented populations. By engaging, inspiring, and training gender and ethnically diverse cancer researchers, CRTEC positions CFCCC to better address the lack of diversity in the biomedical workforce. Through the Cancer Research Training & Education Committee chaired by Nelson, CRTEC leverages pilot grant programs (both internally- and externally-supported) and an extensive mentorship network, including unique components developed at UCI and the CFCCC, to advance the careers of the next generation of cancer researchers. As the UCI College of Health Sciences (COHS) continues to expand with four schools and five institutes and centers of health, CRTEC will take advantage of the COHS mission to provide integrated healthcare to foster and develop unique transdisciplinary cancer research career enhancement programs and further establish CFCCC and UCI as a significant contributor to the pipeline of clinical/translational investigators.

CRITIQUE: CRTEC activities at CFCCC support cancer research education including high school students, undergraduate students, graduate students, postdoctoral associates, medical students and fellows, faculty, clinicians, and community healthcare professionals throughout UCI. CRTEC aims to provide rigorous training in, and conduct of, cancer research; to provide career enhancement activities for trainees to have productive careers as cancer researchers and/or healthcare professionals; and to support a community of cancer care professionals in the CFCCC catchment area. The CRTEC portfolio includes 26 individual awards and institutional grants that total $1.8 million. This includes 9 T32s, 3 F30, 2 F31, 2 R25, 2 K22 awards. A number of diversity initiatives are described; however, the applicaiton is not clear how they interface with CFCCC or the CRTEC.

The CRTEC is overseen by Dr. Edward Nelson, AD for CRTEC, who coordinates and supports research education and training activities within CFCCC and UCI within the matrix structure of the Cancer Center. Dr. Nelson is a physician-scientist and Division Chief of Hematology/Oncology. Dr. Nelson is PI of the American Cancer Society-Institutional Research Grant (ACS-IRG). He attends the annual Cancer Biology Training Consortium retreat, the Southwest Regional CRCE/CRTEC Leadership group, and joint retreats of the UCI and UC Davis Cancer Biology training programs. The CRTEC is guided by its Steering Committee that comprises faculty from major graduate, postdoctoral, and faculty-level cancer research career development programs. This committee also functions as the steering committee for the ACS-IRG. The CRTEC Steering Committee meets twice annually.

Dr. Nelson is assisted by a Senior Program Coordinator hired in January 2021 (with services shared with research programs). She is expected to oversee new and existing programs for cancer research education, mentorship, and career development across the spectrum of trainees and integrate with institutional programmatic efforts, she collects, tracks, and reports on education metrics and other initiatives. They are assisted by an administrator who coordinates several CRTEC activities including the Youth Science Fellowship program, the R25-funded cancer systems biology short course, and the ACS-IRG.

The High School Youth Science Fellowship Program (HSYSF) is supported and sustained by the CFCCC since 1998. Approximately twenty students participate, annually, at no cost and > 95% of these students participate in CFCCC member laboratories. The program has trained >385 total students, to date, with a substantial number (30%) being URM students and 63% female representation. Metrics of follow-up surveys are presented with the majority in the biomedical field. There also are opportunities provided by the UCI Medical Academy and the Summer Healthcare Experience (SHE) programs.

CFCCC faculty are involved in teaching undergraduate students and in mentoring postdocs. Graduate students (50%) are supported on T32 grants, and 17% are MSTP students. Per provided metrics, the majority of trainees continue in biomedical professions. Postdocs have several education courses to choose from for enrichment.

The CRTEC also coordinates and develops programs to foster the career development of CFCCC researchers. These include the UCI NIH Boot Camp, the K Club of the UCI Institute for Clinical & Translational Science, the CFCCC pilot projects program (ROI- 18:1), and ACS-IRG. The ACS-IRG associated Chalk Talks is a nice component to increase the success of ACS-IRG applicants. This program has been very successful in furthering the career of the ACS IRG awardees. There are numerous programs in place to support mentoring of junior investigators. However, it appears participating in mentoring activities for junior investigators is not mandatory. Several CME programs and conference updates are available for clinicians. UCI Health includes 17 residencies and 11 clinical fellowships for training cancer health care providers. CRTEC also helps in planning and conducting the CFCCC annual scientific retreat, individual Program Retreats, and other special meetings. CRTEC partners with other UC medical campuses to provide direction for optimal utilization of available resources and best practices for training grant programs and career development initiatives.

During the last five years, more than 300 laboratory-based research trainees, about 250 clinical trainees, and approximately 300 professionals have received cancer research education and training. Of these trainees, approximately 12% were high school students, 20% undergraduate students, 32% graduate students, 18% postdoctoral fellows, and 8% medical students. 42% of T32 graduates are currently in academic positions at various career stages. There also are other activities including an NIH Resubmission Program and a MET (Mentorship Education and Training) programs.

Notable future plans include developing new clinical research training opportunities, integrating CRTEC activities with COE engagement with specific ethnic OC populations, and development of a “Clinical Investigator Boot Camp” program patterned, in part, after the successful NIH Boot Camp model.

Overall, CRTEC has several impressive programs that span the continuum of trainees and mentees. There are several programs to support cancer research careers of under-represented populations. These include the PRIME-LC academy, Black Thriving Initiative, SAGE Scholars Program, and the LEAD-ABC Program that appears to be largely institutionally run with SOM support. The application is unclear what CRTEC’s role is in some of these activities. The CRTEC collaborates with COE, but few details are offered outside of the AD for COE serving on the steering committee. In summary, this is an outstanding CRTEC activity that brings tremendous value to the training, education, and mentoring activities at CFCCC.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

COMMUNITY OUTREACH AND ENGAGEMENT

DESCRIPTION (provided by applicant): The UC Irvine (UCI) Chao Family Comprehensive Cancer Center (CFCCC) Catchment Area is Orange County (OC) which represents Region 10 of the California Cancer Registry and in which 70% of CFCCC cancer patients reside. OC is the third most populous county in California and the sixth most populous county in the U.S. Nearly two-thirds of county residents are from ethnically-diverse populations and 30% are foreign-born who speak a total of more than 35 different languages at home. Poverty is higher in these OC populations, as 17% of Latinos, 13% of Vietnamese, 13% of African Americans, 13% of Koreans and 10% of Chinese have incomes below the federal poverty line, compared to only 5% of non-Hispanic Whites. Geographically, the majority of these diverse populations reside in central and north parts of OC. UCI is designated by the U.S. Department of Education as both a Hispanic-Serving Institution and an Asian American/Native American Pacific Islander-Serving Institution, and we are the sole NCI-designated comprehensive cancer center based in the county. The mission and long-range goal of the CFCCC’s Community Outreach and Engagement (COE) is to reduce cancer-related burdens in the Catchment Area through cancer monitoring, community outreach and education, leadership on county coalitions and statewide partnerships including the California Cancer Plan, policy advocacy, and facilitation of research that promotes cancer health equity within and beyond the Catchment Area. The Specific Aims of the COE component are: 1) to identify and characterize the cancer burden in OC; 2) to partner with community leaders and organizations for outreach education; and 3) to facilitate community engagement in research. COE is led by Associate Director for Cancer Health Disparities & Community Engagement Sora Park Tanjasiri, DrPH, MPH, a well-established cancer health disparities researcher with deep ties and relationships throughout OC. The Office of COE is composed of a masters-level Director and two community health educators who are supported by CFCCC funds under the authority of the Cancer Center Director. These staff engage in activities covering the continuum of community engagement, including principles of community-based participatory research, to establish and facilitate partnerships with community-based organizations, clinics, and public agencies. Guided by both the overall CFCCC strategic plan and a COE-specific strategic plan, COE works collaboratively with the Community Equity Board to identify cancer education needs and to deliver evidencebased outreach education to address

social, behavioral, and environmental risks within and beyond the Catchment Area, including the California HPV Vaccination Roundtable and pivoting to address urgent COVID- 19 needs across Southern California. Since its inception, COE has strategically guided the design, implementation, and dissemination of research studies that reflect UCI's mission to Discover, Teach and Heal, and the Center's vision to prevent, manage, and cure cancer to promote health and longevity.

CRITIQUE: The mission and long-range goal of the CFCCC's Community Outreach and Engagement (COE) is to reduce cancer-related burdens in the catchment area through cancer monitoring, community outreach and education, leadership on county coalitions and statewide partnerships including the California Cancer Plan, policy advocacy, and facilitation of research that promotes cancer health equity within and beyond the catchment area. The specific aims of the COE component are: 1) to identify and characterize the cancer burden in OC; 2) to partner with community leaders and organizations for outreach education; and 3) to facilitate community engagement in research.

Since the previous renewal the CFCCC has redefined the catchment area, and this process was informed by expertise from the COE. The revised catchment area definition is now focused on Orange County (OC), California. This definition is appropriate as OC is the sixth most populous county in the US and contains rich racial, ethnic, cultural, geographic, and socioeconomic diversity. Narrowing the catchment area is well justified and enhances the cancer center's capacity to have a sustained impact, especially in complex areas of health equity, in their primary catchment area. COE leadership continues to be engaged in regional and state-wide cancer control leadership, demonstrating evidence that CFCCC continues to make an impact in neighboring regions beyond their primary catchment area. It is noted that with the reconfiguration of the catchment area, 30% of patients do not live within OC. It will be important that the COE has processes in place to continue to conduct outreach and needs assessment in these secondary catchment areas.

