AGENDA

Kentucky Lung Cancer Research Program
Governance Board

Council on Postsecondary Education
Wednesday, June 25, 2014
1:00 PM
University of Louisville, Clinical & Translational Research Building

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NOTE: Lunch with Sci-Med Consultants and GB will be held at noon, with GB members and staff.

University of Louisville Clinical & Translational Research Building
505 S. Hancock Street, Louisville, Kentucky 40202

A Review

Report to the Kentucky Lung Cancer Research Program Governance Board

SciMed Consultants

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June 25, 2014

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INTRODUCTION AND SUMMARY OF FINDINGS

Kentucky has the highest incidence of lung cancer in the United States. In 2011, the age-adjusted incidence of lung or bronchus cancer was approximately 93 persons per 100,000 population in Kentucky (from http://www.cancer-rates.info/ky). The Kentucky Lung Cancer Research Program (KLCRP) was established in 2001 by a legislative act using a portion of Tobacco Master Settlement Agreement (MSA) funds. The primary goal of the KLCRP has been to "…reduce the mortality and morbidity of lung cancer in Kentucky" (quoted from the Strategic Plans). The initiative was launched through a collaborative effort between the University of Kentucky (UK) and the University of Louisville (UofL). The program has been administrated by a 9-member Governance Board consisting of representatives of both institutions, members of the Council on Postsecondary Education (CPE), and members-at-large. Use of the Tobacco MSA funds for a cancer research initiative was relatively unprecedented, with only a few other states on record using MSA funds in this way.

In this, the 14th year of the 20 year program, we have been asked to review the accomplishments of the program to date and to provide suggestions for modifications to the program in its final six years. Specifically, we have been asked to assess the degree to which the objectives delineated in the Strategic Plans of the program have been attained. In Part I of this report, we describe our methods and summarize our findings within each of six research priority areas. In Part II of this report, we further describe areas of potential improvement as noted by our panelists, and we provide recommendations for future directions of the program. The individual reports provided by each of our panelists are included in the Appendix.

PART I: METHODS AND SUMMARIES OF REPORTS BY PRIORITY AREA

METHODS

Team Science included six specialists with expertise in the fields of tobacco cessation and smoking prevention, epidemiology, early lung cancer detection, translational research, clinical trials and technology innovation to perform the review of the KLCRP. Five experts were provided with customized lists of questions for each of five priority areas. Our Panel included Bernard Fuemmeler, Ph.D., M.P.H., for tobacco cessation and smoking prevention; Catherine Rahilly-Tierney, M.D. M.P.H., for epidemiology of lung cancer; Peter Mazzone, M.D., M.P.H., for early detection of lung cancer; Pierre Massion, M.D. for the investigator-initiated (II) award program and translational research; Eric Grogan, M.D., M.P.H., for the Kentucky Clinical Trials Network (KCTN) and NCI designation; Kenneth Lieberman Ph.D., for innovation and collaboration.

We provided our reviewers with documents including the state legislation enacting the KLCRP, the original and updated Strategic Plans for the program, annual and financial reports from each of the institutions, and lists of II awardees. The Brown Cancer Center (BCC) and the Markey Cancer Center (MCC) provided supplemental material including lists of "follow-on" funding obtained as a consequence of KLCRP grants, publications based upon KLCRP sponsored research, reports related to lung cancer control, KLCRP and KCTN newsletters, Marty Driesler publications, and II grant program application forms. To gain additional insight into the KLCRP program that went beyond these documents, Drs. Rahilly-Tierney and Lieberman conducted telephone interviews with staff members at BCC and MCC, members of the GB including Joe Graviss, James Roach, M.D., Amullah Kahn, M.D., Harry Carloss, M.D., Debra Armstrong and Connie Sorrell of the Kentucky Cancer Program (KCP), and Jennifer Redmond of the Kentucky Cancer Consortium (KCC).

During review of pertinent documents and telephone interviews, our panelists were asked to identify staff at each site with whom they wanted to speak to gain an in-depth understanding of the KLCRP. Full-day visits to each site were arranged for April 21, 2014 at the BCC and on April 22, 2014 at the MCC. The format of the site visits consisted of a series of formal presentations by selected staff members followed by one-on-one interviews between our panelists and site staff. Presenting and interviewed staff were instructed to focus their presentations and conversation around material related to KLCRP- funded projects and to limit discussion related to research funded by other sources.

SUMMARY OF FINDINGS

Each expert provided us with their own report describing their findings for their Priority Area; these individual reports were reviewed and are summarized below. Panelists' individual reports are included in the Appendix.

TOBACCO CESSATION AND SMOKING PREVENTION

Kentucky has the highest smoking prevalence in the United States, with 28.3% of the adult population and 14.5% of the adolescent population using tobacco. Lowering the percentages of adult and adolescent smoking in Kentucky would have a significant impact on the incidence of lung cancer in the state. Given these facts, the original KLCRP called for expansion of smoking prevention initiatives targeting schools. There was one notable effort toward this end, the "Drive Cancer Out" program. There was no research protocol to evaluate the effectiveness of this outreach program however. Beyond "Drive Cancer Out," the state government contributes some resources to reduce smoking rates by funding Department of Public Health-orchestrated

projects, but minimal KLCRP resources have been directed to research or outreach efforts on reducing tobacco consumption.

The original strategic plan called for studies related to behavioral aspects of tobacco abuse, and the 2010 Strategic Plan called for recommendation for KLCRP funds to be used toward development of lung cancer prevention methodologies. A KLCRP pilot grant of $6000 was awarded to Dr. Ellen Hahn to support her research related to reducing secondhand smoke exposure. With this research as a platform, Dr. Hahn secured a multimillion dollar grant from the National Institute of Environmental Health Sciences (NIEHS) for the collection of more complete data. The original strategic plan named "improvement in lung cancer awareness and activism" as one element that would be necessary to define the KLCRP as successful. The growth of organizations including the Kentucky Cancer Consortium (KCC) and the Kentucky Cancer Program (KCP) supports the contention that cancer awareness in general has increased in the state, and the increase in public non-smoking areas (related to Dr. Hahn's efforts) speaks to the growing activism around reducing tobacco use in the state. However, these efforts to improve public awareness and implement smoke-free public policies were mostly funded outside the KLCRP.

Language including smoking cessation and tobacco control as an objective was missing from later versions of the KLCRP's strategic plans. The slight attention the KLCRP has given to research related to smoking cessation and tobacco control is evident in the publication records from the two institutions. Over the thirteen years of the program no more than five publications originated from KLCRP funding. Explanations for why tobacco control has been overlooked by the KLCRP are unclear. It is possible that the political climate in the state discouraged smoking cessation research. However, research in the area of tobacco control is desperately needed in Kentucky, in particular in-depth exploration on what kinds of programs would be efficacious in bringing an anti-smoking message to hard-to-reach Kentuckians such as those with lower incomes and young adults. The combined strengths and talents of the dedicated staff of UK and UofL could provide fertile ground to promote novel research programs in tobacco control and smoking cessation.

EPIDEMIOLOGY OF LUNG CANCER

In the first KLCRP strategic plan, there was a call for a description of the incidence of lung cancer in the state, using the Kentucky Cancer Registry (KCR) database. The panelist reviewing this area found that annual assessments of cancer prevention and control are provided using the KCR. With the help of the KCR staff, treatment and outcome of lung cancer cases by Area Development Districts (ADD) are provided annually to pertinent stakeholders. The process is

considered to be of high quality, and has been recognized as a model for surveillance programs. From this data, entities such as the KCP and the KCC are able to develop plans for cancer control that incorporate factors such as poverty, smoking behavior, and geographic variability in lung cancer incidence and mortality.

In addition to its role in providing annual statistics regarding lung and other cancer in Kentucky, staff shepherding the KCR have developed an infrastructure that allows for harnessing this resource for research. A data coordination center has been started to help researchers in the accession of data from the KCR database. Staff assists researchers on projects in the utilization of the data according to the methodology of their protocol. Instructions on how to gain access to the data are available on the KCR website. Providers in the community who are seeking basic information on lung cancer incidence and mortality can easily access http://www.cancer-rates.info/ky. In addition, the KCR has implemented a plan to minimize the length of time between diagnosis of a lung cancer case and entry into the registry. Using a technique called Natural Language Processing, the KCR uses this "E-Path" of identifying newly diagnosed cases at the time of diagnosis at any pathology laboratory within Kentucky. This is all accomplished in real time (that is, within days), as the data is immediately entered into the KCR database. This aligns with the goal of "rapid case ascertainment" mentioned in the original strategic plan.

The original strategic plan called for the KLCRP to fund projects that increased understanding of lung cancer across the state. In response to this, important epidemiologic analyses identified several locations in Eastern Kentucky as having high rates of lung cancer. KLCRP-funded research demonstrated that this excess incidence cannot be explained by smoking prevalence alone. Currently, additional research sponsored both by the KLCRP and other sources is underway to further explore the explanation for the high incidence of lung cancer in this area. As an example, a project supported by the Department of Defense is being used to obtain quantitative data on levels of arsenic and other compounds in the local environment and in the human population, and to determine whether there is an association between exposure to such compounds and incident cancers. This important project aligns with an objective mentioned in the 2010 Strategic Plan, namely a call for studies that refine risk factor delineation for lung cancer.

There is some evidence of efforts to educate physicians in Kentucky regarding trends in the incidence and rates of survival from lung cancer, as was called for in the strategic plans. This primarily occurred in the Journal of the Kentucky Medical Association. Several articles dealing with epidemiological and behavioral studies were published in the journal (Wyatt SW, et al. Cancer and incidence mortality in Kentucky and the United States: An overview. *Journal of the Kentucky Medical Association,* 2012; 110:184-188; Hopenhayn C, et al. The burden of lung cancer in Kentucky. *Journal of the Kentucky Medical Association,* 2003; 101:15-20). The original

strategic plan called for development of a website where Kentuckians could read about the risks of tobacco, including lung cancer. There are web-based resources provided by the KCP where Kentuckians can learn about cancer centers or awareness of cancer prevention educational programs, however there was no evidence of websites funded in part or in whole by the KLCRP.

EARLY DETECTION

There was an evolution in the KLCRP strategic plans. The earliest KLCRP of which emphasized development of clinical computed tomography (CT) based lung cancer screening programs, including mobile screening units, as a priority. The strategic plans emphasized the importance of ensuring that screening be available to individuals in the Area Development Districts identified as having the highest incidence of lung cancer, and to individuals residing in areas remote from the cancer centers. Over time, the success of these clinical screening programs was to be assessed with studies that examined trends in rates of screening of high-risk individuals. These clinical programs were to be augmented by research related to molecular predictors of lung cancer risk and novel biomarkers for early lung cancer detection, with these discoveries being incorporated into the clinical screening program. However, these original goals of early detection were premature because guidelines did not recommend lung cancer screening until after the publication from the National Lung Screening Trial (NLST) in 2011. Notably, one site in Kentucky, the Jewish Hospital Heart and Lung Institute (Louisville) participated in the NLST though this effort was unrelated to the KLCRP. Therefore, later versions of the strategic plans reflected a decreased emphasis on clinical CT screening programs, and a heavier emphasis on research related to early detection of lung cancer.

In accordance with the shift in objectives in the Early Detection priority area of the strategic plans, review of documentation and interviews with pertinent staff demonstrated that KLCRP funding was not used to foster clinical lung cancer screening programs until later on in the program, and more so at UK than UofL. Throughout the 14 years since implementation of the KLCRP, UofL did not appear to have any outreach programs for community physicians related to clinical lung cancer screening. With the advent of the new recommendations for CT screening for lung cancer, outreach programs were initiated at UK. These include the Marty Driesler screening program in Appalachia and research to assess attitudes of local physicians regarding lung cancer screening programs. Additional work is being done to develop a network of screening programs and a screening registry for use across the state.

Several of the strategic plans mention the importance of community providers, who are ultimately responsible for lung cancer screening, having adequate educational and resource

support. Jamie Studts Ph.D., an II awardee, is currently completing a project in which he is examining attitudes of community providers regarding lung cancer screening. Findings from this project are expected soon and promise to be interesting.

In accordance with an important objective listed throughout the strategic plans, KLCRP funding has been used to support biorepositories, samples from which have been used in projects aiming to discover high quality biomarkers capable of impacting lung cancer screening programs (metabolomics, microRNA, plasma thermograms, exosomes). Examples of early detection technologies developed with support of KLCRP Investigator-Initiated funding include a unique breath test (volatile organic compounds present in exhaled breath) and novel imaging assessments of lung nodules. In addition to the work in the area of biomarkers and novel imaging techniques in the detection of lung cancer, the KLCRP funded biorepositories at UofL and UK. However, efforts to develop a biorepository at UofL seem modest, with specimen inventory in the 200 sample range. At UK the biorepository was more successful in their efforts with more than 2000 samples available. In general, researchers in the area of Early Detection at UK and UofL unanimously felt that the KLCRP has been instrumental in providing seed funding for projects, encouraging other faculty to do work on lung cancer and enhancing the reputations of the BCC and MCC.

INVESTIGATOR INITIATED PROGRAM AND TRANSLATIONAL RESEARCH

The objectives related to the Investigator initiated (II) program stated in the original strategic plan, namely early initiation of an award program with a rigorous review process including an external advisory grant review panel, were accomplished. The first grants were awarded less than two years after the inception of the KLCRP. The grant review process for the II projects is very good. Science review committees were established at both institutions using an equitable peer review process and feedback to grant applicants was offered. In accordance with objectives listed for the II program in the strategic plans, both basic science and translational research, as well as clinical trials, were supported by the II program. In addition to the pilot projects and clinical trials supported by the II program, biorepositories were established at both campuses, though our panelists did comment that the repository at UK seemed to have more specimens available than the one at UofL. Overall, the II award program has been extremely successful and the balance between clinical, translational and basic science projects well respected.

Researchers felt that the II program of the KLCRP was very helpful in launching pilot projects to procure preliminary data for eventual funding by the National Institutes of Health (NIH), National Cancer Institute (NCI) and other federal agencies. Use of KLCRP funds to “seed” larger

grants from other sources was an important goal mentioned throughout the strategic plans, and it has been accomplished. These funds have been used in part to fund expansion of laboratory space available at both institutions. As a testament to the success of the II award program, there has been an impressive increase in research funding from NIH in particular at both BCC and MCC during the 13 years since the inception of the KLCRP. For every dollar spent on KLCRP II awards, there has been almost triple return in terms of "follow-on" funding from other sources for larger projects. The 2010 Strategic Plan had called for 3-5 NCI-designable cancer research programs to each institution in the range of $12-15 million. The research panel was provided lists of funding to KLCRP-funded investigators that included more than $12 million per institution total from the NCI. This is indicative of growth opportunities KLCRP funding has given to lung cancer research. Researchers at both institutions expressed strong feelings that the present strategic plan is inadequate and needs to be updated. He also noted that improved collaboration both between institutions and between investigators of diverse backgrounds within institutions would be helpful in achieving the goal of producing impactful translational research. Using pilot data from KLCRP II-awarded projects, the program's leaders should consider applying to the NIH for training grants supporting the development of new investigators in lung cancer research.

INNOVATION AND COLLABORATION

Funding from the KLCRP was intended to be made available to all eligible faculty at UK and UofL. Both universities have a broad range of technology oriented academic departments, and can make vitally important fundamental basic and applied research contributions to the KLCRP. These academic departments are largely unaware of the existence of KLCRP funding. It is of critical importance that efforts be made to broaden the potential funding base.

The National Center for Science and Engineering Statistics reports that annually $65 billion is spent on research at US universities. The academic knowledge and expertise in departments *outside* of university medical schools represents a massive resource, which is largely untapped by the medical community. Through the KLCRP and both cancer centers, outreach programs should be implemented to inform researchers in technology-based academic departments outside of the medical schools about available research opportunities and collaborations. In addition, formal meetings should be convened to permit researchers from BCC and MCC to brainstorm potential collaborations utilizing the combined talents of collaborators from diverse disciplines.

Although tobacco is generally recognized as having a negative impact on human health, the plant can be looked at from a different perspective. Researchers in Israel and North Carolina

have been working on the development of alternative uses of tobacco. In Israel tobacco is being used in the production of the antimalarial drug artemisinin and in North Carolina, a Canadian firm is developing an influenza vaccine using the tobacco plant. Given the advances and initiatives already underway utilizing the tobacco plant in applications that are beneficial, not detrimental, to human health, one strategy to consider may be to explore and develop alternate uses of the tobacco plant. Specifically, the Owensboro affiliate of the BCC has the capability of doing this type of research for plant derived drugs, and could serve as a facility in which to develop such initiatives.

CLINICAL TRIALS NETWORK AND NCI DESIGNATION

Development of a network of sites enrolling patients into clinical trials has been a major objective of the KLCRP. The Kentucky Clinical Trials Network (KCTN) has 17 sites in its system and has enrolled in excess of 1800 patients since its beginning. Along with the successful growth of KCTN, there has been an increase in the number of trials, with over 30 active trials underway in 2013. A goal of the KCTN was to increase the number of industry-sponsored clinical trials utilizing the network; this does appear to be taking place separately at the KCTN and at the UofL clinical trials operation. Participation of the KCTN in cooperative studies is taking place, though this represents a small percentage of the overall portfolio of trials underway. Administrative bodies exist at both sites to orchestrate industry sponsorship of clinical trials. As suggested in the strategic plans, there is a central coordination site located in Lexington at a location separated from MCC, which has adequate facilities to perform its work functions. The strategic plans foresaw a site staff training program in which site visits from the coordination center staff would occur on a regular basis. Our panelist reviewing this area found that this does take place, with up to 25 site visits occurring quarterly. The KCTN has the capability to adequately perform lung screening using the resources of the sites in the network and collect specimens to be stored in the biorepository. UofL has its own separate clinical trials effort, with no linkage between the UofL clinical trials network and KCTN. Integration of the two programs would be difficult to implement because the BCC has a strong independent trial support system. Both BCC and MCC perform lung cancer clinical research using KLCRP and cancer center funds.