The COE relies on numerous sources of data to monitor the cancer burden in their catchment area and prioritize cancer research and control needs of its catchment area population. Drs. Bristow and Ziogas lead cancer surveillance for the COE. Data from the California Cancer Registry, the California Health Interview Survey, and the Behavioral Risk Factor Surveillance Survey were used to quantify the cancer burden and health behaviors of the catchment area population living in OC. Cancers accounting for the highest mortality in the catchment area mirrored the U.S. making lung and breast cancer high priorities. Compared to other California areas, catchment area residents were disproportionally affected by breast and ovary cancers for women and melanoma for men. Latino residents had higher rates of cervix cancer incidence and mortality compared to Non-Hispanic Whites. Liver/Bile duct and gastric cancers are also concerns with elevated incidence and mortality among both Latinos and Asian Americans. Notable health behavior concerns include obesity, diet, and physical activity levels of Latino residents. Non-adherence to breast cancer screening among Latino residents and low colorectal cancer screening among Asian American residents were also notable. These data are enhanced and contextualized by numerous forms of engagement with community stakeholders lead by the COE team. However, there is little description provided on how such engagement, or COE-led community needs assessments, helped to inform the COE strategic plan, add nuance to the available surveillance data, or are used to tailor outreach strategies.

A substantial strength of the COE team is the deep connections with community stakeholders representing diverse and/or underserved communities in the catchment area. This community involvement facilitates bi-directional partnerships in prioritizing the cancer control agenda for CFCCC, and the Community Equity Board was involved in developing the CFCCC overall and COE-specific strategic plan. An overall weakness for the COE is lack of adequate description of the COE strategic plan including prioritization, how the strategic plan focuses COE efforts, and associated metrics within the catchment area. The COE has developed, nurtured, and maintained meaningful partnerships with diverse communities and stakeholders throughout the catchment area. These ties support collaborations for outreach, care delivery, and research.

Evidence of impact is clear through the numerous community-based research projects related to health disparities across the three research programs. Dr. Tanjasiri conducts extensive in-reach to promote awareness of catchment area needs, including annual presentations to each program, center leadership, disease site research groups, and webinars to promote catchment area relevant research for the internal grant competitions. The success of this in-reach is well documented, with substantial increases in the number of funded internal grants being catalyzed by catchment area priorities. The COE team supports researchers across the three research programs in conduct of research through supporting participant recruitment and community engagement. Other than the Community Equity Board, specific processes through which COE supports stakeholder participation in planning of research across the basic, clinical, translational and population sciences are not well described. It is not clear that the COE has built the infrastructure to facilitate bi-directional collaborations between basic/clinical/translational researchers and community stakeholders across the research spectrum (e.g. infrastructure to enhance stakeholder engagement in research design, implementation, and disseminating findings to the community).

The COE leads the Advancing Cancer Control Together Initiative, which provides a hub-and-spoke model of enhancing guideline concordant mammography, Pap tests, colorectal screening, and hepatitis B screening. This evidence-based program has made notable improvements in screening rates among underserved communities in OC. Additional programs are described, including interventions related to HPV, tobacco cessation, and hepatitis B and numerous other activities, programs, and policy advocacy initiatives. The engagement of the COE team across many initiatives related to cancer control demonstrates the rich collaborations developed through the COE and meaningful community engagement. There is not discussion of how these initiatives map to the COE strategic plan, making it difficult to assess the sustained or potential longer-term impact of these initiatives on cancer control in the catchment area. During the site visit, Dr. Tanjasiri described ongoing efforts to develop a logic model to guide data collection regarding the process of organization change, valued added to partners, and planning process and tracking. This is an important step and presents an important opportunity to measure COE impact. In addition to the process-oriented metrics described at the site visit there is an opportunity to identify longer-term cancer burden goals to further focus COE activities and maximize impact in the catchment area.

The COE team is exceptional. Dr. Tanjasiri is a leader in cancer disparities and community engaged research. She is supported by faculty colleagues to conduct catchment area surveillance as well as 2.5 FTEs to provide day-to-day support in the office of COE. A new budget recently increased the institutional commitment to 3.0 FTEs to support the COE team. Outside of Dr. Tanjasiri the specific roles and responsibilities of COE team members are unclear.

Overall, the COE is highly effective in supporting collaborations for outreach, care delivery, and research. There are deep connections with community stakeholder, and service to the catchment area is a clear priority.

Assessment: Outstanding to Excellent merit

Budget: The budget is appropriate as requested.

CLINICAL PROTOCOL & DATA MANAGEMENT, DSM, and INCLUSIONS

DESCRIPTION (provided by applicant): Clinical Protocol and Data Management (CPDM) fulfills a vital function within the Chao Family Comprehensive Cancer Center (CFCCC), directing and supporting effective clinical research operations. The CPDM function is conducted by the Sue and Ralph Stern Center for Cancer Clinical Trials & Research (Stern Center), the centralized office for clinical trial operations at the CFCCC. Stern Center leadership has both the clinical and administrative expertise to

nurture a culture of outstanding clinical research. The Stern Center (~80 FTEs) provides a centralized resource for high quality, cost-effective and efficient assistance to investigators in developing, activating and completing scientifically impactful clinical trials. The Stern Center manages the largest portfolio of clinical trials at UCI, with a reputation as a visionary and bestpractice leader in clinical research operations across the institution. The CFCCC Data and Safety Monitoring Board (DSMB) oversees institutional cancer clinical trials that are interventional, as defined by the NCI's P30 Cancer Center Support Grant Data Table Guide. The DSMB is the focal point of the Cancer Center's strategy to ensure the safety of subjects and the validity and integrity of data. The NCI-approved Institutional Data and Safety Monitoring Plan requires that the DSMB review new Investigator Initiated Trials, and monitor and audit trials via a risk-based approach. Audits are conducting by the Stern Center's Quality Assurance Unit according to the Quality Assurance Monitoring and Auditing Plan. Results are reported to the DSMB. The Quality Assurance Unit maintains a culture of excellence, safety, and compliance in order to provide audit-ready operations at all times. The CFCCC-defined Catchment Area is Orange County, which is the third-largest and second-most densely populated county in California, the sixth-most populated county in the United States, and covers nearly 950 square miles. There are 3.2 million people living in 44 cities and towns in the CFCCC Catchment Area, and the population is racially and ethnically diverse. The CFCCC is committed to recruiting women, minorities and individuals across the lifespan to clinical trials. The CFCCC demonstrates equitable and proportionate inclusion in clinical trials of all genders, races, ethnicities, and ages relative to the Catchment Area demographics and patient population of the Center.

CRITIQUE: The Clinical Protocol and Data Management (CPDM) provides support to all clinical research operations in the CFCCC. CPDM functions are carried out by the clinical trials office named the Sue and Ralph Stern Center for Cancer Clinical Trials and Research (Stern Center). The goals of the Stern Center are to support development and implementation of clinical trials, provide quality control of clinical research operations, and ensure training and education services of members. The Stern Center is organized in several functional units: Quality Assurance Unit, Protocol Review and Monitoring, Regulatory Affairs Unit, Clinical Trials Unit, and Clinical Research Finance Unit, which have clearly delineated functions to support clinical research activities in the CFCCC.

The centralized office for clinical trials operations has undergone a dramatic transformation since the last CCSG site review with several notable accomplishments (1) growth of the staff to 80 FTE with creation of a defined career ladder and training (2) unit definition and standardized policies for protocol monitoring, quality assurance and auditing, regulatory, financial and clinical trials management, (3)dramatic reduction in activation timelines to 104 from a range of 200 days with streamlined processes for IRB, budgeting and protocol review (4)CFCCC and medical center salary support for investigators who enroll and/or lead clinical trials (5) increase in the number of Disease Oriented Teams from 6 to 7 with increased support for the DOT clinical research teams as well as alignment with basic scientific investigators to support bench to bedside trials, (6) steady increase in accrual to interventional treatment trials from 205 in 2015 to 297 in 2020, (7) accrual alignment to the racial diversity of the catchment area (23% Asian and 22% Hispanic treatment trial accrual) as well as a balanced gender accrual. An example of restructuring of the clinical trial coordination through the Stern Center is incorporation of Gynecology Oncology and Urology trial management through the CTO. OnCore has been utilized by the Cancer Center since 2009 as enterprise-wide clinical trial management system and Epic is used for EMS. Training programs for staff are clearly described, including a program for new hires and for new PIs. The Quality Assurance Unit has also been restructured and a new Monitoring and Auditing Plan was approved and implemented in 2019. Under this plan, IITs are monitored using a risk-based approach. Trial monitoring begins approximately two weeks after the first patient is accrued, and IITs are monitored approximately every six to eight weeks, 10 to 12 weeks, or quarterly to every six months depending on assigned trial risk. Audits of IITs are conducted annually. For-cause audits may be performed at the discretion of the DSMB. Goals for the coming years include increasing the number of DOTs, adding a Phase I group and increasing the accrual to interventional treatment trials with plans for utilizing genomic outcomes to support this accrual.