NCI designation has been a major objective of the KLCRP since its inception. BCC has a strong infrastructure and stable patient population sufficient to support a successful application, and the review panel surmised that NCI designation is a reasonable goal for UofL. There was ample evidence that the administration at BCC had worked with the NCI to obtain feedback on their P30 application status, and was striving to meet milestones that the NCI had set. However, the amount of funding to this center has not yet expanded to the level required for NCI

designation. Specifically, in order to attain the status of NCI designation within the next five years it will be necessary to procure an additional $30 million to recruit the required research talent. The KLCRP funding has provided BCC the ability to recruit an outstanding group performing research in lung cancer, develop and maintain core facilities supporting research, develop a robust system of clinical trials and seed funding for preliminary data for NIH grants. However, several key researchers with significant NIH support have taken positions at other institutions, and this move may be an additional obstacle to NCI designation for BCC, at least for the short term.

The MCC at UK has obtained NCI designation, and the KLCRP has played a central role in this achievement by supplying nearly five million dollars over 14 years toward this effort. KLCRP funding has permitted MCC infrastructure to grow at a steady rate. With the recruitment of Dr. Mark Evers and the institutional commitment of additional funds, newly recruited investigators have come to the cancer center and have been able to meet the required criteria for NCI designation. At this point MCC is working toward becoming a comprehensive cancer center, and KLCRP support will play a critical role in achieving that goal.

PART II: AREAS FOR IMPROVEMENT AND FUTURE DIRECTIONS

GENERAL OBSERVATIONS

There have been impressive strides made in Kentucky in the area of lung cancer research, and much of this success is attributable to funds from the KLCRP. The program built an infrastructure in which research related to lung cancer could flourish, where before there was very little such research. This is reflected in the publication record at both the University of Kentucky (UK) and University of Louisville (UofL) in the area of lung cancer, which has dramatically increased since the inception of the program. However, there were some general areas of potential improvement noted by several of our panelists, and echoed in conversations between members of our team and members of the Governance Board, staff at both of the institutions, and staff affiliated with other entities working in the area of lung cancer research or prevention in Kentucky.

In general, there was evidence of modest collaboration between the University of Kentucky and the University of Louisville to achieve the overarching goals delineated in the Strategic Plans of the KLCRP. One Panelist remarked that in some instances there appeared to be competition between the two institutions. The original strategic plan called for annual workshops to include researchers from both institutions and across disciplines. There have been 4 joint meetings over thirteen years and no regularly scheduled conferences. Of the hundreds of publications funded by the KLCRP, a crude analysis demonstrated between 6 and 8% of these had authors from both institutions listed. In one of the II grant cycles it was mandated that grant applicants must apply jointly from UK and UL in order to be eligible for the competition. The impact actual impact on collaboration of this one-time occurrence is difficult to quantify. Clinical trial efforts at the two institutions are separate from one another, because KLCRP funds for clinical trials are directed at one of the two institutions. Despite this the clinical trials efforts at UL, largely sponsored by funds from the cancer center itself, are impressive.

Another issue noted by our panelists and mentioned by nearly all staff and faculty with whom we spoke was the diversion of a substantial portion of KLCRP funds toward an ovarian cancer screening program. All of our panelists agreed that this “carve out” of funds handicaps the KLCRP in its efforts toward the overarching goal of reducing the burden of lung cancer in Kentucky. Given the current data on the utility of pelvic ultrasound alone in ovarian cancer screening, the value of the ovarian cancer screening program to Kentuckians might be questioned.

Since the inception of the KLCRP, both institutions have garnered a critical mass of talented faculty with experience in the area of smoking cessation and prevention. However, efforts by outstanding researchers such as Dr. Hahn and Dr. Studts related to tobacco control have mostly

been funded by cancer center pilot funds, National Institutes of Health (NIH), and other sources. In fact, relatively few KLCRP funds have been devoted to tobacco control research since the inception of the program. While entities other than the KLCRP (such as the Kentucky Cancer Program, KCP) have been charged with tobacco control and have been funded using tobacco MSA funds, these entities have focused on service and outreach efforts as opposed to research related to pharmacological or behavioral interventions for tobacco cessation. The recognition of teenage tobacco use as a problem and the intention to reduce teenage smoking in Kentucky via the "Drive Cancer Out" program, sponsored in part by the KLCRP, is to be applauded. Unfortunately this program was not evaluated for its effectiveness and was not based on evidence-based tenets of anti-smoking communication strategies. There did not seem to be programs with a more active approach to smoking prevention, such as telephone outreach or informational brochures, and no evidence of studies looking at trends in knowledge about risks of tobacco abuse in the population, as called for in the original Strategic Plan. There was no evidence of multi-disciplinary clinical programs at the medical centers to assist patients with the smoking cessation process. There were no publications funded by the KLCRP that examined trends in smoking rates, however data from Centers for Disease Control demonstrates there has been little decrease in smoking rates in Kentucky through about 2011. However, the extraordinary potential of each of the two institutions to become leaders in the area of tobacco control research, given the impressive faculty that have been recruited and retained, is recognized. Initiation of KLCRP-funded outreach and research programs, expansion of multi-disciplinary clinical programs for smoking cessation, and assessments of trends in smoking prevalence are areas that the talented faculty at UK and UofL would be well equipped to institute.

The Kentucky Cancer Registry (KCR) has been a leader in the development, maintenance and use of a state-wide registry for surveillance of cancer. However, it was difficult to determine the degree to which the extraordinary effort required to design the registry and assemble the team that shepherds use of the database can be attributed to KLCRP funds as opposed to funds from other Tobacco Industry and non-Tobacco Industry sources. The original strategic plan called for updates provided to Kentuckians regarding innovations in lung cancer treatment and prevention, especially those developed using KLCRP funds. While information related to smoking prevalence and lung cancer incidence and mortality is presented to Kentucky providers via a local medical journal, and there are non-KLCRP funded websites available to the inquiring public, there is little evidence of regular information to the constituency describing the grave problem of the high incidence of lung cancer in Kentucky. There were some impressive KLCRP II pilot projects examining novel predictors of lung cancer incidence and survival. One project sponsored by the Department of Defense, seeks to examine whether non-tobacco exposures, such as arsenic or radon, are related to the high lung cancer incidence in Eastern Kentucky. The original strategic plan called for studies to discover novel genetic factors associated with

prognosis and response to treatment in lung cancer patients. However, there was a noted lack of a research team dedicated to identifying novel genetic tumor signatures that could be used to personalize cancer therapy and predict survival (that is, a genetic epidemiologist). It was also unclear whether lung cancer patients had access to genetic testing of their tumors (ALK testing for instance).

A major objective of the KLCRP as expressed in its strategic plan s and in speaking with shepherds of the program involved since its inception was the support of "high risk, high reward" pilot projects discovering novel biomarkers for lung cancer. In response to this objective, an impressive portfolio of discovery level biomarker projects funded by the KLCRP was undertaken at both institutions. Unfortunately, most of these biomarkers seem to be lacking funding/support for development and translation into the clinical setting, a common obstacle to biomarker development. While lung cancer screening efforts were identifiable as part of various research efforts, there was not a clinical program aimed at capturing high-risk patients for screening either at the centers or through community outreach. An outreach program to educate providers state-wide about the low-dose CT screening guidelines for patients at risk for lung cancer has been initiated, and a project aimed at understanding community practitioners' views toward lung cancer screening is near completion and promises interesting findings. Lung nodule evaluation was not prioritized in the strategic plans; however the panelist reviewing Early Detection noted that such efforts should be incorporated in a lung cancer research program. The development of a biorepository as a resource for researchers at both of the institutions was an important objective in the strategic plans. However, the biorepository at UofL seemed less well developed than that at UK with the reported number of available specimens being small (around 200) in comparison to that at UK (around 2000 samples available).

The II award program was ubiquitously viewed as a success of the KLCRP. Despite that success however, not all KLCRP objectives related to translational research were met. There were some projects related to new drug development and/or immunotherapy, but like discoveries of biomarkers for early detection of lung cancer, many of which lack funding for translation into the clinical setting. Recruitment of new researchers in lung cancer and encouragement of successful researchers in other areas to venture into lung cancer research were both mentioned throughout the strategic plans as an important objective. However, it was difficult to identify new faculty recruits that were focused on lung cancer research, and difficult to identify junior faculty recruits into lung cancer research from other areas of study. Again noted was a lack of a molecular/genetic epidemiologist.

Despite the daunting challenge of initiating and expanding a network of clinical sites with the capacity to add research to their clinical activities, the Kentucky Clinical Trial Network (KCTN) is

now represented in a majority (63%) of Kentucky's counties. As called for in the original strategic plan, a task force ("KLCRP Physician Leadership Team") convened in 2002 to discuss the challenges and priorities pertinent to building a clinical trials network. It is unclear whether such meetings were repeated in later years as the network was built. The strategic plan s called for development of a state-based institutional review board (IRB) to review and approve investigator-initiated or industry-sponsored clinical trials, but this has not occurred. The original strategic plan mentioned the piloting of a web-based enrollment system to be used by sites participating in the KCTN; this does not appear to have occurred. Regular state-wide teleconferences including community-based physicians enrolling into clinical trials were recommended in the strategic plans, but do not appear to be taking place. It was difficult to determine whether the Kentucky Clinical Trials Network Website was used/is useful to patients interested in being enrolled in clinical trials, and a link to information regarding clinical trials for patients could not be identified on the Brown Cancer Center website.

The recent designation of the Markey Cancer Center as an NCI Cancer Center represents a major achievement that required years of dedication from staff and faculty there. Recent loss of a well-funded metabolomics group from the University of Louisville to the University of Kentucky was viewed as a set-back toward the goal of NCI designation by the Brown Cancer Center. In addition, substantial additional funding would be required before the Brown Cancer Center would realistically be considered eligible for NCI designation.

RECOMMENDATIONS FOR FUTURE DIRECTIONS

1. **Consider returning the ovarian cancer screening funds to the KLCRP where the funds could be better utilized to reduce cancer burden in Kentucky.**

2. **Update the KLCRP's Strategic plan.**
    a. Narrow the focus of the objectives to those initiatives that are both feasible and will more directly yield "a reduction in the morbidity and mortality of lung cancer in Kentucky."
    b. Consider tailoring the II-program to include Requests for Applications (RFAs) in the areas of tobacco control, classical epidemiologic research related to lung cancer, and research related to early detection/screening for lung cancer.
    c. Consider re-purposing some KLCRP funds for a training grant program to encourage fellows to direct their careers toward lung cancer research especially in the areas of prevention, epidemiology, and translational research

3. **Systematically encourage collaboration between the two academic institutions.**
    a. Organize biannual meetings to include researchers from both institutions and from departments in and outside the medical schools to discuss current KLCRP-funded research and potential future projects
    b. Consider a monthly journal club
    c. Consider re-defining "collaboration" by assigning complementary priority areas for each of the two institutions, as opposed to expecting both institutions to foster robust programs in all priority areas
    d. Encourage use of both institutions' clinical trial capabilities for each clinical trial proposed; use a common IRB for trials to be implemented at both sites

4. **Systematically encourage multi-disciplinary teams to apply for KLCRP funds.**
    a. Foster increased translation of discoveries in the basic sciences into the clinical setting by encouraging involvement of clinicians and researchers (M.D./Ph.D.) in KLCRP-funded research projects
    b. Encourage cross-disciplinary collaboration by expanding awareness of the KLCRP funding program to University departments outside the medical schools
    c. Consider coordinating with the medical schools to facilitate rotation of M.D./Ph.D. students into KLCRP-funded laboratories

5. **Re-incorporate research in the area of Tobacco Control and Lung Cancer Prevention into the mission of the KLCRP.**
    a. Encourage research in the areas of effective intervention for long-term smoking abstinence, effective communication strategies for hard-to-reach populations, and effective ways to reduce second-hand smoking exposure
    b. Consider using some KLCRP funds to improve the effectiveness of the dissemination of the anti-smoking message, by harnessing evidence-based approaches and technology including social media
    c. Leverage the extant Clinical Trials Network to study novel interventions in pharmaceutical and behavioral science-based interventions to effect smoking cessation

6. **Incorporate a clinical Lung Cancer Screening Program into the mission of the KLCRP.**
    a. Harness the extant Clinical Trials Network to capture and screen high-risk patients
    b. Build multidisciplinary clinics for management of patients with lung cancer nodules

7. **Offer the benefit of recent advances in "personalized medicine" to lung cancer patients in Kentucky.**
    a. Coordinate with clinical departments caring for lung cancer patients to offer genetic testing (such as ALK testing)
    b. Direct some KLCRP funds toward annotating the KCR with genetic testing data on select proven lung tumor genetic signatures
    c. Recruit a genetic epidemiologist with a commitment to utilize the biospecimen repositories to identify novel tumor genetic signatures predictive of survival and response to treatment

8. **Refine the KLCRP's annual reporting process.**
    a. Develop a concise, consistent reporting method standardized across years and between the two institutions
    b. Consider annual dissemination of information about accomplishments of the KLCRP to the public via local television media and social networking (Twitter, Facebook, etc.)

9. **Plan for funding of programs after KLCRP funding draws to a close in 2020.**
    a. Engage both the constituency in Kentucky and the national lung cancer community in dialogue regarding safeguarding the KLCRP's efforts to combat the heavy burden of lung cancer in Kentucky
    b. Consider directing some funds toward early clinical development of biomarkers, vaccines or drug targets previously discovered in KLCRP pilot projects; support junior faculty in seeking industry sponsorship for early phase clinical trials for their discoveries
    c. Consider directing some KLCRP funds toward discovering novel uses of the tobacco plant.

Appendix A

Epidemiology of Lung Cancer in Kentucky

Catherine Rahilly-Tierney, M.D., M.P.H

Kentucky Lung Cancer Research Program: Review of Efforts Related to the Epidemiology of Lung Cancer in Kentucky

Catherine Rahilly-Tierney, M.D., M.P.H.

INTRODUCTION

In the first Kentucky Lung Cancer Research Program (KLCRP) Strategic Plan in 2001, "Early Detection and Epidemiology" is listed as one of 5 of the specific objectives of the program, the others being Early Detection, a Clinical Trials Network, a Basic and Translational Research program, and Constituent Education/Prevention.[1] A timeline in that document project calls for studies that "Describe Epidemiology of Lung Cancer in Kentucky" to take place in the first 5 years of the 20-year program. Specifically, the 2001 Strategic Plan calls for lung cancer incidence to be described and published by Area Development Districts (ADDs) using the Kentucky Cancer Registry (KCR) database. Beginning with the 2006 Updated Strategic Plan, the objectives listed in the Strategic Plan had evolved to include 4 main goals: Investigator – Initiated Research, Early Detection and Prevention, the Kentucky Clinical Trials Network, and NCI Designation as Cancer Centers for each of the 2 sites involved in the program.[2] Although the updated Strategic Plans would not list trending lung cancer incidence as one of the overarching objectives of the KLCRP, tasks related to the epidemiology of lung cancer in Kentucky continue to be included throughout the updated Strategic Plans.

Below, a series of questions in italics related to KLCRP-funded efforts in the area of Epidemiology of lung cancer are addressed. These questions refer to objectives mentioned in one or more of the Strategic Plans. Sources for the answers are referenced and listed at the end of the document.

QUESTIONS

1. ***Have new projects been initiated/funded that "increase understanding of lung cancer in commonwealth of Kentucky"? Is there evidence of studies that describe the epidemiology of lung cancer in Kentucky, through year 5 after the KLCRP was established?***

According to the first Annual Report for the program, early Governance Board (GB) meetings included conversations with Stephen Wyatt DMD MPH, who at the time was associated with the Kentucky Cancer Control Program (this has evolved into what today is the Kentucky Cancer Consortium). During these meetings the GB obtained "…preliminary information regarding the epidemiology of lung cancer in Kentucky." According to that report, the Kentucky Cancer Control Program was charged with performing an epidemiological study.[3] Later Dr. Wyatt did publish at least one piece describing the trends in incidence and mortality though this was later (2012).[4] Efforts to examine trends in incidence and survival in Kentucky were funded to varying degrees via the discretionary funds distributed through the Directors' offices, but also by awarding individual grants for projects through the Investigator-Initiated (II) program. In several reports of expenditures from University of Kentucky (UK), for example, monies spent in the area of "epidemiology" (without details provided) are listed for some, but not all years.[5-8] In minutes from a Governance Board (GB) dated January 13, 2010, some GB members iterate that there are II-funded projects targeting epidemiology-related questions.[9] Claudia Hopenhayn MPH PhD did publish at least one piece describing trends in incidence of lung cancer over time in Kentucky.[10] Sandra Sephton PhD, an early II-awardee, presented some of her work related to cortisol levels as a predictor of survival in lung cancer patients.[11]

2. ***The KLCRP Original Strategic Plan (SP) called for baseline demographics, treatment and outcome of lung cancer cases be published by "Area Development Districts" using Kentucky Cancer Registry. Did this happen?***

   There is evidence of several projects that identified areas in Eastern Kentucky as having particularly high lung cancer incidence. Several of these list the KLCRP as sponsors of the projects. W. Jay Christian, MPH PhD, first-authored several of these.[12-13] These reports demonstrated that lung cancer incidence in coal-mining Appalachian Eastern Kentucky are higher than might be expected when considering tobacco use prevalence alone. Throughout the KLCRP's history, several studies focusing on incidence and trends

in survival in Eastern Kentucky have been funded, some by KLCRP and some by other sources.[5,6] Per our conversation with Tom Tucker PhD, a project funded by the Department of Defense has been garnered to develop a database including not only elements included in the KCR but information on levels of arsenic and other compounds collected from nails, hair, blood, urine, water, and soil specimens in this area.

a. ***Original SP also called for expansion of the KCR to include other variables. Did this happen?***

   The KCR has been a leader in the development, maintenance and use of a state-wide registry for surveillance of cancer. We discussed the KCR in detail in a conversation with Thomas Tucker PhD MPH and Eric Durbin MS. The KCR is part of the national Surveillance Epidemiology and End Results (SEER) program. A few variables were added to the KCR during the existence of the KLCRP, including a smoking variable with is not included in the SEER databases of many other states. The KCR's usability as a source for identifying subjects for both retrospective observational and prospective interventional trials was expanded. During the time period since the inception of the KLCRP, the KCR has standardized its operations in accordance with accepted guidelines for Cancer Registry Management.

b. ***As part of this, they wanted the KCR to be expanded to include molecular biomarkers, did this happen?***

   In our conversation with Dr. Tucker, he discussed that inclusion of biomarkers on all subjects included in such a database beyond subsets of observations included in project-specific datasets, is somewhat unfeasible mainly due to cost issues. There are currently no known biomarkers predictive of lung cancer, and the expense of the effort to add yet-to-be-proven biomarkers variable to KCR would outweigh the utility of having these available to researchers. However, the KCR does contain all variables delineated by the North American Association of

Central Cancer Registries (NAACCR) as standard. As dialogue regarding some select biomarkers that may be useful in the diagnosis and treatment of lung cancer continues among experts in the NAACCR, NCI, and other entities, there is a possibility that some such markers may be added to the KCR in the future.

c. ***Was a data coordinator to manage research projects out of this database hired? Was software making the data accessible to docs who want to add to it OR researchers who want to use it, developed?***

A data coordination center spearheaded by Dr. Tucker and Eric Durbin MS exists to assist researchers in accessing data housed in the KCR database, and has been available for eight years. Staff re available to perform analyses on the datasets constructed on a project-by-project basis. In some cases, raw but de-identified datasets are provided to the researchers and they perform their own analyses. In other cases, the KCR was used to identify cases for enrollment trials or survey studies. Instructions on how to gain access to KCR data are available on the KCR's website. Along with information on obtaining project-specific datasets, the KCR website includes a web-based interactive tool that makes basic analyses with graphs available to anyone with access to the internet. This program, developed by KCR, has been licensed to cancer registries in other states.[14] There are several examples of projects in the epidemiologic and behavioral sciences realms that utilized the KCR as a data source to identify eligible subjects.[15-18]

d. ***One goal listed in the 5-year development section of the original SP was "rapid case ascertainment." Can you determine the length of time between diagnosis of an incident case and the date the case's data is entered into the KCR?***

Using Natural Language Processing technology, the KCR has implemented an "E-Path" method of identifying newly diagnosed cases at the time the diagnosis is made at any pathology laboratory in the state, and adding the case to the KCR

database in real time. Ninety-five percent of lung cancer cases are first reported to KCR via this method. This makes identification of subjects for clinical trial enrollment possible, which has traditionally been difficult given the typically short survival time of diagnosed lung cancer cases. One currently KLCRP II-funded project (Principal Investigator Eric Durbin, funded through 9/30/2015) is entitled "Automated Identification of Lung Cancer Patients for Clinical Trial Recruitment." This project aims to refine the process of utilizing the KCR's rapid case ascertainment system to identify subjects eligible for enrollment into clinical trials. Dr. Hopenhayn is the Principal Investigator on another II-awarded project, "Building the Infrastructure for a Comprehensive Lung Cancer Data Source," funded through 6/30/2014, but unfortunately was not available for comment during this review.[19] The aforementioned Department of Defense-funded project is utilizing the rapid case ascertainment function of the KCR to identify, recruit and enroll subjects newly diagnosed with lung cancer in Eastern Kentucky.

The capturing of cancer cases in real time using NLP to scan pathology reports in laboratories state-wide represents a major advance in the science of disease surveillance. In combination with expansion of lung cancer screening efforts, which in theory could effect a "stage shift" in which the proportion of lung cancer cases identified earlier in the course of disease increases, the KCR's "EPath" technology could ultimately increase patients' access to life-prolonging experimental therapeutics by allowing for rapid identification and enrollment of eligible subjects into clinical trials.

3. ***Original SP called for development of a family registry of lung cancer cases. Did this happen? The 5-year development section of the original SP called for this registry to ultimately have tissue and blood banked. Did this happen?***

In our conversation with Dr. Tucker, we discussed the outdated nature of this as a goal. Given today's technology, we no longer examine genetic factors associated to disease

by examining families. Instead biochemical markers ("gene signatures") on the tumor cells themselves are assayed and examined as potential predictors of survival or response to treatment ("pharmacogenomics"). While KCR does not have the funds nor staff to house specimens, the database does identify the location of tissue from each cancer patient it registers. Such tissue specimens have been collected and included in the Biospecimen Repository at UK for studies in other cancers. For more details on the Biospecimen Repositories, see the report related to Early Detection.

4. ***Original SP called for information re: lung cancer epidemiology be dispersed to the population quarterly. Did/does this happen?***

There is some evidence of efforts to disperse information related to trends in incidence and survival, both to the constituency at large and to Kentucky physicians and other providers. At the end of the KLCRP's first (2001) Annual Report, there is a reprint of a newsletter entitled "Lung Cancer in Kentucky Policy Brief" dated Winter 2001 in which incidence in Kentucky, other states, and the US are compared.[3] We were also provided with another newsletter entitled "Kentucky Lung Cancer Research Program Newsletter" dated 2006.[20] In summary, there were some efforts to disperse information to the public but this was not done with any regularity.

In minutes from a GB meeting on February 12, 2009, the GB Chair Kristie Paris called for the GB to be active in translation of research findings from KLCRP-funded projects into community care of Kentuckians with lung cancer.[7] One way to ensure Kentucky provider awareness of such findings would be publication of results in a journal targeting Kentucky physicians. Several publications related to epidemiologic and behavioral science studies in Kentucky were published in the Journal of the Kentucky Medical Association, so dispersion to the medical community in Kentucky of many important findings from KCLRP-funded efforts presumably did occur.[4,10,13,12,22] There are web-based resources where Kentuckians can learn about research at the cancer centers or educational efforts related to cancers in Kentucky by the Kentucky Cancer Program (KCP, not funded by the KLCRP).[23,24]

In our conversation with Dr. Tucker, he iterated that population-based studies on trends of cancer incidence are most meaningfully done in annual increments, not more frequently such as quarterly.

5. ***The long-range section of the original Strategic Plan called for studies to identify genetic mutations associated with increased risk of lung cancer. Did a screening program for genetic factors associated with increased risk of lung cancer get underway?***

   This reviewer was able to find few publications funded by the KLCRP that identified novel genetic markers associated with long-term risk of incident lung cancer in high-risk patients. However, there have been few such genetic markers for lung cancer published in the literature and widely assayed in general; that is, markers analogous to the multi-gene signatures currently use to guide therapy in early stage breast cancer, for instance.

6. ***Have there been publications reporting trends in incident lung cancer in Kentucky? Publications reporting trends in mortality/survival of incident cases in Kentucky?***

   The UK's 2010 Annual Report mentions re-formulation of the cancer research programs at that center, to include the area of "Cancer Prevention and Control" to be lead by Drs. Tucker and Wyatt.[25] Dr. Tucker and his staff do provide annual assessments of incidence and survival to certain key entities, such as the Kentucky Cancer Consortium. The process they have developed to describe and monitor the burden of lung cancer in Kentucky through time has been widely recognized as a model for such surveillance.[26] These assessments are used to develop statewide cancer control plans. In addition, the KCR is utilized to calculate an index of lung cancer burden, stratified by ADD and incorporating pertinent factors including poverty, smoking behavior, lung cancer incidence, and lung cancer mortality. These indices are presented annually to the KCP's individual District Cancer Councils. Like the statewide trends examined by the KCC, the district-specific lung cancer burden indices are used to focus limited resources where they are most needed. Examples of such efforts include the Cooper/Clayton smoking

cessation program, and the recently initiated efforts at increasing rates of screening among at-risk patients.

There have been efforts not funded by the KLCRP to publish data relating to trends in lung cancer incidence and survival in Kentucky in the medical literature. For example, one publication from the KCP published in 2012 compares incidence and mortality of lung cancer patients in Kentucky versus the US, and mentions trends in these over a period that includes that of KLCRP.[21]

7. ***Has there been an improvement in OS of lung cancer cases in Kentucky?***

Using data from KCR, Dr. Tucker has demonstrated that there has been no significant change in the 5-year survival of lung cancer patients when comparing 2000-2004 to 2005-2009, as demonstrated below (charts derived from his UK Site Visit presentation):

5 Year Survival, Non-Small Cell Lung Cancer, 2000-2004 vs. 2005-2009		
Year	2000-2004	2005-2009
1	51.8%	55.8%
2	39.4%	41.0%
3	34.2%	33.8%
4	30.8%	29.5%
5	27.3%	26.5%

Log-rank test	
Chi Square Value	0.525
P value	0.469

5 Year Survival, Small Cell Lung Cancer, 2000-2004 vs. 2005-2009		
Year	2000-2004	2005-2009
1	34.3%	35.9%
2	14.1%	15.2%
3	9.0%	10.0%
4	7.4%	7.8%
5	6.1%	6.6%

Log-rank test	
Chi Square Value	1.789
P value	0.181

There have been KLCRP-funded II projects examining factors that impact lung cancer survival in Kentucky.[7,8,25] Examples of such publications from such projects were reviewed.[11,16]

8. ***Have there been publications describing a study in which the relationship between emphysema and lung cancer is studied using Kentucky data?***

The Marty Driesler Cancer Project has as its main objective the evaluation of biomarkers that may predict lung cancer. The project has been enrolling both healthy controls and subjects considered at high risk for lung cancer. The latter group is defined by poor lung function defined by pulmonary function testing (PFTs). Subjects meeting PFT-based eligibility criteria are screened using computed tomography (CT), scanning over 3 years; these scans are funded from the KLCRP. Ultimately, nodules identified in this way would be added to the Biospecimen Repository at UK. This Repository in turn would serve as a resource for genetic epidemiology-type research in which relationships between tumor markers, survival, and response to treatment might be examined. Such studies would require not only a populated, accessible repository with merged clinical data, but would require years of follow-up to define relationships between tumor genetic signatures and survival.[20] While the Marty Driesler Cancer Project portends ground-breaking work in genetic epidemiology, realistically such studies would not be expected to have been completed by the year 2014. This is likely why few publications identifying novel genetic predictors for lung cancer could be identified by this reviewer (see answer to question 5 above).

9. ***2010 SP calls for studies that refine methodologies for risk factor delineation – did this happen?***

There is evidence for funding of several II projects that sought to further delineate risk factors for incident lung cancer. Timothy Aldrich, PhD was funded during Cycles 3 and 4 of the II award program for projects related to environmental and occupational factors associated with incident lung cancer, and has published his findings.[27] Dr. Aldrich was unfortunately not available for comment during this review. Other KLCRP II awardees examined novel predictors of stage at time of diagnosis of lung cancer.[22] In financial reports provided from both UK and U of L, there is mention of funding of projects that examine radiation exposure, heavy metal exposure, and high-risk behaviors (such as

smoking) and their relation to incident lung cancer.[5,6,28,29,30] Details of which projects are referred to are not provided in those documents but presumably one such project is the aforementioned Department of Defense-funded project, in which soil and biologic samples (nails, urine) are tested for radon and arsenic levels which will be in turn examined for their association with incident cancers.

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Appendix B

Early Detection
Peter Mazzone, M.D., M.P.H.

REPORT ON THE KLCRP: EARLY DETECTION

Peter Mazzone

Evolution of Strategic Plans

The earliest KLCRP Strategic Plans described the development of clinical CT based lung cancer screening programs as a priority. The early goals included an assessment of the capabilities of all regions of Kentucky to perform lung cancer screening, and support for clinical CT scan based screening programs throughout the state. Separately, CT screening was to be augmented with researcher developed molecular advances in risk assessment and early detection. Results of these clinical and research efforts were to be published and success was to be assessed by the number of patients enrolled and the outcomes of the screening program (improved detection of early cancer, reduction in smoking rates, improved lung cancer overall survival).

By the 2007 Strategic Plan, the goals for early detection appeared to change. Clinical programs were no longer mentioned, while screening and early detection research was highlighted. Biospecimen repository development was stressed and a link to prevention was added. Key research areas were to include the refinement of methodologies for risk-factor delineation, validation of methodologies for lung cancer screening, the development of biomarker correlates of lung cancer and/or lung cancer risk, and the development of methodologies for lung cancer prevention. The programs were still expected to reach into key geographic areas of the state and contribute study results to the literature. Finally, CME programs and templates for early detection were to be made available for Kentucky physicians from each administrative development district.

The evolution of the early detection component of the Strategic Plans mirrored the lung cancer community's acceptance of lung cancer screening. The original goals for early detection were premature. Lung cancer screening was not recommended in any set of guidelines until after the publication of the National Lung Screening Trial in 2011. The shift in focus towards screening and nodule management related research and education was appropriate. This makes it difficult to assess the success of the KLCRP early detection mission based on the initial

goals. As such, the questions I chose to answer focused more on the evolved, and more realistic, goals of the latter Strategic Plans.

Questions to Address

Based on the evolution of the Strategic Plan and the original questions presented for me to address, the following questions were developed:

1. Discuss the evolution of the KLCRP early detection goals, from those related to support of clinical screening programs to those focused on early detection research.
2. Discuss how support from the KLCRP has been used to engage and/or educate community physicians to either develop clinical lung cancer screening programs, or participate in early detection and prevention research.
3. Provide examples of how the KLCRP support of biorepositories has led to research advances related to the early detection of lung cancer.
4. Provide examples of how the KLCRP support of research has led to projects related to the refinement of methodologies for risk-factor delineation, validation of methodologies for lung cancer screening, the development of biomarker correlates of lung cancer and/or lung cancer risk, and the development of methodologies for lung cancer prevention.
5. Discuss KLCRP supported collaborative projects (clinical and/or research), shared by the U of L and UK.
6. Is there evidence to suggest that KLCRP supported early detection and/or prevention projects has led to improved detection of early cancer, a reduction in smoking rates, and/or improved lung cancer overall survival?

Answers to the Questions

The following answers are based on a review of the documentation provided (including strategic plans, yearly reports, lists of awarded grants and publications), in-person interviews, and internet/literature searches. It was challenging to answer some of the questions

completely, as there is a lack of clarity about the proportion of success that can be attributed to the KLCRP, rather than support from other sources.

1. Discuss the evolution of the KLCRP early detection goals, from those related to support of clinical screening programs to those focused on early detection research.

The documentation that was reviewed, and the in-person interviews, clearly showed that KLCRP support was not used to foster clinical lung cancer screening programs. For the first decade of the program this was appropriate, as standard of care lung cancer screening was not recommended. This is an area of transition with implementation of high quality CT-based screening programs now a major focus of early detection nationally. There is a potential for high quality screening programs to become very important in meeting the original mission of the KLCRP.

The documentation that was reviewed, and the in-person interviews, demonstrated a substantial effort in performing discovery level biomarker development projects, potentially capable of impacting screening programs (see below, #3).

2. Discuss how support from the KLCRP has been used to engage and/or educate community physicians to either develop clinical lung cancer screening programs, or participate in early detection and prevention research.

The evidence presented did not suggest engagement or education of community physicians related to clinical lung cancer screening at the University of Louisville. Documentation suggests some biorepository samples were collected from 3 local hospitals. There was community outreach related to prevention (smoking cessation education for youth), to be discussed by another member of our panel.

At the University of Kentucky, the Marty Driesler research project reached into key community sites in Appalachia to perform a screening project. Biologic specimens were collected as part of this research. In addition, research was performed to understand the knowledge level and

attitudes of community practitioners toward lung cancer screening. Projects focusing on behavioral aspects of lung cancer screening are also underway. An education program was developed by Jamie Studts and presented at several community sites across the state. Work is being done to develop a network of screening programs and high quality screening registry for use across the state.

3. Provide examples of how the KLCRP support of biorepositories has led to research advances related to early detection of lung cancer.

The KLCRP has provided support for biorepositories at both the University of Louisville and the University of Kentucky. It was difficult to determine the exact amount of support at each site and the number of lung cancer samples collected to date. The numbers reported to us during our visit to the U of L seemed rather modest (in the 200 range; the documentation reviewed prior to the site visits suggested a larger number of samples had been collected.), while those from the U of K were quite robust (in the 2000 range). Both programs discussed outreach into the community to obtain some of their samples.

The biorepositories have allowed several discovery level biomarker studies to be performed. These projects have included the development of biomarkers related to metabolomics, microRNA, plasma thermograms, and lung cancer exosomes. This work has the potential to impact the early detection of lung cancer. Some of the biomarker research has led to substantial funding to further develop the markers (e.g. metabolomics), while much of the work sits in the chasm between discovery and validation that plagues biomarker development, in hopes of further support.

4. Provide examples of how the KLCRP support of research has led to projects related to the refinement of methodologies for risk-factor delineation, validation of methodologies for lung cancer screening, the development of biomarker correlates of lung cancer and/or lung cancer risk, and the development of methodologies for lung cancer prevention.

In addition to the biomarker work performed using the biorepository materials (see #3), additional research that has been performed, with the potential to impact early detection, includes the development of a breath test (volatile organic compound detection in the breath), and imaging assessments of pulmonary nodules.

The screening projects that have been performed to date have not been large enough to contribute to the validation of methodologies for lung cancer screening. There has been some work performed to determine why areas of the state have elevated lung cancer incidence, in excess of that related to smoking alone. Other studies have not been large enough nor focused on the question of refinement of risk-factor delineation. The more extensive work with biomarkers has been performed at a discovery level with a substantial amount of work left to technically and clinically validate the markers before considering them ready for clinical use. Prevention is discussed by another member of our group.