The Stern Center leadership, CFCCC leadership, and UCI Health have clearly put notable effort into supporting the growth of the clinical research enterprise. Despite these efforts and steady improvements a few weaknesses are noted. UCI Health has seen dramatic growth in the number of cancer patients served. Data Table 3 highlights this growth by cancer type, with 489 patients seen with melanoma, 174 with lung cancer and 135 with oral cancers. The accrual to interventional treatment cancer clinical trials however does not fully reflect the catchment area cancer burden with unclear accrual of melanoma patients, only 5 lung cancer patients and 1 oral cancer patient. There is a clear focus on brain and CNS with strong accrual as well as within the leukemia and lymphoma, GU and GI groups. The accrual is skewed towards industry funded trials with greater than 130 of the accruals within this subgroup and only 80 to institutional studies, the majority of which was from one strong breast cancer study (35 patients). The featured institutional trials (UCI-18-108, 18-128 and 17-28) show significant potential for changing practice in their respective organ sites. NCTN accruals represent only 15% of all enrollment and IITs are at 25%.

Personnel: Leadership of the Stern Center is strong, ensured by Dr. O'Brien (since 2015) and Ms. Ashley Tydon, Associate Director for Clinical Research Operations (since 2019). Dr. O' Brien is a well-established clinical investigator, with a wealth of expertise in clinical research and well recognized for her seminal work in leukemia. Ms. Tydon leads the activities of the CTO focusing on clinical research operations, business and finance management, PI and sponsor relations, and staff mentorship.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

Data and Safety Monitoring

CRITIQUE: The CFCCC Data and Safety Monitoring Board (DSMB) oversees institutional interventional cancer clinical trials to ensure the safety of subjects and the validity and integrity of data. The Institutional Data and Safety Monitoring Plan was approved by the NCI in May 2020. The DSMB is responsible for reviewing data and safety monitoring plans for those institutional studies as well as those multi-center studies for which UIC will be the primary site and assigns risk levels. The first review by the DSMB is performed after PRMC approval. The frequency of review of trials is commensurate with the level of risk with range of review from q 2 months to q 12 months. The scope of the DSMB is well defined with appropriate consideration of level of risk and monitoring frequency.

The committee is chaired by Dr. John Fruehauf, a medical oncologist and includes 7 other members from a broad range of oncological subspecialties inclusive of nursing and a statistician. The DSMB meets bi-monthly (50% membership required) and 75% attendance by committee members is required annually. The Quality Assurance Unit provides the data for DSMB review inclusive of SAEs, AEs, audit reports and CAPAs. The PI is responsible for SAE/AE input into the Oncore database system. The DSMB has a standardized Protocol Template which was updated with addition of the QAU. The DSMB reviewed 11 initial and 19 follow-up protocols in 2020. The DSMB and PRMC are distinct and separate review teams.

In Summary, the DSMP was approved by the NCI in May 2020 and meets acceptable criteria. The frequency of review of trials is commensurate with the level of risk assigned according to established criteria and is clearly specified. Clear procedures for maintaining confidentiality and addressing conflict of interest are in place.

Assessment: Acceptable

Budget: The budget is appropriate as requested.

Inclusion of Women in Clinical Research: The CFCCC has significantly increased representation of women in therapeutic clinical trials since the previous competitive renewal. From 2009-2013, women made up only 31% of treatment trial accruals; this number increased to 51% during the 2015-2020 period. This increase results from a strategic focus on the breast and gynecologic oncology trial portfolios at UCI. Accrual of female patients to interventional non-treatment trials is extremely high in 2020 at 95%, but at the site visit, it was explained that this is due to one high-accruing study. Accrual to non-interventional studies is 38%.

In January 2018, gynecologic oncology clinical trials came under the purview of the Stern Center, and both the breast and gynecologic oncology DOTs have added a dedicated CRM. The existing trial portfolios were reviewed and compared to the catchment area population. New trials have been opened with a goal of enrolling women with cancer types and cancer subtypes that are prevalent in the catchment area.

Plans for ongoing monitoring include providing updates annually at DOT meetings, and meeting quarterly with COE staff to review accrual metrics and discuss opportunities for improvement. These plans for monitoring and improving accruals are appropriate.

Assessment: Acceptable

Inclusion of Minorities in Clinical Research: The CFCCC catchment area is a racially and ethnically diverse geographic area that includes 3.2 million people living in Orange County (OC). Unique features of OC is that Asian Americans make up about 20% of the population, the OC is home to the largest population of Vietnamese Americans in the U.S. Additionally, 34% of OC residents identify as Hispanic or Latino.

In 2020, 23% of accruals to treatment trials, 16% of accruals to interventional non-treatment trials, and 39% of accruals to non-interventional trials were Asian. In 2020, accruals of Hispanic/Latino patients to treatment trials, interventional non-treatment trials, and non-interventional trials were 22%, 17% and 7% respectively. While 34% of the catchment area identities as Latino, a lower percentage of patients treated at CFCCC identify as Latino due to the relative age of Latinos in the catchment area. Latino enrollment in non-interventional trials, which tend to focus on prevention and control, represent an opportunity for the CFCCC to have an increased impact on this significant minority population. Black or African American and Other Races patients make up smaller percentages of CFCCC patients (2% and 3% respectively) and are represented appropriately in clinical trial accruals.

These accrual rates are significantly improved since the last CCSG competitive renewal, reflecting a number of efforts at CFCCC to increase minority accruals. Reducing language barriers is presented as a key strategy for enrolling minority patients in clinical trials. Of note, 20% of the Stern center staff is multi-lingual. In addition, the CFCCC recently received one of eleven NCI P30 CCSG CATCH-UP supplements to enhance recruitment of minority populations to high priority NCI ETCTN trials. Plans for ongoing monitoring include providing updates annually at DOT meetings, and meeting quarterly with COE staff to review accrual metrics. Overall, accruals are representative of the catchment area population and plans for monitoring are appropriate.

Assessment: Acceptable

Inclusion of Individuals Across the Lifespan in Clinical Research: The clinical research services under the CPDM is led by Dr. Susan O'Brien and has specifically defined subpopulations across the lifespan and demonstrated the ability to accrue particularly for older patients as shown in Figure 5 of the CPDM component.

At UCI Health, pediatric cases are referred to Children's Hospital of Orange County (CHOC). While CFCCC has a formal affiliate agreement with CHOC, the center does not directly provide care to pediatric cancer patients; therefore, it is acceptable that the center has few accruals to clinical trials by patients under age 20.

The Hyundai Cancer Institute and Children's Hospital affiliation was just formalized in 2015. More activities to enhance relationships at the younger aged patient populations with perhaps specific leadership and tasking would be appropriate. Furthermore, additional information addressed at the site visit. Suggested that the increased accrual of older adults over age 65 was paralleling an aging population or are truly disproportionate to the index analytic cases.

For inclusion of adults, DOTs review each protocol to determine if any exclusions based on age are necessary. A community advocate reviewer on PRMS is assigned to this review criteria in addition to a primary scientific reviewer. Accrual of older adults has been increasing over the previous award period, and ages of patients accrued to treatment trials are representative of the catchment area population. Adults over 80 have slightly lower participation in clinical trials due to comorbidities. These processes and considerations for including older adults in clinical research are appropriate.

Assessment: Acceptable

PROTOCOL REVIEW AND MONITORING SYSTEM

DESCRIPTION (provided by applicant): The Chao Family Comprehensive Cancer Center (CFCCC) Protocol Review and Monitoring System (PRMS) ensures rigorous internal oversight of the scientific aspects of all cancer-related, hypothesis-driven clinical research studies conducted at the University of California, Irvine. The Disease-Oriented Teams (DOTs) and Protocol Review and Monitoring Committee (PRMC) together comprise CFCCC's two-stage PRMS. The PRMS consists of qualified UCI faculty and staff with the necessary level of expertise within their respective scientific research areas. Committee membership is of sufficient size and breadth of expertise to provide oversight and review of all cancer-related research protocols. PRMS processes are governed by standard operating procedures and guidelines. The PRMS is facilitated and supported by the Sue and Ralph Stern Center for Cancer Clinical Trials & Research (Stern Center), the centralized office for clinical trial operations at the CFCCC. The first component of the CFCCC's two-stage review process, the DOTs, are multidisciplinary groups of basic, translational, clinical, and population health investigators who collaborate on a specific anatomic cancer area in order to further the translation of CFCCC discoveries through the pipeline towards interventional clinical trials. The focus of the DOTs is to ensure rigorous internal scientific review of protocols, manage the clinical trial portfolio, and drive innovation. The DOTs formally score protocols for prioritization based on investigator input, scientific merit, the potential for correlative science and academic credit for CFCCC investigators, study accrual potential, existence of active competing trials and whether the disease under investigation disproportionately affects minority populations in the CFCCC's Catchment Area. The DOTs also perform the assessment of scientific quality for NCTN and industry studies. The PRMC is responsible for the second stage of scientific and feasibility review of protocols and has the sole authority to authorize activation of clinical studies. The PRMC assesses scientific merit and quality for institutional investigator-initiated trials (IITs), determines if the CFCCC has the appropriate resources to support the trial and determines how the trial fits into the broader research agenda of the CFCCC. The PRMC is responsible for the continuing review of open protocols for scientific progress and has sole authority to close trials due to lack of progress, new safety information, or scientific relevance. The rigor of the CFCCC PRMS ensures the scientific quality and progress of clinical research conducted at the Cancer Center and the appropriate management of the Center's resources. The PRMS is critical to the CFCCC's mission to develop new knowledge about the causes, prevention, detection, treatment, and survival of cancer to shift scientific paradigms, change public policy and clinical practice and eliminate cancer health disparities.

CRITIQUE: The Protocol Review and Monitoring System (PRMS) remains a key component to the CFCCC clinical research program and has undergone significant change in the past 5 years in its administrative support, reporting structure, clinical trial review and closure process. The PRMS is now a more formalized two-step process with development and review of a clinical trial protocol within one of 7 Disease Oriented Teams (DOTs) (increase from 6 in 2015) or via an institutional tumor board prior to submission to the Protocol and Review Committee (PRMC). The DOTs are composed of clinical and basic science reviewers.

The PRMS has been structured within the Stern Center with administrative support from the Protocol Review and Monitoring Unit (PRMU). In 2020, the PRMS formalized a scoring system for trials within each DOT with 5 categories of Investigator Input and Academic Credit, Scientific Interest, Accrual potential and Competing Studies. This system's functionality has not yet been realized but will likely be a component of the comprehensive data review by each DOT and PRMC. This new scoring system favors support for IITs and cancer center bench to bedside protocols. The PRMC provides monthly DOT accrual reports, quarterly treatment trial and NCTN accrual as well as flowcharts of trial approval pathways and annual catchment area updates. The PRMC then evaluates the scientific merit, PI track record, feasibility and resource utilization of the protocols and has the sole authority to authorize activation of clinical studies. The CFCCC leadership has clearly prioritized support for the DOTs and internally and externally derived clinical trials as well as strengthened the review process and oversight during the past 3-5 years. The PRMC has created a formal SOP for monitoring study accrual as well as defining the process for protocol closure by the PRMC. The numbers of clinical trials reviewed by PRMC is continuously increasing (up to 200 trials in 2020). Approximately 10-15% pf trials reviewed by the DOT are disapproved, this number was higher in 2020. Ten protocols were closed to accrual in 2020. Each of the PRMS changes have improved activation times (below 100 days), a new scoring system for protocol review and processes for trial closure. As this program moves forward focus will be placed on malignancies that are prevalent in the catchment area. Future goals include DOT expansion as well as integration of the ePRMS system.

In summary, clear evidence is presented that the PRMS is working well with improved processes for review, activation and closure based on defined metrics. Overall, the CFCCC has the necessary components for their PRMS and has put a number of new policies in place to ensure more efficient operations. The program will seek to increase prioritization processes for catchment area malignancies in the upcoming years.

Personnel: The PRMC is co-chaired by Drs. Joseph Carmichael (new leader) and Christine McLaren who are appointed by the Stern Center Director and CFCCC Director. The committee has representation from adult and pediatric oncologists (the latter ad hoc), radiation oncologists, surgeons, biostatisticians and representatives from pharmacy and nursing as well as a community representative. The committee meets monthly and will extend time for the meeting based on the number of trials requiring review. In the last 3 years the PRMC has reviewed 50 national, 5 externally peer-reviewed, 50 institutional and 175 industry studies.

Assessment: Satisfactory

Budget: The budget is appropriate as requested.

DEVELOPMENTAL FUNDS

DESCRIPTION (provided by applicant): The Chao Family Comprehensive Cancer Center (CFCCC) utilizes Developmental Funds to support critical priorities, aligned with strategic planning, in order to grow and enhance key scientific areas. Prior funds provided support for staff investigators, faculty recruitment and pilot project funding. In the future funding period, investments will continue to be focused in these three areas: Faculty Recruitment: CFCCC has been extensively focused on the

recruitment of cancer-focused faculty recruitments during the current funding period and this remains a priority as outlined in the 2020-2025 CFCCC Strategic Plan. CFCCC requests Cancer Center Support Grant (CCSG) funds for partial support of strategic faculty recruitments. Pilot Project Funding: The investment in research proposals to pursue innovative ideas and stimulate high priority research areas (e.g., population science, translational research, research on underrepresented populations, and early phase clinical trials) are critical to ensure a high likelihood of future extramural grant awards. CCSG Developmental Funds will supplement additional funds provided through the Anti-Cancer Challenge (a peer-to-peer fundraising initiative established by Center Director Richard Van Etten, MD, PhD), philanthropic, and other institutional funds. Research Staff Investigators: CFCCC staff investigators are supported through CCSG Developmental Funds to foster the advancement of key strategic objectives of the Center. Staff Investigators enable the advancement of priority strategic objectives of the CFCCC. The funded researchers are CFCCC members who are important contributors to the scientific, translational, and clinical research activities of the Center and who serve in a significant role in helping the Center achieve scientific objectives above and beyond their own research. During the future funding period, support will be provided for Farshid Dayyani, MD, PhD and Edward Uchio, MD who are disease leaders of and significant contributors to clinical research activity, enrolling a large number of patients in trials and developing and writing investigator-initiated trials with specific regard to CFCCC's Catchment Area.

CRITIQUE: During the current funding period Developmental Funds have been distributed among three major areas including Staff Investigators, Pilot Projects and Faculty recruitment. Several measures have been taken to enhance the prioritization and evaluation of these funds. Key priorities are tied to the center's strategic plan, as well described in the application. Additional input on the prioritization of funds use is provided by the EAB, the IAB and the recently formed Community Equity Board (CEB). The details of EAB input are clearly provided, but it is less clear as to the specific input of the CEB.

A large number of pilot grants supported by CFCCC are listed in the application and an increased number of pilot grants in cancer control have been funded, proportional to the other programs. The stated ROI for the CCSG pilot grants is 12:1, which is an impressive yield. However, the details of the ROI for the specific projects supported is not provided in adequate detail. This is especially true given the large number of pilots projects supported by other CFCCC funds, and in those the representation of cancer control projects seems less than for other programs. Overall, however, the types of projects supported are appropriate and in alignment with the priorities of the center.

A total of 22 new faculty recruitments were partially supported by Developmental Funds. The individuals recruited are in alignment with the center's strategic goals. The amount of extramural funding garnered by these recruits is quite impressive, but again it is not clear what portion of each individual's recruitment was supported by CCSG Developmental funds.

Pilot project funding is sought to continue support of projects that address specific priorities of the CFCCC strategic plan. However, It is not clear from the application, how many such projects will receive CCSG support or the amount of support per award, especially since it seems that the same types of awards will be supported by the Anti-Cancer Challenge funds which are substantially more than the CCSG funding requested. Support is also requested for 25 faculty recruits in line with strategic prioities. Of note, only three of the 25 planned recruits are proposed for the CC program.

In summary, Developmental Funds have been used effectively to advance the priorities of the CFCCC and significant steps have been taken to address concerns raised in the previous review. The proposed use of future funding is likely to lead to advancement of the major strategic goals and increased scientific impact of the CFCCC. The stated return on investment on pilot projects and faculty recruitment is quite high, but the role of Developmental Funds versus other funding sources is somewhat unclear.

Assessment: Excellent to Outstanding merit

Staff Investigators: Highly capable and well qualified Staff Investigators have been supported in the current funding period. Dr. Min-Ying (Lydia) Su, Professor of Radiologic Sciences, and Dr. Krishnansu Tewari, Director of the Division of Gynecologic Oncology, have made significant contributions to the basic/translational and clinical objectives of the CFCCC.

New funding is proposed to support the two Clinical Staff Investigators: Dr. Farshid Dayyani, who has led a large number of IIT's in GI cancers and led the effort to increase the number accruals to GI cancer interventional treatment trials by 9-fold to a total of 48 in 2020; and Dr. Edward Uchio, who is a Professor and Director of Research in the Department of Urology and is involved in clinical trial research and collaborations with health services researchers with an emphasis on health disparities. The stated intent of supporting these Staff Investigators is to support the strategic priority of increasing clinical trial research with an emphasis on translational investigator-initiated trials. Both investigators are highly qualified to do so and have made significant contributions to the center already. Their appointments are approved.

Assessment: The proposed Staff Investigators are Acceptable.

Budget: The budget is appropriate as requested.

LEADERSHIP, PLANNING AND EVALUATION

DESCRIPTION (provided by applicant): The Chao Family Comprehensive Cancer Center (CFCCC) has established leadership, planning, and evaluation processes that have significant impact on the CFCCC's development, growth, and ability to capitalize on strategic opportunities. The CFCCC performs regular needs assessments and evaluations that are vitally important to strengthen its basic, translational, clinical, and population sciences research, training and education, and outreach efforts, all of which serve the needs of the CFCCC Catchment Area of Orange County. The Associate Director's Committee, Program Leaders and Shared Resources Committee, and the Senior Leadership Council are internal groups that serve as decision-making bodies for the CFCCC. The External Advisory Board (EAB), Internal Advisory Board (IAB), and Community Equity Board (CEB) provide critical feedback and advice to aid the CFCCC in planning and evaluation activities, with the CEB bringing perspective from the community to the CFCCC's efforts. Through these groups, the CFCCC develops coordinated plans, evaluates progress, addresses challenges, identifies opportunities, and maximizes potential impact. Evaluation is a priority for the CFCCC and is used to ensure that resources and efforts are aligned with CFCCC priorities and strategic planning. Based on input from advisory boards the CFCCC has strategically reviewed Cancer Center membership, and evaluated and improved CFCCC Programs and Shared Resources. On an ongoing basis, and re-evaluated every five years, the CFCCC engages in a detailed process of strategic planning. Most recently, the 2020-2025 Strategic Plan was finalized and forward action on individual tactics has progressed. Implementation of the 2020-2025 CFCCC Strategic Plan is integrally woven into the overall planning and evaluation processes of the Cancer Center. The Specific Aims of Leadership, Planning & Evaluation are to facilitate CFCCC growth with a transdisciplinary leadership team to guide and encourage cancer research collaborations and foster research discovery, proactively establish CFCCC priorities and implement goals, strategies, and tactics, and ensure progress with continuous assessment and thorough evaluation to match resources toward established goals.