5. Discuss KLCRP supported collaborative projects (clinical and/or research), shared by the U of L and UK.

In the area of early detection there was no evidence to suggest projects were being shared by the U of L and UK. Investigators and administration at both sites felt that there were no major hurdles, beyond distance and the phase of the projects that were being performed, to collaborating. A few investigators appear to have left one of the sites and now work at the other. For at least one of these there was a sense of frustration that a tremendous amount of support was provided to the investigator at the initial site then the investigator left for the other site once a substantial grant was obtained to further the research.

There was a description that one of the granting cycles required investigators from both sites. I did not have a clear sense of the success of this one time mandate in fostering collaboration. There was also a description of a few joint meetings between researchers at the sites. These seemed to be well received but did not occur frequently or with any regularity.

6. Is there evidence to suggest that KLCRP supported early detection and/or prevention projects has led to improved detection of early cancer, a reduction in smoking rates, and/or improved lung cancer overall survival?

The screening programs connected to the KLCRP have been relatively small research projects. They have shown promise for early detection in even the rural areas of Kentucky but have not been large enough to expect an impact on meaningful outcomes. Clinical screening has not evolved to the point where improved early detection and overall lung cancer survival have been impacted. The data presented to us supports this.

There has been a substantial effort to reduce smoking rates. This is discussed by another member of our team.

Messages from Interviews

1. There was a desire to have closer collaborations with clinicians.
2. It has been difficult to move some of the biomarker work beyond the discovery level.
3. It is time to have an updated Strategic Plan that reflects recent advances in early detection.
4. Collaboration across institutions has been minimal. Barriers were not identified but systematic encouragement has been inconsistent.
5. There is no plan in place to sustain the aspects of the early detection programs that have been supported by the KLCRP if/ when the KLCRP ends.
6. Every person interviewed felt the KLCRP has been instrumental in providing pilot funding for projects, attracting researchers to lung cancer, and growing the lung cancer programs.
7. There hasn't been much focus on lung nodule evaluation.
8. It was difficult to determine how much of the successes to date could be credited to the KLCRP.

Recommendations

This is an unprecedented time for the early detection of lung cancer. The benefit of lung cancer screening has been proven. Debate remains about the proper implementation of screening, with a recognition that the development of successful screening programs requires appropriate patient selection and the minimization of potential harms. There are also great opportunities to advance the science of screening by improving risk prediction and nodule management. The successful development of high quality state-wide screening programs has the greatest potential to meet the mission of the KLCRP, "To reduce morbidity and mortality from lung cancer".

1. Incorporate clinical aspects of lung cancer screening into the strategic plan. Ensure at least one award at each site per year is dedicated to aspects of the implementation of lung cancer screening programs. Examples include education programs, systems for nodule management, incorporating smoking cessation, and systems to identify high risk patients.
2. Encourage clinician involvement with bench/translational researchers. Consider mandating a clinician be included in every grant application.
3. Encourage collaboration between institutions in the implementation of lung cancer screening through sharing of best practices and collection of outcomes data.
4. Incorporate biomarker development into screening programs. Aim to move current biomarkers from discovery to validation phases.
5. Develop a sustainability plan for the programs being supported by the KLCRP.
6. Engage the national lung cancer community and industry to assist with recommendations 4 and 5.

Appendix C

Consultation Report
Bernard Fuemmeler, Ph.D., M.P.H.

CONSULTATION REPORT

Prepared by Bernard Fuemmeler, Ph.D., M.P.H.

Background and Purpose of Consultation:

The Commonwealth of Kentucky solicited a review of the Kentucky Lung Cancer Research Program specific to the program priority areas in lung cancer epidemiology, early detection and treatment, research and translational activities with regard to incidence and mortality reduction and clinical trials.

I was asked to review the success of the KLCRP program with respect to translational activities specifically related to tobacco control efforts. Materials reviewed included: 1) Original legislation establishing the KLCRP and the Governance Board (GB) that oversees it; 2)Original Strategic Plan (SP) for the KLCRP as developed by the GB in 2001, with updates in 2006, 2010, and 2012; 3) Annual reports prepared by GB and the office of Continuing Postsecondary Education (CPE) about the program, from 2006 through 2013; 4) Financial reports prepared by staff at University of Kentucky (UK) and University of Louisville (U of L) spanning years from 2007 through 2013; 5) Lists of grant awardees at UK and U of L and success of these grantees; and 6) websites or other resources discovered or provided by the institution.

Additionally, I was part of a site-review committee that visited both UofL and UK on April 21st and 22nd, respectively. During my visit I attended a group presentation arranged by the heads of each program, Dr. Donald Miller from UofL and Dr. Mark Evers from UK. I also meet independently with representative from both UofL and UK, specifically from Drs. Michael Bousamra, Goetz Kloecker, Wolgang Zacharias, and Kavitha Yaddanapudi from UofL and Drs. Jamie Studts, Audrey Darville, and Ellen Hahn from UK.

Strengths:

Both cancer centers at the UofL and UK are ideal settings in which to develop nationally and internationally recognized programs in lung cancer research. Research directed at lung cancer has the potential significantly reduce cancer morbidity and mortality. A focus on lung cancer research also has the potential to bring together scientists from a number of disciplines

because the etiology is distinguished by both social and biological factors. Developing a cutting-edge scientific program in lung cancer research will distinguish UofL, UK and the state of Kentucky and be helpful in the anticipated applications for National Cancer Institute (NCI) comprehensive cancer center status at the respective institutions. There are a number of strengths that will distinguish UofL and UK as leaders in the field of lung cancer prevention and tobacco control with continued support and potential expansion of the KLCRP.

1) **Unmet need to reduce smoking**

   Unfortunately, Kentucky has the highest smoking rate in the nation at around 28.3 percent of the adult population and 14.5 percent of the adolescent population. Reducing the rates of adult smoking and teen smoking initiation in Kentucky will have a tremendous impact on lung cancer incidence and mortality within the state. The state is already contributing resources to this effort and traditionally few resources from the KLCRP have been devoted specifically to research on tobacco control. Much of the work devoted to tobacco control through both non-KLCRP funds and the minimal funding by the KLCRP have been on service-related or outreach programs, with little attention to evaluation of efficacy of these programs. Support from the KLCRP funds directed at tobacco control research would likely have a large impact in contributing to the success of UofL and UK institutions having first-rate tobacco control research programs.

2) **Growing expertise in lung cancer research**

   Because of the continued support of the KLCRP, programs at UofL and UK have begun to amass a number of researchers with expertise in lung cancer research. Researchers in this area are well positioned to contribute to transdisciplinary research that would facilitate translational research. For instance, the knowledge gained from developing a lung-cancer clinical trials network could be leveraged to develop clinical trials network devoted to testing novel smoking cessation interventions and products.

3) Potential for collaborations

UofL and UK are in a unique position to contribute significant research on tobacco control. UofL and UK Schools and Departments of Nursing, Public Health, and Psychology have several talented behavioral science faculty with expertise in smoking cessation and prevention. For instance, Dr. Ellen Hahn and her collaborator Jamie Studts have been conducting very novel and innovative research aimed at improving indoor air pollution, including reducing second hand smoke exposure. Support from the KLCRP for efforts like these that would support behavioral and population sciences around tobacco control have the potential to impact smoking prevalence and contribute uniquely to the advancing behavioral science related to tobacco control.

Weaknesses and Challenges:

Over the past 13 years the KLCRP program has been inattentive to advancing pharmacological or behavioral science research related to smoking cessation and tobacco control. This is quite apparent when examining the publication history of investigators funded by KLCRP program. Between the two institutions there are no more than 5 publications that originated from KLCRP funding that address tobacco control over the 13 years of the program. Research support from the KLCRP program on smoking cessation or prevention has been absent and opportunities to support research capable of follow-on funding in this area have been overlooked. The explanations for why behavioral science research on tobacco control has been overlooked by the KLCRP program are not entirely clear. Investigators from the institution indicated that, in the early years of the KLCRP program, the political climate of the state and the KLCRP program discouraged research on smoking cessation and tobacco control. One investigator with knowledge about the early RFAs for the KLCRP program recalled that KLCRP pilot funds restricted applicants from submitting proposals that focused on smoking cessation. Despite this, there have been a few examples of the KLCRP program supporting tobacco control efforts. For example, at the UK, Dr. Hahn received a small amount of money (~$6,000) to support pilot data collection for a grant on second hand smoke. Dr. Hahn was able to secure a multi-million dollar grant from the NIEHS that followed from this work. Fortunately, Dr. Hahn

had additional resources to collect the pilot data she needed to advance her research. UofL devoted a moderate amount of funding (~$12,000) to an anti-tobacco campaign (Drive Cancer Out) directed by Dr. Bousamra. Dr. Bousamra was able to raise additional funds from charitable organizations to support his Drive Cancer Out program which focused on anti-smoking messaging with teenagers in the school setting. The program's signature was a sports car emblazoned with the anti-smoking DCO logo (Note: no funds were used from the program to purchase the car). The program appeared to be popular with children and the school system, but given that it was not based on behavioral science or evidence-based anti-smoking communication strategies, the program likely had very little effect on reducing teen smoking initiation and it is not clear if it could have increased smoking initiation.

In sum, smoking cessation and tobacco control research has been neglected in the portfolio of funding from the KLCRP program. This is in contrast to some of the earlier goals of KLCRP strategic plan which suggested tobacco control efforts be a part of the KLCRP portfolio. Later strategic plans did not contain some of this language. In the area of tobacco control, continued research is needed on more effective ways to improve long-term smoking cessation. In addition, research is urgently needed on disseminating effective smoking cessation programs, especially to difficult to reach populations, such as those with lower income and teenagers. Research is also needed on effective communication and prevention strategies directed to teens. Programs like the "DARE" and "TRUTH Campaign" have been shown to be mostly ineffective and research is needed on how to improve our prevention approaches. Research on reducing second hand smoke exposure especially for children also needs to be advanced. Reducing smoking will likely have the largest impact on the incidence of lung cancer in the state of Kentucky. The strengths of the UofL and UK institutions have the potential to lead novel research in tobacco control. Cutting edge pharmacological and behavioral science research in tobacco control would advance the cancer institutes likelihood of achieving NCI comprehensive cancer center status. Funds from the KLCRP program could be directed toward these ends. If funds were directed toward serious and meaningful cutting edge research on tobacco control, it is likely to make a significant difference on the rates of smoking in the state.

Recommendations

Given the importance of tobacco control research to lung cancer incidence and mortality, the following recommendations are suggested for inclusion in future KLCRP strategic plans and goals.

1. **Articulate a vision that better integrates tobacco control research as part of the KLCRP and embark on action steps in this direction**

   The most successful programs in tobacco control are those with strengths in both basic pharmacological and behavioral science research. In addition, rigorous research on dissemination and implementation of smoking cessation and prevention also contribute to the success of tobacco control programs. While discrete areas for research emphasis are open, multi-disciplinary scientific teams will advance the most cutting edge research. The use of technology to improve dissemination of smoking cessation programs and methods to include difficult to reach populations should be considered. With all efforts, the highest standards of evidence-based approaches should be a priority.

2. **Align currently silo programs/resources for collaboration within the respective institutions and across institutions**

   Aligning disciplinary scientists for a shared mission is challenging, however, the products of this type of work are likely to have a larger impact. Different approaches should be considered, such as incentivizing collaboration through the grants program or supporting supplements to existing awards that would allow scientists of different disciplines to collaborate. Supporting large-scale center grants are also methods to foster interdisciplinary collaboration.

3. **Assure optimal funding for tobacco control efforts**

   The KLCRP program has not traditionally supported tobacco control research. These efforts could be supported with set-aside funds or RFAs specific to tobacco control could be considered.

4. **Foster strong leadership in tobacco control**

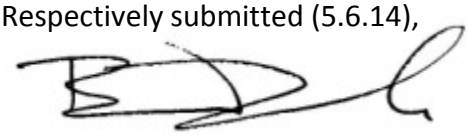
   Support from the KLCRP could be used to advance working groups and meetings that would help accelerate research in tobacco control.

5. **Cultivate training opportunities**

   Post-doctoral training opportunities for tobacco control efforts could be considered. Additionally, supporting organizational interdisciplinary colloquium series would facilitate training in tobacco control.

Thank you for the opportunity to visit and learn about the KLCRP. The KLCRP provides a unique opportunity to advance research pertaining to lung cancer. Attached are supplementary files that were used to during my review. Please do not hesitate to contact me if I might provide any additional information.

Respectively submitted (5.6.14),



Bernard Fuemmeler, Ph.D., M.P.H.
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Supplemental Material A:

Pre-site review of documents

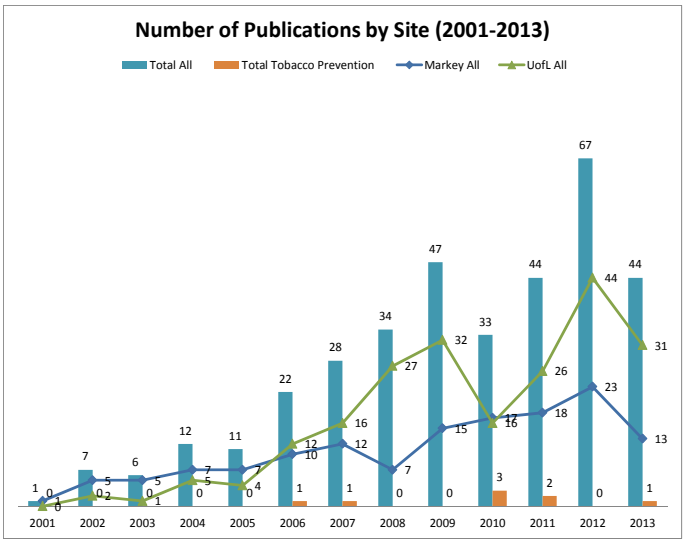
Questions provided by review committee to guide content of review based supplied documents:

1) The lung cancer research program was originally intended to be a collaboration between UK and U of L. Is there evidence of collaborations between researchers at each of these institutions?

There is some evidence of organized collaboration between the two institutions, but this was minimal over the first 13 years of the program. In recent years investigators have been developing some cross-institution collaborations. According to the publication information supplied by the institutions, a joint grant with the two institutions was initiated in Cycle 10, Nov 1 2010. According to UofL Annual Report 2010, the first joint Univ of Louisville, Univ of Kentucky Lung Cancer symposium was held on Nov 21st. Cross-institution collaboration on areas of tobacco control could be enhanced in future years as there was very little documentation of tobacco prevention/control research between the two institutions.

2) Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place?

See overall plots of number of publication by year and publications on tobacco prevention. Publications titles were reviewed to determine if they related to tobacco prevention (i.e., etiology research on smoking behavior, prevention, or treatment). From 2001-2013 Markey had 3 publications in prevention and University of Louisville had 4 publications. Between 2001 and 2006, Markey had 35 publications overall and



between 2007-2013, Markey had 105 publications. This represents 3-fold increase in publications. Between 2001 and 2006 University of Louisville had 24 publications and between 2007 and 2013 UofL had 192 publications. This represents an 8-fold increase in publications. Efforts to direct funding specifically to areas related to smoking prevention, cessation and control will likely result in greater numbers of publications in these areas.

3) The original SP called for improvement and expansion of smoking cessation/prevention initiatives targeting schools. Is there any evidence that extant programs were expanded or new ones initiated?

Across both sites there is very little evidence of expansion in the areas of smoking cessation/prevention. There is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports. Note: See supplemental material from site review for description of other activities related to smoking prevention.

4) The original SP called for "clinical implementation of smoking cessation" – interpretation of this might be the initiation or augmentation of clinics that specifically work with patients toward smoking cessation. Is there any evidence that such clinics were set up at one or both of the cancer centers?

There is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports.

5) The original SP called for the development of behavior studies on smoking cessation and tobacco abuse.

a. Can you find evidence of such studies being initiated and published?

UofL publications show work on tobacco prevention (secondary or primary)

- Knudsen HK, **Studts JL**. The implementation of tobacco-related brief interventions in substance abuse treatment: a national study of counselors. Journal of Substance

Abuse Treatment Apr;38(3):212-9, 2010. doi: 10.1016/j.jsat.2009.12.002. Epub 2010 Feb 8. PMID: 20116960; PMC2864720

- Knudsen HK, **Studts JL**, Boyd S, Roman PM. Structural and cultural barriers to the adoption of smoking cessation services in addiction treatment organizations. Journal of Addiction & Disease Jul;29(3):294-305, 2010. doi: 10.1080/10550887.2010.489446. PMID: 20635279; PMC2922688
- **Studts JL**, Matera EL, Worth CT, Ghate SR, Miller BF 4th, Thomas SD, Sorrell CL. Tobacco cessation treatment knowledge, attitudes and practices of Kentucky physicians. Journal of the Ky Medical Association Oct;105(10):497-507, 2007. PMID: 18038512.
- **Studts JL**, Ghate SR, Gill JL, Studts CR, Barnes CN, LaJoie AS, Andrykowski MA, LaRocca RV. Validity of self-reported smoking status among participants in a lung cancer screening trial. Cancer Epidemiol Biomarkers Prev Oct;15(10):1825-8, 2006. PMID: 17035388.

UK/Markey publications show work on tobacco prevention (secondary or primary)

- Hopenhayn C, Christian WJ, Christian A, Studts J and Mullet T. Factors associated with smoking abstinence after diagnosis of early stage lung cancer. Lung Cancer 80:55-61, 2013.
- Luftman V, Martin CA, Guenthner G, Arnold SM, Mullett TW and Jhaveri M. The Power of Videotaped Personal Statements of Patients With Lung Cancer: A Recruitment Strategy for Smoking Prevention and Cessation Programs. Oncol Nurs Forum 38:11-4, 2011.
- Christian J and Hopenhayn C. Early stage lung cancer survival in Kentucky: Associations with smoking history and Appalachian geography. Journal of Kentucky Medical Association 108:97-105, 2010.
- Hahn EJ, Rayens MK, Hopenhayn C and Christian WJ. Perceived risk and interest in screening for lung cancer among current and former smokers. Research in Nursing & Health 29:359-70, 2006.

UK/Markey

- 2010 FY Report. UK Project: Examining lung cancer survival: smoking cessation, quality of life, environmental exposures.
- 2009 FY Report: Prevention Study: lung cancer patient statement to smoker family member with participation in cooper Clayton smoking cessation program.
- 2009 Annual Report: Northern Kentucky clean air project. These funds served as matching funds for a grant from RWJ Foundation to identify highly toxic indoor air sites and develop appropriate intervention strategies.

b. **Can you find evidence that advances in smoking cessation (one example might be availability of support for safe use of varenicline) being incorporated into any *clinical programs focused on smoking cessation?***

There is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports.

6) The 5-year section of the original SP called for the development of a website where Kentuckians could read about the risks of tobacco use including lung cancer.

7)

a. Does such a website exist?

The below websites were found. It is not clear if Quit Now Kentucky received money from or organization input from the KLCR program.

https://www.quitnowkentucky.org/

http://www.nkyhealth.org/quitnow.aspx

b. Is there any evidence for more active programs targeting smoking prevention and cessation, such as phone outreach programs or informational brochures made available through schools/mailing campaigns, etc?

There is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports. Information is provided by Quit Now Kentucky (at above websites).

8) The long-term section of the original SP called for updates provided to Kentuckians regarding innovations in lung cancer treatment and prevention. Presumably such updates would be available through mass media (articles in the lay press) or on the aforementioned website. Can you find evidence that such updates were made available at any time to the lay public?

There is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports.

9) The Assessment of Success section of the original SP called for assessments of trends in knowledge of Kentuckians related to risks of tobacco use and related to therapies of lung cancer.

a. Have there been any studies looking at trends in knowledge of the population in Kentucky?

b. Is there evidence of public activism (non-for-profit organizations focused on prevention and cessation, etc)?

Although, there are efforts to improve knowledge about the harms of smoking through other organizations, there is no evidence from publications, grants allocated from the pilot funding mechanism, or year-end reports that this was supported by the KLCRP.

Note publication of potential relevance: Christian J and Hopenhayn C. Early stage lung cancer survival in Kentucky: Associations with smoking history and Appalachian geography. Journal of Kentucky Medical Association 108:97-105, 2010.

10) Are there any publications that demonstrate trends in smoking rates in adults and adolescents in Kentucky? If so, is a decrease in such rates over time demonstrated?

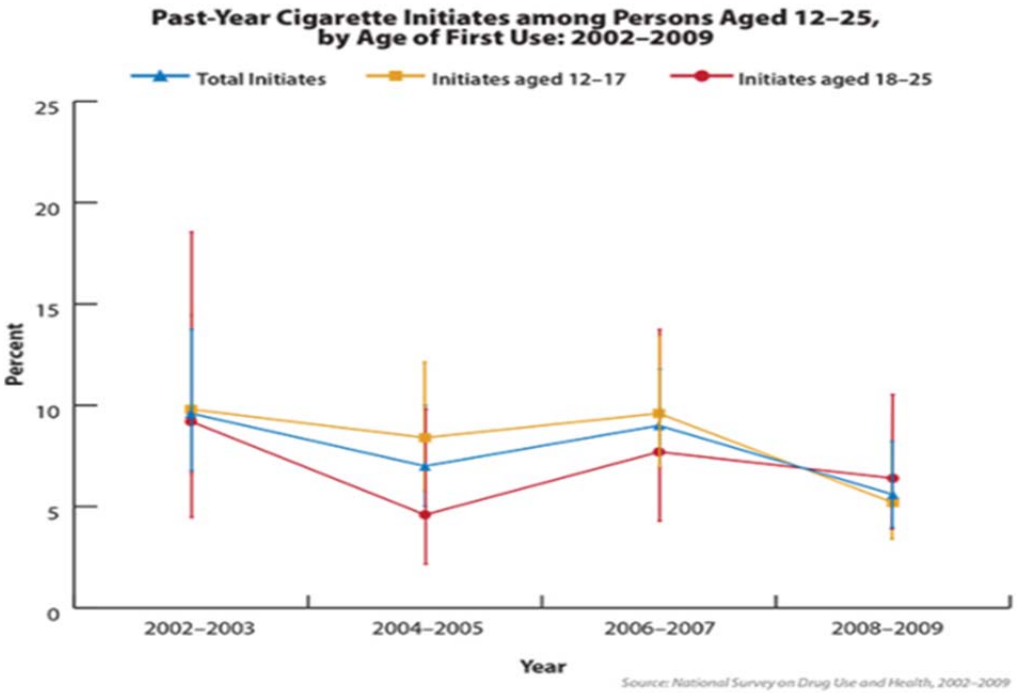
The KLCRP has not traditionally supported tobacco surveillance research. The following documents highlight pertinent information on tobacco use in Kentucky.

http://www.cdc.gov/tobacco/data_statistics/state_data/state_highlights/2012/pdfs/states/kentucky.pdf

http://impacteen.org/statetobaccodata/chartbook_final060409.pdf

Highlights from CDC report:

- In 2011, the percentage of youth who currently use tobacco in Kentucky was 31.9% compared to 23.4 nationally. Kentucky ranked 36th among 36 states reviewed.
- Past year cigarette initiates have decreased, but not markedly. In 2008–2009, of all Kentucky youth ages 12–17 who had never smoked, 5.2% smoked a cigarette for the first time in the past year. This ranked 10th in the nation, with a range of 3.3%–9.2% among the states.
- Adults in Kentucky rank 51st among the states who report that their homes are smoke free.
- In 2010, Kentucky was below the national average for efforts aimed at anti-tobacco media campaigns.



11) The 2010 updated SP calls for development of lung cancer prevention methodologies without being specific. Can you find any evidence that any KLCRP funding went toward lung cancer prevention programs?

Dr. Studts has received funding twice from the KLCRP program. He is leading innovative and successful research in the area of lung cancer screening.

Supplemental Material B:

Notes from interviews and site visits with selected staff from UK and U of L.

NOTES – University of Louisville

- 25% Kentucky Healthcare improvement authority
    - 70% Kentucky access
    - 20% KLCRP (5% of total)
    - 10% Smoking Cessation (2.4% of total)
- Impact of KLRCP on BCC
    - More than 20 research groups
    - Early research funded by KLCRP
- KLRCP – Dataseam Partnership
    - Funded students to come to UofL - outreach to community – computer program
- Leveraging of funds
    - Cigarette excise tax
    - Advanced Cancer Therapeutics – bio-drug development within coordination of BCC
    - "Bucks for Brains"
- Lung Cancer Prevention
    - Colored berries to alter high risk biomarkers in cancer patients
    - Embryonic stem cell vaccine to prevent the development of lung cancer
- Partnership with Owensboro
    - Tobacco-based research program
    - Plant based vaccines
        - HPV vaccine (oral)
        - Oral Cholera toxin B vaccine
            - Inexpensive and rapid turnaround
            - May prevent colon cancer development in animal models

- Early detection of lung cancer
    - "Breath test" for lung cancer
- Lung Cancer Manhattan Project

There is a significant funding being used from smoking cessation (not from KLCRP)

- Haven't funded many tobacco control research investigators
    - Not many applications coming from investigators from behavioral science areas.
    - 60 scientists and around 25 R01 among those fundees

Sandie Sephton Presentation

- Fundee of KLCRP
- Psycho-oncology and behavioral neuroscience
    - Mindfulness and stress biology

Goetz Kloecker

- Survey on primary care physicians and systemic therapy for lung and breast cancer
- 10 million Bristol myers squib – educating primary cancer physicians
    - This work is possible because of the clinical trials network.
    - The plan will be to implement an education program

Michael Bousamara

- Drive Cancer Out
    - 2006-2010
    - Not for profit program
        - Bring the clinic to the classroom
        - Motivate medical students and undergrads to be health leaders and educators
        - Make it fun – young leaders : "smoke free ford gt"
        - Market the anti-smoking message (conjunction with Truth campaign)

- Clinic to the classroom
    - Cancer survivor volunteers; surgical instruments, videos; plastinated cancerous lungs; multiple other visual displays; homework; go to areas hit hardest, inner city and low income areas
    - 30 different schools; 12-15 schools a year
- Student Leaders
    - Classroom educators, trained to lead school programs
    - Volunteered at multiple activities
    - Involved UofL student athlete volunteers;
- Make it Fun
    - Ford GT concept
    - 14,000 promises not to smoke
    - Big car events
- Market the anti- smoking message
    - Two high quality PSAs
    - Governor meeting with cancer survivor
    - Worked on tobacco legislation

Epidemiologist – Kathy Baumgartner

- leading/assisting to develop lung cancer cohort

http://louisville.edu/sphis/fac_staff_dir/kathy-b-baumgartner.html

Drive Cancer Out Program

From 2006-2010 Dr. Bousamra led the Drive Cancer Out Program (DCO). The DCO program was an organization that is supported by medical students, health care providers, and cancer survivors. The DCO was implemented mainly as an educational outreach program to increase health literacy of youth. The KLCRP program contributed $30,000 to its initiation (only ~$12,000 was actually spent). Other funds were raised through fund-raising campaigns and industry support, including some funds from tobacco industry. The program's signature was a sports car emblazoned with the anti-smoking DCO logo (Note: no funds were used from the

program to purchase the car). In addition, a website was developed with education materials (no longer an active website) and two public service announcements (e.g., http://www.youtube.com/watch?v=Qz5MY5VpsGI). The funds were mainly used to fund project coordinator time and for t-shirts with the logo to give away at school visits. There was some coordination with the Campaign for Tobacco Free Kids program. Funds were also used to do a pre-test post-test evaluation of the program (~10,000 to a statistical consulting firm), which was published in the Kentucky Medical Association Journal (KMA, vol 106, No.12). The evaluation was not designed to evaluate efficacy of the program. The program design was loosely based off of the "truth campaign." The program was not based evidence-based programs for prevention. The program depended heavily on Dr. Bousamra's leadership and could not be sustained once he was unable to have the sports car as part of the educational program.

Meeting with Goetz Kloecker

Dr. Kloecker has been working recently on evaluating methods for increasing education about lung cancer treatment among primary care physicians. He is coordinating efforts with Dr. Jamie Studtz (UK) to develop a comprehensive physician training program sponsored by BMS – Dr. Studtz is the PI.

Meeting with Dr. Kavitha Yaddanapudi

Dr. Yaddanapudi is a new assistant professor who is a recent recipient of a KLCRP two-year grant. She is doing work on a vaccine for lung cancer using embryonic stem cells. She is using a mouse model to test this new therapeutic. Pilot data is supporting new grant initiatives through the "free to Breath Foundation" in which she received $100,000 grant and she is also working to submit NIH follow-on grants.

Meeting with Dr. Wolfgang Zacharias

Dr. Zacharias is a two-time recipient of KLCRP research grants. The funding mainly was used to examine a model that he was previously examining in oral cancer and apply it to lung

cancer. The funds were used to support a post-doc to help with this research. Attempts were made to develop NIH/NCI follow-on grants, but these were unsuccessful.

Overall Impressions

- Lack of research in tobacco control
- The behavioral sciences is underrepresented
- Education and outreach is present, but no work to evaluate these efforts.
- Hard to see how some of the funded work will support NCI funding in tobacco control and behavioral science

NOTES – University of Kentucky

Ellen Hahn – spoke on prevention efforts of lung cancer

- These efforts include
  - Smoking cessation and prevention initiatives
  - School and colleges smoking policies
  - Website
  - Lay public & activism
  - Public knowledge
  - Trends in smoking

- Impact of KLCRP funding
  - The level of KLCRP funding has been nominal in this area.
  - The focus on lung cancer on which the KLCRP has mobilized interest and synergy has allowed for collaborative efforts.

Meeting with Dr. Studts, Hahn, & Darville

In addressing some of the discrepancies between why prevention and tobacco control had not been of higher priority Dr. Studts mentioned that tobacco cessation was explicitly excluded for

funding consideration in the call for proposals. Some of his earlier work was on patient provider communication.

Dr. Hahn mentioned that the KLCRP program has provided a way to connect with collaborators – Dr. Hahn connected with Dr. Studts when he was at U of L through his KLCRP grant.

Dr. Studts recent funding through the KLCRP is providing funding for a novel intervention trial of smoking cessation in lung cancer survivors.

Moving forward the group offered a few suggestions for way to improve prevention and tobacco control.

1) A renewed focus on prevention should be instituted.
2) Investigator initiated grants could be used to further foster collaborations and call for proposals should be written to attract prevention scholars to lung cancer research.
3) Grants or funds could also be used to supplement ongoing R01 to collect data that will further help build more funding in lung cancer and tobacco control and prevention.
4) Grants or funds could also be available for bridge-fund applications.

Appendix D

Investigator-Initiated Program and Translational Research
Pierre P. Massion, M.D.

KLCRP – INVESTIGATOR-INITIATED PROGRAM AND TRANSLATIONAL RESEARCH

Review by Pierre P. Massion, M.D.
April 21 and 22, 2014

Content of your review. We would like you to think about the following specific questions as you review these sources.

1) ***The lung cancer research program was originally intended to be a collaboration between UK and U of L . Is there evidence of collaborations between researchers at each of these institutions? 6 (satisfactory)***

   The KLCRP has clearly established collaborations between the 2 sites. The success of this collaboration is rated as satisfactory only. The investigators have managed to set only 4 retreats over 13 years and no regular encounters for specific programs. Individual collaborations are better in number but overall difficult to quantify. The clinical trial network has been more successful and engaged the 2 institutions. Although the trials are opened on both CCs, UK seems to have benefited more from the infrastructure/leadership that is established in Lexington.

2) ***Is there evidence of a trend of increasing number of publications each year coming out of UK and U of L? Specifically, the 2006 updated SP calls for a 300% increase in publications between 2000 and 2008. Did this take place? 3 (excellent)***

   The publication record is strong at both places. The publication rates went from 15 publications / year in 2010 to 30 in 2013. A small % are in collaboration publications however.

3) ***What is the process for grant review for investigator-initiated projects?***

   a. ***The original SP called for the selection by the GB of an External Advisory Committee to evaluate new proposals within the first 2 years of the program. Was such a Committee established?***

b. ***Is there adequate internal review (i.e. by the GB) of internal grant proposals prior to funding such projects? What criteria does the GB use to evaluate investigator initiated proposals? 3 (excellent)***

Scientific committee established on both side with good peer review process and feedback provided to investigators. The investigators have all mentioned that the program has really served the purpose of jumpstarting new investigators and launching new projects for successful RO1 funding.

4) ***The original Strategic plan foresees Investigator Initiated projects funded starting during year 2 of the LCRP. Did this take place?***

a. ***Can you determine when the initial RFPs for the first funded projects were made available? OCT 2001- Have additional RFPs been made available each year for Kentucky researchers?***

b. ***The original RFPs from the GB were supposed to be in the areas of both basic and translational research. Can you identify evidence that projects in these areas are funded?***

c. ***The original SP also called for funding of investigator-initiated projects/studies related to improving radiation therapy techniques and better chemotherapy regimens, including new drug development and immunotherapy, for lung cancer patients. Is there evidence that such studies were/are funded in Kentucky? 3 (excellent)***

The first awards were provided in the year 2 (2001) of the KLCRP grant. RFPs were initiated yearly and about half of the total budget was dedicated to the support of Investigator initiated grants, 13 funding cycles thus far. Both basic science and translational research were supported including clinical trials. The program was really successful. All programs seem to have benefited from these grants and the balance between clinical, translational and basic science projects was well respected.

5) ***The original Strategic Plan called for annual workshops open to investigators of varying disciplines and importantly from both institutions. Can you find evidence that such workshops take place? 8 (poor)***

Annual workshops did not happen. I have found evidence for workshops between 2003-2008 and not thereafter.

6) ***The original SP called for recruitment of a molecular epidemiologist within the first 2 years of the program.***

   a. ***Was such a researcher recruited? Who?***
   b. ***The 2006 updated SP called for the ongoing recruitment of additional scientists into both the cancer centers. Can you find evidence that both young investigators and established investigators are continuously being recruited to either of the cancer centers?***
   c. ***In addition to recruitment of new faculty, the 2010 updated SP called for existing faculty at the 2 institutions to direct some of their focus to lung cancer. Is there evidence that tenured faculty at either institution instigated new projects related to lung cancer? 8 (poor)***

I have found no evidence for hiring a molecular epidemiologist at U of Louisville. Recruitment of additional researchers happened and the KLCRP clearly contributed to this effort with at least 25% of the budget dedicated to faculty recruit/NCI designation. Recruits in lung cancer were no clearly delineated on either side. The lung cancer focus is particularly not strong at the Markey cancer center. I could not find the list of recruits provided apparently by UK.

7) ***The original SP called for a Task Force to set up a state-wide system for acquiring and banking tissue, harnessing the expertise of UK and U of L pathologists and molecular biologists. Was such a program initiated? Is it operational today? 5 (good)***

Tissue banking was clearly initiated on both campuses but the enterprise is minimal at Uof Louisville and much stronger at UK. Neither site could provide the exact number of individuals in the tissue bank but it is very substantial at UK (over 2000 individuals have at least blood in the repository). Such effort has been supported by multiple sources including the KLCRP.