CRITIQUE: The leadership planning and evaluation processes of the CFCCC are well described and successful in fulfilling strategic priorities. These include both internal and external advisory groups, community outreach panels, and the internal leadership that guides the CFCCC on a weekly, monthly and yearly basis. CFCCC leadership consists of the Center Director, Deputy Director, Associate Directors for Clinical Science, Basic Science, Population Science and Cancer Control, Cancer Health

Disparities and Community Engagement, Cancer Research Training and Education, and Administration and Finance. The senior leadership meets twice monthly as the Associate Directors Committee to define and advance research, community outreach and engagement, and training and education at CFCCC.

Dr. Richard Van Etten has served superbly as CFCCC Director since 2013 and was named Senior Associate Dean and Associate Vice Chancellor for Cancer at UCI in 2019. He has been continuously funded by the NCI for over 25years, PI of 14 R01s over that time, participated in numerous cooperative grants, and currently serves as a member of the NCI Cancer Centers Study Section (A).

The senior leadership includes Dr. Marian Waterman, Deputy Director, who has served in this role since 2014. She previously served as a Program Leader (2004-2014) and Associate Director for Basic Sciences (2014-2020). Dr. Waterman research focus is on the role of Wnt signaling in somatic stem cells and cancer stems cells. She is well-funded most notably as the MPI of the U54 Center for Cancer Systems Biology and an NCI R25 training grant on Cancer Systems Biology.

Dr. Susan O'Brian is the Associate Director for Clinical Science and has served in this role since 2015. She is a world-renowned researcher and clinical investigating and treating acute and chronic leukemia. She has been the PI of over 50 funded clinical research protocols, authored more than 800 articles in peer-reviewed journals, and received the Irwin H. Krakoff Award for Excellence in Clinical Research at MD Anderson Cancer Center in 2014.

Dr. Karen Edwards is the Associate Director for Population Science and Cancer Control and the Chair of the Department of Epidemiology. She has served in this role since 2019. Dr. Edwards has led and worked on numerous genetic and epidemiologic studies that involve a range of disease phenotypes and interactions between genetic and environmental / lifestyle factors and have worked on large interdisciplinary projects, including several Centers of Excellence.

Dr. David Fruman is the Associate Director for Basic Science and Acting Director of the Cancer Research Institute. He has served in this role since October 2020, prior to which he served as Program co-Leader for the Systems, Pathways and Targets Program for six years. His research focuses on PI3K/mTOR signaling pathway and is currently funded through the DOD and Leukemia and Lymphoma Society.

Dr. Sora Park Tanjasiri is the Associate Director for Cancer Health Disparities and has served in this role since 2018, when she was recruited from California State University, Fullerton. There she served as Chair for Health Science and Director of the Health Promotion Research Institute. She is well-qualified for this leadership role having worked for over 30 years applying community-based participatory research to the development and testing of cancer prevention (tobacco, nutrition, physical activity, and HPV vaccination), early detection and survivorship interventions for disparity populations.

Dr. Edward Nelson is the Associate Director for Cancer Research Education and Training and has served in this role since 2017. He is Chief of the Division of Hematology/Oncology and oversees the division's fellowship program, as well as the UCI PI for the ACS-IRG. As a physician scientist and medical oncologist, Dr. Nelson has maintained an active research program and been a PI of both cooperative group and hypothesis-driven investigator-initiated clinical studies.

Ms. Christine Hui is the Associate Director for Administration and Finance/Chief Administrative Officer and has served in this role since September 2019. She has over 15 years of experience managing and overseeing research administration operations, and since 2014 served as the Administrative Director for Clinical Research Operations at CFCCC.

The senior leadership structure of the CFCCC is appropriate and well described in the application. The leaders are each highly qualified for the roles that they serve. The need for three Associate Directors given the presence of only three programs is understandable given the supervisory roles that these three Associate Directors play in shared resource management and center operations. The application describes a much more effective working relationship among senior leaders particularly through the Associate Directors Committee. The relationship between the mission of the CFCCC and the UCI Health System is better clarified in this application compared to prior submissions. There is a now a Director of the Service Line who has a reporting relationship to Dr. Van Etten.

Internal planning and evaluation is woven through several internal committees that establish, coordinate and support the vision and strategic objectives of the CFCCC. These include the Associate Directors Committee (meets twice monthly) that serves as the principal scientific and administrative advisory body for Director. This committee was formed in response to the need to facilitate bilateral communication amongst the CFCCC Director, Deputy Director and Associate Directors. The Associate Directors Committee appears to be the main mechanism by which the Director is able to discuss strategy and implement the overall strategic plan. Both progress of the research programs as well as the performance of the shared resources are reviewed in this key committee. The Program Leaders (meet monthly) and Shared Resource Directors Meetings (attend quarterly) discuss progress toward scientific goals, coordinate strategies to enhance research collaboration, and develop new scientific directions. This committee reviews membership applications and reviews Shared Resources on a quarterly basis. It is unclear whether the Associate Directors overseeing the Research Programs, Drs. Edwards, Fruman, and O'Brien, attend this committee and how they interact regularly with the Program Leaders to facilitate research at the center.

The Senior Leadership Council (meets quarterly) brings together the Associate Directors Committee and key institutional senior leadership to advise on the planning and resourcing of strategic priorities, the acquisition of institutional resource commitments, and overall planning and assessment of Cancer Center initiatives. This council oversees progress to the Strategic Plan and facilitates bilateral communication between CCCC and stakeholders at UCI and UCI health. Dr. Van Etten chairs the Associate Directors and Senior Leadership Council meetings and attends the Program Leaders meeting. With Dr. Van Etten's new direct influence and shared authority of clinical research operations, a Cancer Clinical Operations Committee was formed and meets monthly. There is no mention of the Cancer Research Training and Education Coordination Steering Committee or the Shared Resource Internal Advisory Committees and the role they play in shaping strategic initiatives for CFCCC and broader planning and evaluation activities.

The CFCCC maintains three advisory boards including External and Internal Advisory Boards, and a Community Equity Board. The center has made outstanding use of its external advisory board. The board is chaired by Dr. Louis Weiner and is exceptionally well balanced for clinical, basic, and population scientists. In addition, there are several cancer center directors who serve on the EAB. Table 2 in the application describes more than a dozen specific recommendations of the EAB that have been followed and implemented by leadership. These are not trivial observations and directives from the EAB but rather substantial actions that have led to marked improvement in several features of the center. This reflects both the outstanding contribution of the external advisers as well as the nimble executive abilities of the leadership team. However, the EAB does not adequately include a member who is an active Associate Director for Administration at an NCI-designated cancer center.

The Internal Advisory Board is chaired by the UCI Provost and includes key senior institutional leadership. It is unclear if this board meets once or twice annually, however, the impact and effectiveness of this Board is apparent with the substantial increase in CFCCC space and institutional commitment based on EAB and leadership recommendations. The Community Equity Board is comprised of 11 local cancer community leaders and advocates based in Orange County. This board meets twice annually and provides input, perspectives, and engagement from the Orange County

community to identify the unique cancer needs within the CFCCC Catchment Area and inform research priorities. CFCCC has utilized several ad hoc advisory boards to address specific recommendations made by the EAB.

Strategic planning is a priority of the leadership team. Development of a 2020-2025 CFCCC Strategic Plan, began in November of 2017, and included input from CFCCC senior leadership, UCI and community stakeholders, shared resource directors, and culminated in final presentation and approval by the CFCCC IAB and EAB in 2020. This plan intentionally aligns resources and strategic objectives with the new strategic plans for both UCI and UCI Health. There are seven goals that include expanding the cancer science enterprise and target new areas for development, increase the translation of CFCCC discoveries, grow clinical cancer research enterprise, fulfill the commitment to CFCCC Catchment Area, grow philanthropic sources of support, train and mentor next generation of diverse cancer scientists and health professionals, and position UCI Health as the premier provider of cancer care and research in Orange County. While the goals of this strategic plan are overly broad, detailed tactics provide direction for the plan. However, the timeline is unclear for development of specific metrics to measure success for each of the tactics. While the implementation of this plan appears to be well-structured, the oversight structure seems overly complex. However, in favor of the process is the fact that this strategic plan has been reviewed and approved by both the EAB and the IAB and is likely to be solid guide to effective planning and strategic work.