8) ***The 2006 updated SP called for identification of molecular abnormalities for lung cancer susceptibility. Can you find any studies or publications that describe novel biomarkers/genetic factors from investigators at UK and/or UofL? 3 (excellent)***

Biomarkers studies are many. It is a relative success of the program yet none are considered ready for clinical utility. Most are in early phases of development. Most of them are published in mid to low tier journals. These include a miRNA signature from UofL, a breath test from UofL, cortisol rhythm as predictor of lung cancer survival from UofL, autoantibodies for the early detection of lung cancer from UK, Estrogen receptor expression in lung adenocarcinoma (UofL).

9) ***The 2006 updated SP calls for an increase over time in NIH, DOD, and NCI Program Project investigator-initiated research.***

a. ***Is there evidence that of increasing numbers of funded projects from these sources?***
b. ***Is there evidence of NCI multi-project grants, SPORE grants, and or NCI cooperative grants? 5 (good)***

There are two of such examples: PO1 from Drs. Fan, Higashi, Moseley, Lane, with collaboration of UofL Dr. Yan. There was no SPORE, nor NCI Cooperative grant. This is a really difficult bar to reach in the field. This PO2 in metabolomics is a major accomplishment. Another example is the DOD award to UK investigators. The NCI designation from the UK Markey CC in July 2013 is also in part credited to the KLCRP.

This comment should be pondered by the tremendous growth in peer review funding at both institution which speaks for the progress made at both CC and this growth is clearly credited in part to the success of the KLCRP. Research funding has almost tripled in 13 years. This is a remarkable achievement.

10) ***The 2006 updated SP calls for expansion of the available space for bench research. Is there evidence of expansions/new facilities being built at either cancer center? 2 (outstanding)***

Yes on both side. Bench research is well supported. At UK the Research space has increased by 97% since 2009

11) ***The 2010 updated SP called for mentorship/development of early stage investigators in the area of lung cancer. Is there evidence of an environment that fosters such mentorship/growth of young investigators at these 2 institutions? 5 (good)***

Junior investigators recruit happened at Markey not so much at Brown.

12) ***Starting with the 2006 updated SP, there is a call for expanding the LCRP to include support for research related to cancers other than lung, that are associated with smoking. Is there evidence for support of research on non-lung, smoking –related cancers at these 2 institutions? 2 (outstanding)***

Absolutely, effort in renal cell ca (AS1411), immunology, cervical cancer vaccine (Gardasil) , HN cancer, neuroblastoma (AS1411).

Comments:

- Overall the scientists are delighted to have such program supporting pilot grants and seed money for larger NCI applications.
- Researchers all commented on how this KLCRP foster new lung cancer research, attract new investigators in the field. They would love to see grants going fomr75K / year to

higher level of support and / or maybe to spend the money over a 3 year period instead of 2. Allowing carry forwards is discussed with PROs and CONs.

- The development of the clinical trial network and tissue procurement tremendously facilitates the effort of going from the bench to the bedside.
- Researchers identified a need for core facility for example in pharmacology and animal model. They need to further consolidate the effort with UK and UofL to share reagents, expertise and have retreats more frequently. There is a good virtual screening drug discovery lab at UofL but a need for a stronger development phase program.
- Research awards are relatively well balanced between basic, translational and clinical sciences. 4-6 projects were funded annually at both sites.
- There is a definite need to update the strategic plan and foster more collaboration between basic and clinical sciences.
- Researchers underlined the wish to emphasize areas of research in the future including the development of a state wide database for CT screening, augmentation of the effort on biomarker development and validation for lung cancer, and drug development with special emphasis on lung cancer.
- Some of the awards were made collaborative based on mandatory collaborations in the RFA. These initiatives have not been strongly enforced. There is a need for a multidisciplinary approach to one disease and a clear need for physician scientists. That is clearly missing at UofL and to some extent at UK as well.
- Researchers recognized the need for more MD PhD students to rotate in the labs. Collaboration with the School of Medicine could be stronger. Translational research should be more emphasized. There could be a stronger path to train from basic sciences to translational medicine.
- A screening program is not opened at UK or UofL. They contributed to the NLST but there are no services currently at either CC offering screening for lung cancer with a multidisciplinary clinic following up lung nodules. Implementation f LC screening program starts at home. There is a plan at UK and this will hopefully opens in the network.

- The CCs do not offer directly molecular testing for lung cancer diagnosed in the clinic beyond EGFR and AKL mutations. No SNAP shot or Foundation medicine genotyping supported by the program. Suggestions are provided at www.mycancergenome.org
- Researchers express a wish to have a joined Journal Club on a monthly basis.
- Applying for a training grant supporting the development of new investigators in lung cancer research could be a major accomplishment of the KLCRP.

Appendix E

Clinical Trials Network
Eric Grogan, M.D., M.P.H.

KENTUCKY LUNG CANCER RESEARCH PROGRAM: CLINICAL TRIALS NETWORK

From KLCRP 1st Strategic Plan 2001

Mission: To reduce the morbidity and mortality from lung cancer. Initial focus areas included early detection and epidemiology, development of statewide clinical trials network, and striving for NCI designation of the cancer center from each university.

Strategic Plan Update - January 2012

GOAL 3: Kentucky Clinical Trials Network

"164.476(5)(b) Establish a statewide clinical trial network to make university-based clinical trials available to the community physician in order to bring the most innovative cancer treatments to all Kentuckians in need of these treatments."

Improvements in the effectiveness of new cancer treatments are accomplished through a series of phased clinical trials: Phase I. – identify maximum tolerated doses of new drugs and dose-limiting toxicities; Phase II – test the study drug's effectiveness in specific cancers; Phase III – compare new treatments with established protocols. All of today's recognized cancer treatments were proven by clinical trials before they became generally available. Despite that record of success, most people do not know that cancer clinical trials are the means by which cancer research becomes cancer treatment.

Thousands of cancer clinical trials are underway in the United States. The National Cancer Institute, cooperative groups, academic medical centers, community hospitals, physician practices, and pharmaceutical companies sponsor cancer clinical trials. Of the 1.3 million people who will be diagnosed with cancer this year, only three to five percent will participate in cancer clinical trials.

The University of Kentucky and the University of Louisville have worked together to establish a Kentucky Clinical Trials Network to educate patients and physicians about the benefits of clinical trials and trial availability, and to assist physicians with planning and implementing trials.

Objectives

1. Increase number of Kentuckians with access to and participating in lung cancer clinical trials.
2. Develop and maintain a critical mass of trained professional staff to support multi-site clinical trials.
3. Offer and manage industry-sponsored lung cancer clinical trials through the Network.
4. Identify and develop investigator-initiated clinical trials at both universities that can be offered to patients in diverse settings.
5. Continually improve the Network's services with input from practicing Kentucky physicians.

Priorities for 2012-2014

- Efficiently and effectively process and manage clinical trials for the Network.
- Increase the number of industry-sponsored trials.
- Increase the number of therapeutic trials.
- Increase the number of cooperative group trials.
- Expansion of investigator-initiated clinical trials from both institutions.
- Improve training sessions with site investigators and site coordinators.
- Increase number of patient accrual to Network trials.

Endpoints in 2014

- The Network has a continuing stream of novel therapeutic trials available to patients.
- The Network has an increasing stream of patient accrual.
- The Network provides training and information to physicians and citizens throughout the Commonwealth, including updated clinical trial results and new standards of care.
- Clinical trials are accessible for all Kentuckians.

Important information Annual Reports

2006 Annual Report:

- 5 investigator initiated studies, five industry studies, one cooperative study, and a community hospital study.
- Budget to date - $1.3M, Expenses to date - $0.4M.

2010 Annual report

- Patient population served by KCTN sites and enrolled to KCTN studies to 57/120 counties; 48% of state.
- Total patients accrued to KCTN studies is 178.
    - Therapeutic Intervention: 95
    - Epidemiologic/Observational: 83

2012 Annual Report

- Enrolled 736 patients residing in 71/120 counties (59%) to KCTN trials. 16 sites.
- In total, over 30 different clinical trials offered during funding period.
- 4.3 million spent to date – approximately 400k per year
- Visit 25 sites per quarter

Salary supports:

Clinical Director	**Tim Mullett**	**10.00%**	**Existing**	**$16,016.28**	**$3,339.33**
Asst. Director for Clinical Studies	**Kris Damron**	**100.00%**	**Existing**	**61,353.96**	**19,527.84**
Clinical Research Assistant II	**Michele Hughes**	**100.00%**	**Existing**	**51,119.90**	**17,124.00**
Clinical Research Assistant I	**Melinda Dowden-Kruger**	**100.00%**	**Existing**	**34,981.32**	**11,705.11**
Administrative Research Assistant	**Trey Alexander**	**100.00%**	**Existing**	**36,735.45**	**16,746.94**
Research Admin Coordinator - Clinical	**Lara Sutherland**	**10.00%**	**Existing**	**4,147.20**	**1,560.84**
Temp Tech/Paraprofessional	**Teresa Foody**	**25.00%**	**Existing**	**7,020.00**	**604.88**
Epidemiologist	**Amy Christian**	**18.75%**	**Existing**	**10,321.23**	**3,606.58**
Epidemiology - Lung Cancer	**Claudia Hopenhayn**	**7.47%**	**Existing**	**7,991.67**	**2,309.65**
	Total	**4.71**		**$229,687.01**	**$76,525.17**

2013 annual report

- Enrolled 1,553 participants residing in 71/120 counties (59%) to trials.
- Sites located in every federal congressional district in Kentucky.
- Meetings with MCC to evaluate opportunities to expand access to trials to selected affiliate centers. Anticipate FY 2014 impact to increase IIT accrual at new sites.
- KCTN Medical Director attends selected external Tumor Boards and directly participates in patient care discussions and screening for trials.
- Continue work with 16 research sites, including Academic Centers, Community-based hospitals and private practice physicians; experience ranging from vast research enterprises to no existing research program.
- Resource tools & training provided to increase screening & enrollment of patients to studies. KCTN PCs and Director visit sites, directly assist in screening for trials.
- Sites have established enrollment to trials or increased their previous overall enrollment performance. Data for selected sites that hold accreditation with the American College of Surgeons, Commission on Cancer indicate verifiable numbers of increased participation and access to trials in FY 2013.

    1. Site #13: Community Hospital Cancer Program: No trials, no accruals prior to participation in KCTN. Hospital service area of 6 counties, with patients accrued to trials from 5 area counties; anticipate saturation to exceed service areas in FY 2014 as this site will serve as a regional role in an upcoming KLCRP sponsored IIT. Site has expanded research nurse team to 1.5 FTE, with prn effort of others. Achieved commendation level from CoC for enrolling 7% of lung patients to trials.
    2. Site #01: Teaching Hospital Cancer Program: Enrolled 41 patients from 32 area counties. Enrolled 10% of lung patients to trials. Expanded IITs to multi-site.

    Study Spotlight - Investigator-Initiated Intervention Trial:

    • IIT collaboratively developed, by MCC clinician, behavioral scientist, KCTN Medical Director and Director. Utilizes innovative statistical design, MOST to identify optimal

smoking cessation intervention strategy for newly diagnosed patients; pharmaceuticals and high intensity counseling. Funded with KLCRP cycle 12 award, with additional grants submitted to pharma and philanthropy. Received positive feedback from pharma on innovative design and well-written protocol.

Clinical Trials (G3)	Clinical Director	Tim Mullett	10.00%	Existing	$ 17,727.38	$ 3,433.14
	Asst. Director for Clinical Studies	Kris Damron	100.00%	Existing	$ 61,353.96	$ 18,413.76
	Clinical Research Assistant II	Michele Hughes	100.00%	Existing	$ 51,119.90	$ 17,124.00
	Clinical Research Assistant I	Melinda Dowden-Kruger	100.00%	Existing	$ 49,783.40	$ 15,900.35
	Administrative Research Assistant	Trey Alexander	100.00%	Existing	$ 37,440.00	$ 16,400.81
	Research Admin Coordinator - Clinical	Lara Sutherland	37.50%	Existing	$ 16,891.20	$ 6,093.63
	Temp Tech/Paraprofessional	Teresa Foody	25.00%	Existing	$ 15,336.00	$ 1,301.83
	Epidemiologist	Amy Christian	18.75%	Existing	$ 6,728.82	$ 2,654.08
	Database Specialist	Bryan Baseheart	5.00%	Existing	$ 2,900.95	$ 951.27
	Admin Support Associate I	Wanda Matthews	45.00%	Existing	$ 14,322.19	$ 5,835.51
		Total	5.41		$ 273,603.80	$ 88,108.38

Kentucky Clinical Trials Network Coordinating Center

KCTN website: http://www.kctn.org

Very general information provided. Contact information for the directors and administrators at both university sites is provided. Not sure how frequently it is accessed or how useful it is to patients.

TEAM:

Timothy Wm. Mullett, MD, FACS
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Coordinating Center Contact Information

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Kentucky Clinical Trials Network
2347 Sterlington Rd., Suite 310
Lexington, KY 40517
Hotline: (859) 323-1109
Toll-Free: (866) 972-2984
Fax: (859) 257-1343

Listed clinical trials on website

Protocol No.	Title	Status
AMGEN-20070782	A Randomized, Double-blind, Placebo-controlled Study to evaluate the Long-term Safety and Efficacy of Darbepoetin Alfa administered at 500 ug once-every-three-weeks in Anemic subjects with Advanced Stage Non-small cell lung cancer receiving multi-cycle chemotherapy	Open
CTN-1301	Optimization of Smoking Cessation Strategies in Community Cancer Programs for Newly Diagnosed Lung and Head and Neck Cancer Patients	Not Open
IMCLONE-CP12-0917	An Open-Label, Multicenter, Randomized, Phase 2 Study of a Recombinant Human Anti-VEGFR-2 Monoclonal Antibody, IMC-1121B in Combination with Platinum-based Chemotherapy versus Platinum-based Chemotherapy Alone as First-line Treatment of Patients with Recurrent or Advanced Non-small Cell Lung Cancer (NSCLC).	Open
PFIZER-A7471009	A Randomized, Double-Blind, Phase III Efficacy and Safety study of PF-00299804 versus Erlotinib for the treatment of Advanced Non-Small Cell Lung Cancer following progression after, or intolerance to, at least one prior chemotherapy	Closed
STEREO	STEREOtactic Radiation and Adjuvant Chemotherapy in Lung Cancer (STEREO) BCC-LUN-10-STEREO	Open

Brown Cancer Center Clinical trials*

http://www.browncancercenter.org

Lung cancer screening program

http://www.browncancercenter.org/programs-services/cancer-screenings/lung-cancer-screening/

Lung cancer clinical trials

http://browncancercenter.org/programs-services/clinical-trials/

18 matches found

- 05.0523Preoperative Metabolomic Analysis of Primary Lung Cancer: a Translational Clinical Trial of the Brown Cancer Center (Study # BCC-LUN-05-002)
- 12.0409A Phase IIb/III randomized, double-blind, placebo-controlled study comparing first-line therapy with or without TG4010 immunotherapy product in patients with stage IV non-small cell lung cancer (NSCLC) (Study Number TG4010.14)
- 10.0390CLOSED - An Open-label, Multicenter, Randomized, Phase 2 Study of a recombinant Human Anti-VEGFR-2 Monoclonal Antibody, IMC-1121B in Combination with Platinum-based Chemotherapy versus Platinum-based Chemotherapy Alone as First-line Treatment of Patients with Recurrent or Advanced Non-small Cell Lung Cancer (NSCLC) (Study # IMCL CP12-0917 (I4T-IE-JVBL))
- 13.0106Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced Non-Small Cell Lung Cancer (NSCLC) (Study Number RTOG 1106/ACRIN 6697)
- 13.0337The effect of pentoxifylline in preventing radiation-induced toxicity in the treatment of recurrent or new primary non-small cell lung cancers using stereotactic ablative radiotherapy (SABR) in patients previously treated with thoracic radiation (Study Number BCC-RAD-13-Pentoxifylline)
- 08.0388Protocol for the Cancer Database and Specimen Repository (CDSR) at the James Graham Brown Cancer Center (Previous Lung Repository) (Study # BCC-CA-09-002)
- 13.0195A Single-Arm, Multicenter, Open-Label, Phase 2 Study of Gemcitabine-Cisplatin Chemotherapy Plus Necitumumab (IMC-11F8) in the First-Line Treatment of Patients With Stage IV Squamous Non-Small Cell Lung Cancer (NSCLC) (Study Number: I4X-MC-JFCK)
- 11.0218RETIRED - Salvage Therapy with Docetaxel and Blueberry Powder in Non-Small Cell Lung Cancer (BIT-2) - BCC-LUN-BIT-2
- 12.0200ENDED - A Randomized Phase III Study of Sublobar Resection (+/- Brachytherapy) versus Stereotactic Body Radiation Therapy in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC) (Study # RTOG 1021)
- 12.0265A Randomized Phase II Study of Pre-Operative Chemoradiotherapy +/- Panitumumab (IND # 110152) Followed By Consolidation Chemotherapy In Potentially Operable Locally Advanced (Stage IIIA, N2+) Non-Small Cell Lung Cancer (Study # RTOG 0839)
- 08.0041Beta-glucan?s Effect on Cetuximab Induced Cytotoxicity in Non-Small Cell Lung Cancer (Study # BCC-LUN-07-005)
- 08.0040RETIRED - Berry Interventional Trial (BIT) in Resected Non-Small Cell Lung Cancer (Study # BCC-LUN-07-002)
- 09.0075 CLOSED - A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients with Completely Resected Stage IB (≥ 4cm) ? IIIA Non-Small Cell Lung Cancer (NSCLC) (Study # E1505)

- 12.0299CLOSED - A randomized, open-label Phase III trial of afatinib versus erlotinib in patients with advanced squamous cell carcinoma of the lung assecond-line therapy following first-line platinum-based chemotherapy (Study Number 1200.125)
- 09.0451Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer also Receiving Cisplatin and Etoposide (Study # RTOG 0538 / CALGB 30610)
- 10.0659STEREOtactic Radiation and Adjuvant Chemotherapy in Lung Cancer (STEREO) (Study # BCC-LUN-10-STEREO)
- 11.0573A Feasibility Study Using Four-Dimensional CT Imaging to Evaluate Lung Strain in Patients Treated with External Beam Radiation Therapy for Primary Lung Cancer (Study # BCC-RAD-11-02 4D-CT)
- 11.0621Randomized Phase II Study Comparing Prophylactic Cranial Irradiation Alone to Prophylactic Cranial Irradiation and Consolidative Extra-Cranial Irradiation for Extensive Disease Small Cell Lung Cancer (ED-SCLC) (Study # RTOG 0937)

*No web links to the KY Clinical Trials Network from the Brown Cancer Center.

Summary:

The Kentucky Clinical trials Network (KCTN) has built a 17 site network and has enrolled over 1700 patients into trials since the inception of the program. Therapeutic trials have been responsible for over 250 of these patients. A large biorepository has been built that is accessible to investigators. The first 5 years were slow in the development of the network but the last 5 years have seen a substantial improvement in enrollment with the inclusion of epidemiology based trials. Cooperative group trials have remained a smaller percentage of the overall portfolio. A successful coordinating center has been set up in Lexington separate from the main campus with adequate office space to accomplish the necessary work. The site was visited and seems to be an excellent working environment.

Going forward, with the approval of CT lung cancer screening, the KCTN is in a good position to study the implementation of screening and assist with this process with the network and continue to collect specimens for research. Use of a common IRB platform such as IRB share will improve efficiencies between institutions. It is apparent that the University of Louisville has a robust clinical trials portfolio that is separate from the KCTN. There is no link in the U of L clinical trials website and the CTN program. Dr. Chesney who runs the clinical trials office at UofL stated that there is no interaction with the CTN from an administrative level. Challenges are present with the integration of U of L and the CTN because U of L is a separate site with a very strong independent clinical trial support system through the JGB Cancer Center.

The cancer centers at both Louisville and UK support lung cancer clinical research at the individual institutions with cancer center funds in addition to the monies given from the KLCRP. Each of these institutions has larger portfolios than the KCTN as some of these studies may not be financially viable for the KCTN to accomplish at the satellite sites in the community.

Suggestions to improve the collaboration of the network include 1) pursuit of improving use of IRB Share between UK and Louisville. 2) Incentives for investigator initiated trials that are tied to the previous KLCRP funding from UK and Louisville with support from the KLCRP research project funds so that they can be financially viable for the CTN external sites outside of the university settings.

The KCTN is in a unique position to serve as a conduit for the study of lung cancer screening in Kentucky. Continuation of funding from settlement is needed from the state going forward to reduce lung cancer mortality in the state. I would recommend that return of the ovarian cancer screening funds occur to the KLRCP for the lung cancer screening effort. These monies can be made available for research projects on lung cancer screening in KY and establishment of a lung cancer screening network that will promote research and high quality clinical care. It would layer on top of the existing trial network and quality standards will ensure the reduction in lung cancer mortality see in the National Lung Screening Trial.

Ongoing funding will be critical after 2020 to reap the benefit if the inertia created by the robust KCTN and continue its expansion.

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Appendix F

National Cancer Institute Designation
Eric Grogan, M.D., M.P.H.

NATIONAL CANCER INSTITUTE DESIGNATION

From KLCRP 1st Strategic Plan 2001

Mission: To reduce the morbidity and mortality from lung cancer. Initial focus areas included early detection and epidemiology, development of statewide clinical trials network, and striving for NCI designation of the cancer center from each university.

GOAL 4: NCI-Designation as Cancer Centers

"164.476(5)(c) Leverage the resources earmarked for the Lung Cancer Research Project toward the certification of the cancer program at the University of Kentucky and the University of Louisville by the National Cancer Institute as a cancer center[.]"

The Cancer Centers Program of the NCI supports major academic and research institutions throughout the United States to sustain broad based, coordinated, interdisciplinary programs in cancer research. These institutions demonstrate scientific excellence and the ability to integrate a diversity of research approaches to focus on cancer. The NCI and its Cancer Centers Program are dedicated to advancing cancer research to ultimately reduce cancer incidence, morbidity, and mortality.

Designated Cancer Centers receive funds from NCI for scientific infrastructure of the center, including such elements as scientific leadership and administration; shared/core research resources that give ready access to state-of-the-art technologies; and flexible program development funds that help the center and its associated faculty pursue its planned objectives and take immediate advantage of new research opportunities.

The University of Kentucky and the University of Louisville are each pursuing NCI designation as cancer centers to provide Kentuckians and the nation advanced understandings of and improved interventions in our fight against cancer. Support from the KLCR Program has provided vital financial resources to both institutions during a critical stage of development. The goal of NCI Designation requires a continued investment in scientific expertise, equipment, space and financial resources.

Objectives

1. Expand the base of cancer research expertise, particularly in translational research, with the recruitment of both promising young scientists and established investigators working at the front lines of cancer research.
2. Develop diverse cancer research programs with a high degree of inter- and intra-team collaboration.
3. Provide and promote interactive research opportunities.
4. Offer expanded innovative clinical trials, building on combined research underpinnings of the two centers.

Priorities for 2012-2014

- Continue to expand the overall research bases at each institution, particularly in Translational and Clinical Research.
- Increase extramural funding with emphasis on funding from the NCI.
- Increase NCI multi-project grants including program projects, SPORE grants and NCI cooperative grants.
- Expansion of research laboratory space.
- Develop a more broadly inclusive smoking-related cancer program that involves lung, head & neck, pancreas, cervix and bladder cancers.
- Provide all support necessary to process and support submissions for the Markey Cancer Center and James Graham Brown Cancer Center for NCI designation.
- Continue to develop multidisciplinary clinics for lung cancer patients.

Endpoints 2014

- Document 3-5 firmly established NCI-designable cancer research programs at each institution, with an emphasis on translational and clinical research.
- Growth of NCI funding at both institutions in the range of $12-$15 million.
- Meet with, receive and respond to recommendations of an External Advisory

Committee.

- Meet with, receive and respond to recommendations of the NCI Centers Branch Director.
- Submit P30 application for NCI-designation.

Markey Cancer Center – University of Kentucky

** NCI designated cancer center – July 13, 2013 announcement

Dr. Mark Evers

Arrived in 2009 University invested 90-100 million

Current 2014 funding grown from almost 12.8 million in 2006 to 23.8 million

http://www.ukhealthcare.uky.edu/markey/director-message-042012/

Markey Cancer Center Affiliate Network

ARH Cancer Center
Hazard
606-487-7902
www.arh.org/Hazard

Frankfort Regional Medical Center
Frankfort
502-875-5240
www.frankfortregional.com

Georgetown Community Hospital
Georgetown
502-868-1100
www.georgetownhospital.com

Harrison Memorial Hospital
Cynthiana
859-234-2300
www.harrisonmemhosp.com

Norton Cancer Institute
Louisville
502-629-HOPE (4673)
www.nortoncancerinstitute.com

Our Lady of Bellefonte Hospital
Ashland
606-833-3333
www.olbh.com

Rockcastle Regional Hospital and Respiratory Care Center
Mount Vernon
606-256-2195
www.rockcastlehospital.org

St. Claire Regional Medical Center
Morehead
606-783-6500
www.st-claire.org

Listed lung CA trials on UK Markey website

http://www.ukhealthcare.uky.edu/markey/Researchers/Clinical-Trials/Find-a-Clinical-Trial/

Protocol No.	Title
07-RAD-01	07-RAD-01/UK/P4: Stereotactic Body Radiation therapy for Post-chemoradiation Residual Disease in Stage II/III Non-small Cell Lung Cancer (IRB #07-0601-F1V)
09-RAD-01	09-RAD-01: Conformal High Dose Intensity Modulated Radiation Therapy for Asymptomatic Metastatic Disease to the Thoracic and Lumbar Spine (IRB #09-0625-F6A)
11-LUN-87-BMS	11-LUN-87-BMS: (CA184156) Randomized, Multicenter, Double-Blind, Phase 3 Trial Comparing the Efficacy of Ipilimumab plus Etoposide/Platinum versus Etoposide/Platinum in Subjects with Newly Diagnosed Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) (IRB #12-0503-F1V)
11-LUN-90-MCC	11-LUN-90-MCC: A Non-Randomized Phase II Protocol of Irinotecan for Subjects with Previously Treated Advanced ISG15 - Positive Non-Small Cell Carcinoma of the Lung (NSCLC) IRB #12-0854-F2L
2012-034	Appalachian Kentucky Lung Cancer Study of Soils
CALGB-30610/RTOG-0538	Comparison of Thoracic Radiotherapy Regimens+Cisplatin+Etoposide in SCLC patients
DOD2011-193	Study of Lung Cancer in Appalachian Kentucky: The Role of Environmental Carinogens
RTOG-0937	Study Comparing PCI Alone to PCI+Consolidative Extra-cranial Irradiation for ED-SCLC
S0819-MASTER	Carboplatin/Paclitaxel or Carboplatin/Paclitaxel/Bevacizumab +/- Cetuximab in NSCLC patients

Budgets

	Budget	Budget	Budget
	TOTAL REVENUE 2000-2012	**FY 2010-2011 Allocations**	**FY 2011-2012 Allocations**
ADMINISTRATION	**$15,877,362.00**		
I-I GRANTS FUNDING	**$ 14,278,491.00**		
Administrative Carry Forward (FY10-FY11)			
I-I Grants Carry Forward (Cycles 9-10)			
Administration (FY12)		$1,677,418.00	$1,428,308.00
I-I Grants Reserve (FY 10-12) Cycle 11 &12		$ 523,344.00	$732,123.00
Other Grants/Contracts			
TOTAL INCOME	**$ 30,155,853.00**	$2,200,762.00	$2,160,431.00
GOAL 1: Investigator Initiated Research	$10,913,646.60	$523,344.00	$732,123.00
GOAL 2: Research in Early Detection/Prevention	$3,055,709.36	$274,739.00	$150,000.00
GOAL 3: Kentucky Clinical Trial Network	$ 4,341,165.00	$411,289.00	$394,016.00
GOAL 4: NCI Designation (Comp Cancer Center)	$ 4,479,768.00	$877,390.00	$737,292.00
Administration	$1,910,742.90	$114,000.00	$147,000.00
Epidemiology	$422,410.40		
Endowed Chair	$492,494.00		
TOTAL EXPENSE	**$25,615,936.26**	**$2,200,762.00**	**$2,160,431.00**
Balance	**$4,539,916.74**	**$ -**	**$ -**

Goal 4: NCI-Designation as Cancer Centers (KRS 164.476 (5)(c))			
4a.	Expand the base of cancer research expertise, particularly in translational research.	Recruit both promising young and proven mature scientists.	Recruited 37 new faculty since 2009; diversity of disciplines represented.
4b.	Develop diverse cancer research programs with a high degree of inter- and intra- team	At least 3 designated Program Areas.	Have 4 mature program areas and 3 developing areas.
4c.	Provide and promote interactive research opportunities.	30% of grants and publications collaborative.	Since 2007, as measured through publications alone, 20% and 13% of publications have been intra-programmatic and inter-programmatic, respectively.
4d.	Offer expanded innovative clinical trials, building on combined research underpinnings of the two centers.	Accrual of at least 10% of patients to innovative clinical studies.	Approx. 9.9% accrual from May 2011 through April 2012; over 50% of patients accrued to clinical studies are residents of Appalachian eastern Kentucky; We are expanding our Affiliate Network to offer clinical trials throughout the state.

Kentucky Lung Cancer Research Program							
FY12 Payroll Expenditures							
Acct No	Initiatives by Goal	Role	Individual	FTE %	New/Existing	Salary	Fringe
3048106808	Investigator Initiated Research (G1)	Basic Scientist	Younsoo Bae	10.00%	Existing	$ 2,242.20	$ 709.97
3048106846	9	Basic Scientist	Rolf Craven	5.00%	Existing	$ 1,795.65	$ 600.55
3048106832	9	Basic Scientist	Wooin Lee	10.00%	Existing	$ 3,739.93	$ 1,079.87
3048106824	9	Basic Scientist	Craig Vander Kooi	5.00%	Existing	$ 1,875.65	$ 611.07
3048106799	9	Basic Scientist	Thomas Roszman	Cost shared	Existing	$ -	$ -
3048107864	10	Basic Scientist	Younsoo Bae	10.00%	Existing	$ 8,970.26	$ 2,840.73
3048108111	10	Basic Scientist	Rolf Craven	Cost shared	Existing	$ -	$ -
3048107852	10	Basic Scientist	Vivek Rangnekar	Cost shared	Existing	$ -	$ -
3048108571	10	Basic Scientist	Edward Hirschowitz	Cost shared	Existing	$ -	$ -
	10	Basic Scientist	John Yannelli	Cost shared	Existing	$ -	$ -
3048107842	10	Basic Scientist	Zhigang Wang	Cost shared	Existing	$ -	$ -
			Total			$ 18,623.69	$ 5,842.19
3049024117	Early Detection (G2)	Clinician Scientist	Susanne Arnold	12.00%	Existing	$ 27,603.80	$ 6,654.44
		Radiologist	Michael Brooks	4.00%	Existing	$ 12,675.64	$ 2,663.16
			Lara Sutherland	58.75%	Existing	$ 26,655.75	$ 10,110.24
			Total	0.75		$ 66,935.19	$ 19,427.84
3049024113	Clinical Trials (G3)	Clinical Director	Tim Mullett	10.00%	Existing	$ 16,016.28	$ 3,339.33
		Asst. Director for Clinical Studies	Kris Damron	100.00%	Existing	$ 61,353.96	$ 19,527.84
		Clinical Research Assistant II	Michele Hughes	100.00%	Existing	$ 51,119.90	$ 17,124.00
		Clinical Research Assistant I	Melinda Dowden-Kruger	100.00%	Existing	$ 34,981.32	$ 11,705.11
		Administrative Research Assistant	Trey Alexander	100.00%	Existing	$ 36,735.45	$ 16,746.94
		Research Admin Coordinator - Clinical	Lara Sutherland	10.00%	Existing	$ 4,147.20	$ 1,560.84
		Temp Tech/Paraprofessional	Teresa Foody	25.00%	Existing	$ 7,020.00	$ 604.88
		Epidemiologist	Amy Christian	18.75%	Existing	$ 10,321.23	$ 3,606.58
		Epidemiology - Lung Cancer	Claudia Hopenhayn	7.47%	Existing	$ 7,991.67	$ 2,309.65
			Total	4.71		$ 229,687.01	$ 76,525.17
3049024114	NCI-Designation (G4)	Faculty - Basic Scientist	Heinz Kohler	95.00%	Existing	$ 140,886.84	$ 37,702.20
		Faculty - Biostatistics Core	Bin Huang	1.25%	Existing	$ 1,365.94	$ 389.44
		Faculty - Biostatistics Core	Brent Shelton	38.92%	Existing	$ 69,940.84	$ 17,111.51
		Faculty - Pharmaceutical Science	Markos Leggas	25.00%	Existing	$ 23,501.87	$ 7,045.68
		Faculty - Pharmaceutical Science	Esther Black	20.00%	Existing	$ 17,467.74	$ 5,069.23
		Faculty - Clinician Scientist	John D'Orazio	55.00%	Existing	$ 81,646.32	$ 20,318.69
		Faculty - Basic Scientist	Steve Schwarze	7.40%	Existing	$ 12,276.48	$ 4,149.33
		Faculty - Basic Scientist	Xianglin Shi	10.00%	Existing	$ 22,871.14	$ 5,194.28
		Faculty - Biostatistics Core	Heidi Weiss	34.68%	Existing	$ 66,554.04	$ 15,992.82

UK Markey Summary:

The University of KY has met the NCI designation goal. KLRCP funding has provided nearly 5 million dollars as a backbone of funds over the past 14 years to support this mission. The majority of the NCI designated funds are used for support of the core facilities. The clinical trials network is based at UK. This has benefitted UK with the access to specimens and a clinical trial consortium. The KLRCP funding has allowed the cancer center infrastructure to grow at a slow steady rate for the first 9 years of the program. With the recruitment of Dr. Evers and the institutional commitment with substantial additional funding to bring funded investigators to UK (90-100million) to increase the NIH funding, UK has been able to pass the difficult threshold to be able to achieve NCI designation. This has resulted in additional funding, recruitment, and an increase in clinical volume of 25-30%. KLRCP funding provided necessary support but without a recent university commitment and the successful recruitment of well-funded investigators, NCI designation would have been delayed many years. The Markey Cancer Center desires to become a comprehensive cancer center. Continuation of the KLRP is critical to obtaining this goal and maintaining NCI designation.

University of Louisville James Graham Brown Cancer Center

UofL has not achieved NCI designation but the applications are forthcoming. In discussions with the NCI, Dr. Miller reported that they were 6 R01's short of having enough grant funding to submit. All other areas were ready for submission.