The leadership has overseen growth of CFCCC during the current project period. NCI funding has increased by 18% (from $7.9 million to $9.3 million) and overall peer-reviewed cancer-relevant funding by 18% ($24.8 million to $29.2 million). In the current project period, there was an increase in CFCCC-controlled wet laboratory space representing a ~70% increase. The CFCCC now directly manages ~172,000 sq ft of administrative, basic, translational, and clinical research space. A major goal of the effective leadership strategy and planning is building the scientific depth of the center. It is noted that more than 90 new investigators have been added to the CFCCC during the current funding period. These new investigators have addressed many of the needs that were identified in the past as well as input from the internal and external advisory panels at the center.

The CCSG application itself is a great reflection of leadership planning and evaluation of any cancer center. The application is complete with appropriate attention to detail and there are very few errors noted.

There are multiple retreats, seminars, and symposia managed by the CFCCC leadership, including an annual CFCCC Scientific Retreat, however, further details on the frequency, depth of scientific expertise, field of study, and attendance to these events is unclear, which makes the impact difficult to assess.

In summary, while the leadership team at the CFCCC is relatively new, it has demonstrated strategic growth in critical areas in the last several years including space, institutional commitment, and key recruitments. Planning and evaluation are done through a series of meetings, both internal and external, which focus on the status of the research and clinical enterprises, education and training, and community outreach and engagement. These meetings also interface with key institutional stakeholders to facilitate bilateral communications. CFCCC has a strong External Advisory Board that has provided critical input and advice to CFCCC and UCI leadership during the current project period. The advice of the EAB and the center’s response have been critical in obtaining the notable achievements made. The ability and progress made from implementation of the findings of the EAB and IAB are examples of progress of the center and its ability to lead and plan.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

ADMINISTRATION

DESCRIPTION (provided by applicant): The vision of the Chao Family Comprehensive Cancer Center (CFCCC) is to “Prevent, Manage and Cure Cancer so that All People Live Healthier, Longer Lives.” The mission parallels that of UC Irvine (UCI), the parent institution, to Discover, Teach, and Heal within the broad discipline of cancer medicine. CFCCC Administration is directed by the Associate Director for Administration and Finance, Christine Hui, MPH. She serves as a Cancer Center senior leader and reports directly to the Cancer Center Director. Administration provides effective centralized organization, infrastructure, and support that enables the CFCCC to function efficiently and cohesively in line with the CFCCC’s mission. Administration works with leadership to foster scientific and intra-institutional collaborations to support cancer-focused research, strategic goals, and the CFCCC mission and vision. Administration oversees the management of programmatic membership, strategic planning, leadership meetings and scientific retreats, coordination and management of pilot project competitions, coordination of all Cancer Center Support Grant (CCSG) data management and reporting, space management, participation with faculty recruiting and onboarding, and fiscal control and management of all accounts ensuring compliance with all UCI institutional policies and federal requirements. Administration also provides centralized clinical research infrastructure through the Sue and Ralph Stern Center for Cancer Clinical Trials and Research (Stern Center), which reports to the Associate Director for Administration and Finance. This support includes managing the trials from activation to close-out, budget and contract negotiation, and study and data management. Staffing and coordination for clinical research review committees, including the Disease-Oriented Teams, Protocol Review and Monitoring Committee, and Data and Safety Monitoring Board are also managed through the Stern Center. The majority of the costs for support of Administration are covered by institutionally-provided discretionary funds under the authority of the CFCCC Director. The Administration Core budget request represents 9% of the overall CCSG budget.

CRITIQUE: The CFCCC Administration supports the oversight of the Cancer Center Support Grant (CCSG), shared resource management and compliance, coordination of pilot project programs, management of space utilization, organization and staffing of planning and evaluation activities, oversight of budgets and finance, participation with faculty recruitment and onboarding, and management of data, reports and data systems. Four administrative units, with 88 staff members, span Administrative Programs, Finance, Informatics, and Clinical Research Operations.

The qualifications of administrative staff members for their proposed roles are superb. Ms. Christine Hui, Associate Director for Administration and Finance and Chief Administrative Officer, leads the Administrative team with over 15 years of experience managing and overseeing research administration operations, including ten years of experience at NCI-designated Comprehensive Cancer Centers. She was recruited into the Associate Director role for CFCCC as interim in February 2019 before being appointed in a permanent capacity in October 2019, after serving for five years as the Administrative Director for Clinical Research Operations for CFCCC. While Ms. Hui has been the Associate Director for a relatively short period, her experience at CFCCC over the last six years will be an asset. During her tenure in this role, Ms. Hui has been supported by an experienced Administrative Director for Clinical Research Operations and Director for Administrative Programs. The recent recruitments of a Finance Operations Manager and Informatics Program Manager will continue to enhance the effectiveness and output of the Administrative team. Overall, the relative newness of the lead administrative team makes it difficult to fully evaluate progress in the assigned roles, however, the strong progress and key initiatives that have been implemented to date demonstrate a positive trajectory for the coming years. Career development for Administration is facilitated through participation in national conferences and in-house opportunities for career development and training.

Administrative oversight of the CCSG application process is evident throughout the application. The current CCSG application is aligned with the CCSG guidelines and review criteria. Generally, accuracy

and completeness of CCSG reporting are evident throughout the application with demonstrated consistency in structure and common information cited across the different CCSG components. However, there are several inconsistencies with this oversight for required attachments, namely missing required data per the CCSG-guidelines on clinical trial oversight for proposed Clinical Staff Investigators, the wrong budget justification in PRMS, and the wrong Systems, Pathways, and Target Program Research Program (SPT) other attachments for Program-related publications and clinical research. Once notified of these missing components, the Administrative team did quickly provide this information for review during the site visit. It is reasonable to assume some errors do occur in applications of this size, especially given the number of Administrative team members working on the application; however, new and/or enhanced SOPs or workflows would assist in future applications to enhance data accuracy and application completeness.

Administrative responsibility for space management has grown from the prior competing renewal, with new policies and evaluation metrics created in response to the prior critique. Administration made significant improvements in space management during the current project period, including a newly-codified policy that governs the assignment and review of space under the CFCCC Director's authority. Administration manages policies on assignment and retention of space, optimizing space utilization based on usage, maximizing program-promoting proximities and collaborative opportunities, and enhance shared capabilities. There is a Cancer Center Space Committee overseen and managed by Ms. Hui, that meets annually to evaluate space allocations, under the guidance of the CFCCC Space Policy, with ad hoc meetings as needed.

The CFCCC Administration provides oversight for seven CCSG-supported Shared Resources, with six jointly managed with UCI departments and one solely managed by the Cancer Center. Along with the Deputy Director and Associate Directors for Basic, Population and Clinical Sciences, a representative from Administration attends the annual Shared Resource Internal Advisory Committee meetings. To evaluate trends in CFCCC member usage, services, and monitor correlations with CCSG funding, Administration receives data quarterly from the Shared Resources and manually enters it into a Microsoft Access Database. In December 2020 the center began using Agilent's iLab tool which should be fully integrated by Summer 2021. This will be a significant improvement for Administration, CFCCC leadership, and Shared Resources in the evaluation and monitoring of the CCSG-supported Shared Resources, allowing real-time data and utilization metrics. Ms. Hui's leadership in this acquisition and implementation should be commended. Every five years, Administration partners with the School of Medicine to survey CFCCC membership and other users to evaluate Shared Resources and solicit feedback. Optimally this would be a yearly exercise allowing Administration to follow trends in satisfaction with Shared Resources overtime and optimize research support. Administration has plans to issue the survey on an annual basis, in addition to the recent hiring of a Senior Program Coordinator, to support Shared Resource management which will further strengthen the ability of Administration to provide feedback and improvements for CFCCC Shared Resources.

CFCCC has effective financial management led by a Finance Unit that reports directly to Ms. Hui and provides all accounting and financial services for the CFCCC total annual budget of ~$14 million, including discretionary and other institutional, philanthropic, and CCSG funding. The CFCCC budget is developed annually in coordination with the School of Medicine. CCSG financials are reviewed quarterly with the Center Director.

The processes for CFCCC membership (now totaling 195) are managed by Administration, and governed by a CFCCC membership policy, with final approval by the Program Leaders and then the Director. On the advice of the External Advisory Board in 2020, membership categorization was simplified to two categories. There are continued concerns about the broad criteria for membership, even with this new policy, given the large membership of two of the three Research Programs, and relatively low level of peer-reviewed research funding. Administration should consider further refinement and development of this plan. CFCCC purchased and implemented Advarra Forte's EVAL in

Spring 2020 and transitioned all CCSG data, including membership to this new system. As CFCCC membership is the foundation of the majority of CCSG required metrics, Administration effectively managed this transition by creating and implementing multiple SOPs, work instruction guidelines, and templates to accurately abstract, clean and manage this data. well documented. As a matrix center, faculty recruitment and retention are coordinated and managed within each respective department or division, however, CFCCC partners with the departments and divisions on cancer-focused recruitments and initiates targeted recruitments emerging from the strategic plan. CFCCC participated in the recruitment of >90 cancer investigators with financial contributions ($9.7 million in start-up funds, $650 thousand in equipment, and six FTEs) made to 29 of these recruits. Administration has effectively launched a new onboarding program for incoming cancer-focused faculty, with 36 cancer-focused faculty members participating to date, which effectively contributes to the integration of these faculty into the CFCCC community.

CFCCC Administration actively supports, arranges and documents center meetings including Associate Directors, Senior Leadership Council, Research Program, Shared Resource Operation and Internal Advisory Boards, additional meetings and retreats, and CFCCC External and Internal Advisory Boards.

CFCCC has a pilot project program, Anti-Cancer Challenge, which is the largest pilot project program within the UCI. This program is effectively managed by the CFCCC Administration; from solicitation and review to awarding to progress and final reports, including return-on-investment. Administration helps facilitate alignment of the requests for proposals with the strategic plan. At the time of submission, the progress/final reports and return-on-investment data are being integrated into the EVAL system which will further enhance reporting capabilities for this program. Additional specificity on the utilization of CCSG developmental funds in support of specific pilot projects, as well as the subsequent return-on-investment, is not well addressed. Other pilot project programs (e.g., ACS-IRG) are managed outside CFCCC Administration; however, integration of these funding mechanisms and associated data/outcomes into the fold would provide added value to both CFCCC and those funding mechanisms.

Administration has contributed significantly to CFCCC strategic planning as is evident in the development, organization, and implementation of the CFCCC 2020-2025 Strategic Plan. Administration is responsible for facilitating the implementation and monitoring process in support of this plan and participates in the Strategic Plan Coordinating Committee.

CFCCC communications rely on a new bi-monthly CFCCC Bulletin and an expanded tri-annual Center newsletter. Administration has implemented a new communication strategy through the purchase of an email marketing platform, which will provide trackable data on user interest in newsletter content. In partnership with the School of Medicine, the CFCCC website was redesigned from 2019 to 2020 and launched in January 2021.

The infrastructure of the Stern Center grew significantly during the current project period, with a 260% increase in staffing noted. Administration played a critical role in obtaining institutional support for these positions using national benchmarking standards and in determining optimal staffing levels for current and future clinical trial accrual volume. These efforts have led to more appropriate workloads for staff, increased morale, increased protocol compliance, and better audit and monitoring outcomes for clinical trials.

In summary, CFCCC Administration has been strengthened with the recent addition of Ms. Hui. In this short time, she has made significant strides in creating an effective team, increasing capabilities in data analysis and collection, shared resource and space management, communications, and strategic planning. During the current project period, progress has been made to address the concerns from the previous critique and strengthen CFCCC Administration, including the development of a new space management policy, cancer-relevance policy, and membership policy. Ms. Hui and her team should also receive credit for the significant growth in the Clinical Trials Unit, including the substantial decrease

in protocol activation time. While Ms. Hui directly oversees the administration of the Clinical Trials Unit, her oversight of administrative activities for Cancer Research Training and Education and Community Outreach and Engagement is not well-defined. There are some data reporting and component discrepancies in the CCSG application; however, with the implementation of EVAL and the significant increase in Administrative personnel under Ms. Hui's leadership, these will likely not be an issue in the future. CFCCC Administration has set itself up well for the future project period with investments in analytics tools, processes, and personnel which will assist in the continued growth of this team.

Personnel: Ms. Christine Hui, Associate Director for Administration and Finance/Chief Administrative Officer, has served effectively in overall administrative management, including implementation of new initiatives, processes, and systems for the Cancer Center in the short time since her appointment in 2019. She brings relevant experience from her prior role as the CFCCC Administrative Director for Clinical Research Operations.

Assessment: Outstanding merit

Budget: The budget is appropriate as requested.

ESSENTIAL CHARACTERISTICS

Physical Space is rated Outstanding. CFCCC basic, translational and clinical cancer research, shared resource, and administrative space is spread across scattered sites at two principal locations, UCIMC in Orange, and the UCI main campus in Irvine, which are separated by 12 miles. The Cancer Center's physical facilities are adequate and appropriate with substantial increases noted during the current project period. There was a 70% increase in wet laboratory space. The CFCCC Director controls ~172,000 sq ft of administrative, basic, translational, and clinical research space, including CFCCC outpatient building (58,000 sq ft), administrative space in 200 Manchester building (19,000 sq ft), and laboratory space in Shanbrom Hall (12,000 sq ft) and Sprague Hall (83,000 sq ft).

Clinical facilities are largely located on the UCIMC Orange campus houses in the CFCCC outpatient building (Radiation Oncology, multidisciplinary outpatient clinics, infusion center, outpatient surgery, administration, Stern Center Biospecimen processing lab, CRC), with other clinical care outpatient facilities and research activities taking place in multiple nearby buildings. Three additional satellite clinical care and research facilities include the UCI Health Cancer Center Newport Beach which opened in 2016 and includes breast, neuro, and medical oncology, surgical oncology, infusion, and clinical trials; UCI Health Yorba Linda which opened in 2019 and offers breast oncology and imaging, with plans to expand to medical and radiation oncology, and clinical trials in 2021; and UCI Health Newport-Birch Street which opened in 2019 and offers genitourinary oncology and clinical trials. CFCCC controls research space on one floor of Shanbrom Hall on the UCIMC Orange campus.

The UCI main campus houses the majority of basic and translational research space and shared resources, primarily in Sprague Hall. CFCCC controls and manages Sprague Hall which is occupied by 22 CFCCC investigators from all three Research Programs. In addition, the building houses two of the seven Shared Resources. The remaining Shared Resources are located in other buildings on this campus within walking distance. It is difficult to assess whether the distance between UCIMC and UCI campuses hurts Shared Resource usage by members and although it is stated that ETR, BSR and IVFOI are located on both campuses, the exact location on the provided maps is not clear. However, access to Shared Resources appears to be appropriate. Plans for the UCIMC Irvine-Newport on the UCI campus will have a significant impact on fostering collaborations between CFCCC clinicians, clinical investigators, and basic/translational investigators. These new facilities will have a phased opening between 2023 and 2025.

Space allocation is determined by the CFCCC Space Committee according to its Space Policy, with space allocations reviewed annually or more often as needed. Additional space commitments for the next project period are significant and include 25,000 sq ft of laboratory space, which is in addition to the 10,000 sq ft of CFCCC laboratory space currently available for future recruitments.

In summary, CFCCC facilities are appropriate and have grown significantly in the last five years, with plans for additional space increases in the coming project period. While clarification was provided at the site visit on the planned use and location of the newly committed laboratory space, the actual use and implementation will be an essential metric to evaluate whether it strategically addresses planned recruitments aimed at supporting the vision and mission of CFCCC.

Organizational Capabilities is rated Outstanding. The CFCCC has an effective and improving programmatic structure with appropriate linkage to the leadership committees, as well as the senior leadership teams, with overall reporting and direction from the center leadership. Dr. Van Etten, as Center Director, occupies upgraded leadership positions within the institution enhancing integration of the center. This is facilitating a stronger impact within the UCI as well as new investments in the cancer center. The leadership team has been evolving recently and the Center Director and Deputy Director have well defined organizational capabilities and leadership roles. The role of the new Associate Director for Basic Research is less well defined. In addition, the effort for Associate Directors (5%) is modest and suggests that they might have difficulty leading the expansive portfolios described in the application. The Deputy Director addressed this at the site visit, ameliorating this issue. The EAC is appropriate, has been indispensable as advisors and advocates, and has a strong group to assess and contribute to Dr. Van Etten's leadership and decision-making process. Dr. Van Etten has led a new round of strategic planning for 2020-2025. Membership and training are well described and appropriate.

The status of the CFCCC has been upgraded within the UCI with new co-management authority by the Center Director over the cancer service line and a new revenue stream from the clinical operations. The compensation structure to support clinical investigators' research time is better defined and creative, given that this is a new enhancement available to Dr. Van Etten. In terms of the organizational and administrative structure although there a number of committees such as the Associate Directors Committee, the Senior Leadership Council, the Cancer Clinical Operations Committee, Overlap of Membership and how these are different such as between the Associate Directors Committee and the Senior Leadership Committee would be benefitted by how decisions are deployed, as well as how other leaders across the center can percolate good ideas or needs up through these organizational structures.

There are 6 Associate Director level positions that oversee the center and get input from the Center Director and advisory committees (Basic Sciences, Clinical Sciences, Health Care Disparities and Community Engagement, Administration and Finance, Cancer Research Training and Education, Population Science and Cancer control). The CFCCC has an executive steering committee, which is comprised of the Center Director, CEO and COO of UCI Health, Chief Ambulatory Officer, and Deans of the Medical School and Clinical Affairs. There are 3 additional executive level committees: Associate Directors' Committee, Senior Leadership Council, and Cancer Clinical Operations Committee. These committees meet at appropriate regular intervals. There are multiple advisory committees comprised of capable members with appropriate expertise for the components they inform and include a Community Advisory Board. There has been considerable attention paid to the strategic plan, with modifications of the plan to allow the center to be responsive to evolving review criteria for NCI centers and the needs of the catchment area. There are also an appropriate number of meetings, retreats, special symposia, and organ site specific conferences to facilitate collaborative cancer research within the institution.

Transdisciplinary Collaboration and Coordination is rated Outstanding. There has been a strong and ongoing effort at the CFCCC to improve collaboration and coordination across the center from the

time of the last review. The CFCCC leadership fosters collaboration through symposia, scientific retreats, and seminars with outside scientists.

The primary mode of catalyzing transdisciplinary collaborations is through Disease Oriented Teams and pilot funds. Seven Disease Oriented Teams are designed to facilitate translational research and have resulted in several new investigator-initiated trials. Institutional pilot funds have supported new team science projects that have resulted in new ITTs and intra-programmatic NCI funding. At a center level, the programs have been consolidated in a fashion that should allow for increased transdisciplinary collaboration from the time of the last review. A specific effort from the time of the last review has been reinvigoration of the leadership of the center through strategic recruitment of new program directors and faculty, while simultaneously constructing more active Disease Oriented Teams to interact with those reorganized programs. When increasing the integration of peripheral sites like the VAMC and the Children's hospital, attention has been paid to strategically integrating the translational science and population-specific issues into the center's research portfolio. These efforts are not longstanding, however, so additional time will need to pass to examine the efficacy of these integrations.

Inter- and intra-programmatic publications have shown improvements with intra-programmatic publications ranging from 11%-20% and inter-programmatic publications ranging from 13%-20%. Inter-institutional publications range from 48%-68% across the three programs. Importantly, there are a number of new collaborative grants and initiatives at the center, and these awards are a testament that work performed to foster additional collaboration across the programs and center is effective. Collaborations with other cancer centers have been formalized through the University of California Hematologic Malignancies Consortium, which has grown to a newly formed UC Cancer Consortium in 2017. This infrastructure for collaboration has yielded several intra-institutional IITs and SPORE application developed by the intra-institutional UC Pancreatic Cancer working group. Significant examples of late translation of science into advanced preclinical and clinical models has occurred since the last review as well, and most of these involve intra-programmatic, inter-programmatic, and inter-institutional collaborations. Further, these efforts have fostered industry collaborations as well, as a mechanism to get the science into patients. Successful funding in the U54 cancer systems biology program should be very fruitful and emblematic for the way in which transdisciplinary collaboration has improved. These achievements reflect well on the mission and vision of the center.

Cancer Focus is rated Excellent to Outstanding. There are three cancer focused research programs at the CFCCC to fulfill the mission of the center. Currently, the CFCCC peer reviewed funding base is $29.2 million with $9.3 million in NCI-supported direct costs, $13.1 million in other NIH supported direct costs and $6.7 million in other peer reviewed cancer funding. If non peer review funds are included the total is $41.1 million compared to $31.9 million at the time of the last renewal. This represents a 28% increase in overall cancer focused funding. The center has an established system to assign degree of cancer relevance to all grants based on specific aims. However, some listed grants have unclear degrees of cancer relevance. Overall, there has been significant sharpening of the cancer focus of the center research from the time of the last review.

Institutional Commitment is rated Excellent. While substantial changes have been made to the institutional prominence of both the Center Director and the CFCCC overall there is room for improvement in the overall financial support for this dynamic and productive center. A notable example of the institution meeting prior commitments is the elevation of the CFCCC to school status rather than department status in the current organizational structure. This has been accompanied by the Center Director reporting to the Vice Chancellor for Health Affairs. It is noted that there has been a near complete turnover in medical school and health system leadership since the last submission. Importantly, the Center Director sits on several relevant UCI committees that allows influence over priorities set by both the school and the health system. The Center Director also has appropriate control over membership of the center. Given the matrix nature of the CFCCC, it is entirely appropriate that recruitments are done in conjunction with academic departments.

At the site visit it was announced that the UCI and the UCI Health will support $25 million ($12.5 million from each) in funding for the CFCCC over the next 5 years. In addition, 5 faculty FTE lines in the UC system along with start up packages are part of the next 5 years commitment. It is also noted that the new leadership has committed an additional 25,000 square feet of space for the next funding period. This represents a modest but real increase in laboratory capacity for the center. In addition, the application notes that $6.2 million will be provided for support of shared resources. This is a meaningful start and critical for the science of the center.

The CFCCC has appropriate influence and control of philanthropy activities. There are four dedicated staff members who raise funds for the CFCCC. While the endowment is modest at $25.8 million, the Center Director has been able to increase the size of this endowment over the last five years.

The application describes a funds flow mechanism from the oncology service line that provides support for clinical investigator time and effort. The cancer patient population has grown substantially, and it is not clear that the institutional support from the service line has grown to the same degree. It is also not clear if there is sufficient distribution of service line proceeds to the center to enable growth. It is encouraging that the service line director now has a reporting relationship to the Center Director and. At the time of the site visit, presentations stressed that any financial deficits for the Stern Center are backstopped by the institution which is a significant level of support. Finally, there has been some progress in developing a formula to support clinicians for the work involved in the process of clinical trial design and accrual.

The application describes an appropriate process for appointing an interim Center Director as well as a commitment to a broad national search for a permanent replacement should one be needed. Furthermore, there is recognition of the importance of team science in the appointments and promotions process.

In summary, there has been a consistent increase in financial support for the programmatic expansion of the CFCCC in terms of research space, funding, and personnel. The institutional financial support for the center could be significantly greater given the dramatic increase in the patient population seen at the center. However, institutional support for the Stern Center is terrific and a wonderful improvement in clinical trial metrics have occurred, though the overall accrual to trials is somewhat modest.

Center Director is rated Outstanding. After a national search, Dr. Richard Van Etten became the CFCCC Director in 2013. Prior to his appointment as Center Director he served as Cancer Center Director at Tufts University School of Medicine from 2009 to 2013. Dr. Van Etten is a highly accomplished translational/clinical cancer researcher with over 30 years of experience and has had continuous funding from the NCI since 1994. He currently serves as PI on an NCI R01 grant and Project Leader on a U54 grant as part of the NCI Systems Biology Consortium. He is widely recognized for his research on hematologic malignancies and has made significant scientific contributions in this field, earning him national recognition. He has served on a number of NIH review committees as well as serving as the local PI for an institutional Eastern Cooperative Oncology Group grant and as a member of the ECOG Leukemia Committee.

Soon after assuming the directorship at CFCCC, Dr. Van Etten began an extensive process of reorganization and recruitment. Since then he has led the process of re-organizing the scientific programs of the center in response to the previous CCSG review and with significant input from the External Advisory Board. He has co-recruited over 90 basic, translational, clinical and population researchers since 2015 and appointed new senior leaders, as well as those focused on the catchment area, diversity, and a new Associate Director for Basic Research. He has also launched and expanded philanthropic activities to expand and deepen the financial stability with endowment funds. Dr. Van Etten is considered a national leader and highly respected in the cancer centers community as well as

obviously at his own institution, evidenced by the new financial commitments, additional wet lab space and augmented authorities.

During the current funding period, Dr. Van Etten has gained additional authority over cancer research and clinical affairs at the institution through a new reporting structure in which he reports to the Vice Chancellor for Health Affairs with additional reporting to the Dean of the School of Medicine and CEO of UCI Health. This provides additional authority over both academic and clinical cancer resources including a shared oversight of clinical operations.

In summary, Dr Van Etten is highly qualified to serve as Center Director of the CFCCC and he has the necessary authority to carry out this role. During his time as Center Director he has been very effective in leading the extensive growth and planning for the future growth of the center which will likely increase the overall impact of the CFCCC.

BUDGET RECOMMENDATION

The site visit team did not make any reductions from the total direct costs of the CCSG. In total direct costs, the current budget is $1,516,678 (from Data Table 5); requested budget is $1,959,450 (from Data Table 5 and the Face Page); and the recommended budget is $1,959,450. The site visit team recommends that the budget be evaluated by the Cancer Center Support Grant (P30) Special Emphasis Panel, as needed.

The budget tables that follow are provided as informational item only. The official recommendation for support will be provided under the heading, RECOMMENDED BUDGET/CANCER CENTER SUPPORT GRANT (P30) SPECIAL EMPHASIS PANEL, after that 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 $
Program Leadership (including other budget categories, where appropriate)	89,778	89,778
Research Programs (non-salary)		
Biotechnology, Imaging and Drug Development	15,000	15,000
Systems, Pathways and Targets	15,000	15,000
Cancer Control	15,000	15,000
Cancer Research Career Enhancement and Related Activities	82,094	82,094
Leadership, Planning and Evaluation	214,388	214,388
Developmental Funds (including staff investigators, where appropriate)	174,464	174,464

Administration	148,188	148,188
Shared Resources: Salaries	597,334	597,334
Shared Resources: Operating Costs/Activities	103,444	103,444
Community Outreach and Engagement	141,165	141,165
Clinical Protocol & Data Management (CPDM) Data & Safety Monitoring	202,915	202,915
Protocol Review and Monitoring System	110,680	110,680
Total Direct Costs	1,959,450	1,959,450

SUMMARY OF RECOMMENDED BUDGETS/SITE VISIT TEAM'S RECOMMENDATIONS

Budget Categories	YEAR 24 $	YEAR 25 $	YEAR 26 $	YEAR 27 $	YEAR 28 $
Salary, Wages and Fringe Benefits	1,616,006	1,616,006	1,616,006	1,616,006	1,616,006
Equipment	54,410	54,410	54,410	54,410	54,410
Travel	0	0	0	0	0
Participant/Trainee Support Costs	0	0	0	0	0
Other Direct Costs (excluding Consortium)	289,034	289,034	289,034	289,034	289,034
Consortium Costs	0	0	0	0	0
Direct Costs	1,959,450	1,959,450	1,959,450	1,959,450	1,959,450
Indirect Costs	1,085,873	1,085,873	1,085,873	1,085,873	1,085,873
Total Costs	3,045,323	3,045,323	3,045,323	3,045,323	3,045,323