Summary from meeting with Dr. Miller

- Need 30 million to push over the edge to get NCI designation to recruit and keep.
- Loss of Metabolomics group - big loss
- Building infrastructure slowly but sustainable
- Strong clinical trials

Budget

NCI-Designation						
	Instructor, Term - Vaccinology Lab	Joh, Joongho	50.00%	Existing	$ 26,449.98	$ 6,657.46
	Biostatistican III - Biostatistics Core	Pan, Jianmin	68.67%	Existing	$ 49,108.74	$ 12,360.67
	Biostatistican, Director, Biostatistics Core	Rai, Shesh Nath	36.75%	Existing	$ 50,192.42	$ 12,633.43
	Instructor, Term - Human Molecular Biology	Sedoris, Kara Joyce	100.00%	Existing	$ 55,260.00	$ 13,908.94
	Manager, Tissue Repository	Smolenkov, Andrei	100.00%	Existing	$ 51,200.04	$ 12,887.84
	Sr Biomedical Engineer - Flow Cytometry Core	Worth, Christopher	100.00%	Existing	$ 59,241.96	$ 14,911.20
	Graduate Research Assistant	Dinc, Gunes	17.00%	Existing	1,083.32	$ 272.67
	Graduate Research Assistant	Barsoumian, Hampartsoun	92.00%	New	$ 20,166.63	$ 5,075.94
	Student Assistant - Human Molec Biol	Malik, Danial	16.00%	New	$ 2,108.10	$ 530.61
	Post-Doctoral Associate - G. Clark Lab	Clark, Jennifer	4.00%	New	$ 1,095.07	$ 275.63
	Senior Associate Director	Pierson, Milton	25.00%	Existing	$ 37,800.02	$ 9,515.27
		Total			**$ 353,706.28**	**$ 89,029.66**

Clinical Trial Program						
	Manager, Regulatory Affairs	LaDuke, Christina	25.00%	New	$ 14,499.99	$ 4,623.50
	Laboratory Research Coordinator	Hall, Melissa	91.00%	Existing	$ 41,614.59	$ 13,269.05
	Clinical Research Coordinator	Kantardzic, Belma	50.00%	Existing	$ 28,924.95	$ 9,227.37
	Clinical Research Nurse	Schoenbachler, Jennifer	100.00%	Existing	$ 60,065.04	$ 19,156.75
		Total			**$ 145,104.57**	**$ 46,276.67**

Clinical Trials

- 17 active clinical trials in lung cancer (at the JGBCC)
- >20% accrual of patients to available trials in lung cancer

Summary

UofL JGBCC has a strong infrastructure and patient base to support a successful NCI application. Funding has been sustained in the past few difficult years but not increased. Erosion of talented investigators with large grant funding has threatened the ability to ensure a current successful application. If NCI designation is going to be successful in the next 5 years then a substantial investment of at minimum 30 million dollars to recruit successful investigators is necessary. This will need to come from the University of Louisville or the State. As with the University of KY, KLRCP funding has provided a critical mass of lung investigators, allowed the JGBCC to maintain core facilities, support robust clinical trials, and provide grants to investigators to obtain preliminary data to transition to extramural funding.

Appendix G

Innovation and Collaboration
Kenneth W. Lieberman, Ph.D.

INNOVATION AND COLLABORATION

Kenneth W. Lieberman, PH.D.

The funding from the KLCRP was originally intended to be available to all eligible faculty at the University of Kentucky and the University of Louisville. Both universities have a broad range of technology oriented academic departments including engineering disciplines, physics, chemistry and the life sciences. UK has an excellent College of Agriculture Food and Environment. Most of the funding awarded by the KLCRP in the Investigator Initiated Program has been to faculty associated with the Schools of Medicine at UK and UL through the Markey Cancer Center and the Brown Cancer Center.

The technology based academic departments at both universities, UL and UK, can make potentially fundamental basic and applied research contributions to the lung cancer program, but they appear to be largely unaware of the existence of the KLCRP funding. It is of critical importance that efforts be made to correct this situation and broaden the potential funding base.

The National Center for Science and Engineering Statistics reports that each year $65 billion is spent on research at US universities. The academic knowledge and expertise represents a massive resource, which is largely untapped by the broader community. Through the KLCRP program and both Cancer Centers outreach programs should be implemented to inform technology academic departments about available research opportunities and collaborations. In addition, formal meetings should be convened to permit researchers from both the Cancer Centers and the technology departments to brainstorm potential collaborations areas of investigation utilizing the combined talents of all collaborators. Collectively, both the Brown and Markey Cancer Centers have a number of drugs and vaccines sponsored by KLCRP funding in various stages of development for the treatment of lung cancer. A productive research partnership between Chemical Engineering and the Brown Cancer Center has resulted in a unique device for the diagnosis of lung cancer using four components of exhaled breath as a clinical indicator, and is currently being evaluated for clinical efficacy as a

screening tool. This is an excellent illustration of what collaborations between technology-based academic departments and the Cancer Centers can produce.

Three members of the Department of Bioengineering and a single member of the Department of Chemical Engineering at the University of Louisville are teaming with the Brown Cancer Center in active research programs with some KLCRP support. The participating faculty are Hermann Frieboes, Ayman El-Baz and Rob Keynton from Bioengineering and Sean Fu from Chemical Engineering.

Although tobacco is generally recognized as having a negative impact on human health, the plant can be looked at from a different perspective. Recent research developments in Israel and North Carolina are both alternative uses of the plant. Researchers in Israel have used unique methodologies to manufacture a malaria treatment drug artemisinin in large quantities using the tobacco plant as a vehicle for its production. In North Carolina, a Canadian company built a large manufacturing facility in the Research Triangle area for the purpose of using tobacco for the manufacture of influence vaccines.

Kentucky Lung Cancer Research Program
Governance Board Meeting Minutes
February 26, 2014

Present: Dr. Jim Roach - Chair (MAL), Dr. Mark Evers (UK), Dr. Don Miller (UofL), Joe Graviss (CPE), Dan Flanagan (CPE); Absent: Drs. Joshi, Amdullah, and Mullett. Guests: Nathan Vanderford and Beth Yost of UK; Milton Pierson of UofL; Kris Damron (KCTN); and Rebecca Bowman, Travis Powell, Linda Linville of CPE.

The Governance Board of the Kentucky Lung Cancer Research Program (GB) was called to order by Dr. Roach at 3 PM, on February 26, 2014, at CPE offices in Frankfort.

Minutes of the November 21, 2013, were approved by motion by Dr. Miller, 2nd by Mr. Flanagan.

Discussion of interviews and scope of work as performed to date by the program reviewers, SciMed Consultants, was favorable, with comments as to their understanding of the program and discovery through various documents very positive.

Drs. Evers and Miller presented the Investigator-Initiated grant proposals as recommended by their respective institutions. After a brief description of each, the following proposals were approved for funding, motion by Mr. Flanagan, 2nd by Mr. Graviss. (See attached.) These proposals will span the FY 14-16 biennium, and total $1,350,000.

The U.S. Preventive Services Task Force Recommendation Statement on "Screening for Lung Cancer" had been circulated to all members. These recommendations call for *annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 3o pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.*

Discussion was brief with the anticipation of the screening to be covered by insurance and acknowledging the study evolving out of clinical trial into 3rd-party payors' responsibility for costs.

Dr. Miller presented some work on another Lung Cancer Screening project underway at UofL with more current and heavy smokers, that is a breath sample analysis.

Kris to provide KCTN Report HERE.

- Manuscript – survey of primary care providers
- Pizer - investigator gran with nasal NRT, investigator drug @ UK
- Hazard – 1st study, survey and education with survey
    - 60 patients in one day enrolled
- Hardin Memorial in Elizabethtown, now a KCTN site

Dr. Miller spoke of recent study at UofL working with the Kentucky Cancer Registry, that indicates only 300% of lung cancer patients ever see a cancer specialist, and many receive no treatment at all. This work is being done by Dr. Klocher. Dr. Miller also indicated the interest of Bristol Meyers in investigating the psychosocial issues in assisting with the education of providers. Additional pharmaceutical development is underway.

Dr. Roach asked if anyone at KY's research center was doing any work related to the association of estrogen receptors and lung cancer.

Rebecca Bowman, Administrative Office at CPE, presented some fund balance calculations calling for an alignment of budgeted numbers moving into FY 14-15 and prior to the actual allocation for FY 13-14 as yet not received. Both UK and UofL were in agreement to have a session with Rebecca and her staff to determine fund balances in both categories of programs and grants, as well as those funds allocated for ovarian cancer, and being held as interest earnings.

A motion was made to delay funding of the new II grants until such a time as the fund balances were deemed acceptable by all parties. Mr. Graviss motioned and Dr. Miller 2nd motion, with all in favor.

Action Item: Meet with cancer center business administrators to determine fund balances prior to disbursement of any II research funds.

Travis Powell, General Counsel for CPE, indicated that there had been no change in the shortfall to the Tobacco Master Agreement Settlement revenues, but that the legal debate at the national level at this time were not impacting the location expectation for FY 14.

There being no further business, a new meeting date was not determined, anticipating the SciMed Consultant report in mid-summer and in anticipation of including their summary at the GB's next meeting. Meeting adjourned at 4:00 PM.

Submitted as draft 3/5/2014, Linda Linville

Investigator	Application Title	FY 13-14	FY 14-15
Suzanne Arnold	A randomized phase II trial of induction chemotherapy and low-dose fractionated radiation in head and neck cancer with correlative evaluation of DNA repair.	$ 75,000	$ 75,000
Tadahide Izumi	Establishment of Buccal Cell Biomarkers for Carcinogenesis Related to Tobacco Product Consumption	$ 75,000	$ 75,000
Jeremiah Martin	A Singleparm, Phase II study of thoracoscopic lung cancer staging with the use of intraoperative ultrasound at the time of definitive resectin.	$ 75,000	$ 75,000
Jamie Studts	Disseminating LCS through Shared Decision Making: A Web-based CE Intervention for Primary Care Providers	$ 75,000	$ 75,000
Total UK Funding Recommendation		*$ 300,000*	*$ 300,000*

Investigator	Application Title	FY 13-14	FY 14-15
Sucheta Telang	Co-Targeting 6-Phosphofructo-2-Kinase/Fructose-2,6-Biphosphaatase Isoform-e(PFKFB3) and -4 (PFKFB4) as a Strategy Against Lung Cancer	$ 75,000	$ 75,000
Sandie Sephton	Understanding the Prognostic Significance of Circadian Disruption in Lung Cancer, and Piloting an Intervention	$ 75,000	$ 75,000
J. Christopher Sta	Targeting the Anaphase Promoting Complex as Lung Cancer Chemotherapy	$ 75,000	$ 75,000
Levi J. Beverly	The N-end rule Ubiquitination Pathway as a Novel Driver and therapeutic Target of Human Cancer	$ 75,000	$ 75,000
Xiao-an Fu	Analysis of Cancer Metabolites in Exhaled Breath for Diagnosis of Lung Cancer	$ 75,000	$ 75,000
TOTAL UofL Funding Recommendations		*$ 375,000*	*$ 375,000*

		FY 14-15	FY 15-16
		$ 675,000	$ 675,000
TOTAL FUNDING APPROVED by Governance Board 2/26/14		**$ 1,350,000**	

6349 WDI0 - Council on Postsecondary Education
Lung Cancer Research, Tobacco Settlement
FY13 and FY14 Cash Activity
as of 6-23-14

	Date	Description		Interest	Ovarian	Combined LC Pool	UK Lung Cancer Grants	UK Lung Cancer Programs	UofL Cancer Grants	UofL Cancer Programs	Total Allocation (Calculated)	CASH
2013		**FY allocation per distribution formula reviewed**			775,000.00		750,000.00	1,593,724.00	750,000.00	1,154,076.00	5,022,800.00	
2013		**FY13 allocation calc error**						(449,500.00)		(325,500.00)	(775,000.00)	
2013					**775,000.00**		**750,000.00**	**1,144,224.00**	**750,000.00**	**828,576.00**	**4,247,800.00**	
2013	04/23/13	Revenue/Cash Transfer into CPE	4,247,800.00									
2013		**Total Revenue/Cash into CPE FY10**	**4,247,800.00**									4,247,800.00
2013		Interest Income YTD FY13		2,294.22								2,294.22
2013	07/16/12	UL grants							(732,123.00)			(732,123.00)
2013	07/16/12	UK grants					(473,344.00)					(473,344.00)
2013	11/15/12	UK grants					(50,000.00)					(50,000.00)
2013	03/11/13	UK grants					(150,000.00)					(150,000.00)
2013	04/04/13	UK ovarian			(775,000.00)							(775,000.00)
2013	04/15/13	UK prog exp					(300,000.00)	(1,593,724.00)				(1,893,724.00)
2013	05/02/13	UL prog exp & grants							(750,000.00)	(1,154,076.00)		(1,904,076.00)
2013	06/27/13	Interest Exp APA office (FY12 audit)		(5,814.00)								(5,814.00)
												-
		FY2013 cash totals		**124,092.62**	**-**	**-**	**1,035,846.44**	**(449,500.00)**	**548,351.94**	**(325,500.00)**	**933,290.99**	**933,290.99**
		Adjustment for FY13 calculation error					**(449,500.00)**	449,500.00	**(325,500.00)**	325,500.00		
		Final FY13 carryforward balances		**124,092.62**			**586,346.44**	**-**	**222,851.94**	**-**		933,290.99
2014		**Interest Income YTD FY14**		766.15								934,057.14
2014	03/12/14	SciMed Consultants KLCRP Cancer Research PRG Review- Phase 1		(15,900.00)								918,157.14
2014	05/21/14	SciMed Consultants KLCRP - PHASE II		(3,900.00)								914,257.14
2014	06/06/14	SciMed Consultants KLCRP CET Cancer Research Prgm PHASE 2		(24,197.00)								890,060.14
2014	06/16/14	SciMed Consultants KLCRP CET PHASE II		(2,309.32)								887,750.82
		FY14 balance as of 6-23-14		**78,552.45**			**586,346.44**	**-**	**222,851.94**	**-**		**887,750.82**
		Revenue of $4,187,8000 FY14 not yet received										

6349 WDI0 - Council on Postsecondary Education
Lung Cancer Research, Tobacco Settlement
FY14 to FY16 Allotments
as of 6-23-14

	FY 14	FY 15	FY 16
TOBACCO FUNDS (TF)			
Research Challenge Trust Fund*			
Lung Cancer Research	3,412,800.00	4,197,500.00	2,832,500
Ovarian Cancer Screenings	775,000.00	775,000.00	775,000
	4,187,800.00	**4,972,500.00**	**3,607,500**

FY14 unresolved

FY13-14 allotment allocation scenarios			
with database coordinator position	**FY 13-14**	**without database coordinator position**	**FY 13-14**
LC and OV Total	4,187,800.00	LC and OV Total	4,187,800.00
Ovarian distribution	(775,000.00)	Ovarian distribution	(775,000.00)
LC allocation total	3,412,800.00	LC allocation total	3,412,800.00
LC grant distribution	1,500,000.00	LC grant distribution	1,500,000.00
LC position funded by both UK and UL	75,000.00		
LC program distribution total		LC program distribution total	
UK 58%	1,065,924.00	UK 58%	1,109,424.00
UL 42%	771,876.00	UL 42%	803,376.00
	3,412,800.00		3,412,800.00

ADAM H. EDELEN
AUDITOR OF PUBLIC ACCOUNTS

Robert King, President
Kentucky Council on Postsecondary Education
1024 Capital Center Drive, Suite 320
Frankfort, KY 40601

Independent Accountant's Report

We have reviewed the expenditures of the Lung Cancer Research Fund from July 1, 2012 to June 30, 2013. The Council on Postsecondary Education, University of Kentucky and the University of Louisville are responsible for the expenditures of the Lung Cancer Research Fund.

Our review was conducted in accordance with attestation standards established by the American Institute of Certified Public Accountants and the standards applicable to attestation engagements contained in *Government Auditing Standards* issued by the Comptroller General of the United States. A review is substantially less in scope than an examination, the objective of which is the expression of an opinion on the expenditures of the Lung Cancer Research Fund. Accordingly, we do not express such an opinion.

Based on our review, nothing came to our attention that caused us to believe that the expenditures of the Lung Cancer Research Fund are not completely and accurately recorded, in all material respects, in the enhanced Management Administrative Reporting System (eMARS).

This report is intended solely for the information and use of the Council on Postsecondary Education, Governance Board of the Kentucky Lung Cancer Research Project and the Legislative Research Commission and is not intended to be and should not be used by anyone other than these specified parties.

Respectfully submitted,

Adam H. Edelen
Auditor of Public Accounts

June 3, 2014

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Markey Cancer Center
FY15-16 Biennium
KLCR Budget request

		PERSONNEL	TRAVEL	OPERATING	Total Expense	
	Estimated 6/30/14 Balance Available	Personnel + Fringe Benefits				Requested Revenue FY2015
GOAL 1: Investigator Initiated Research	$ -	$ -	$ -	$ -	$ 750,000.00	$ 750,000.00
GOAL 2: Early Detection/ Prevention/Marty Driesler	$ 158,821.00	$ -	$ -	$ -	$ -	$ -
GOAL 3: Kentucky Clinical Trial Network	$ 724,584.00	$ 431,600.00	$ -	$ -	$ 431,600.00	$ 431,600.00
GOAL 4: NCI Designation (Comp Cancer Center)	$ 88,037.00	$ 1,132,950.00	$ -	$ -	$ 1,132,950.00	$ 1,132,950.00
Prime Transfers	$ -	$ -	$ -	$ -	$ -	$ -
Administration	$ 61,160.00	$ -	$ -	$ -	$ -	$ -
TOTALS	**$ 1,032,602.00**	**$ 1,564,550.00**	**$ -**	**$ -**	**$ 2,314,550.00**	**$ 2,314,550.00**

		PERSONNEL	TRAVEL	OPERATING	Total Expense	
		Personnel + Fringe Benefits				Requested Revenue FY2016
GOAL 1: Investigator Initiated Research		$ -	$ -	$ -	$ 750,000.00	$ 750,000.00
GOAL 2: Early Detection/ Prevention/Marty Driesler		$ -	$ -	$ -	$ -	$ -
GOAL 3: Kentucky Clinical Trial Network		$ 213,200.00	$ -	$ -	$ 213,200.00	$ 213,200.00
GOAL 4: NCI Designation (Comp Cancer Center)		$ 559,650.00	$ -	$ -	$ 559,650.00	$ 559,650.00
Prime Transfers		$ -	$ -	$ -	$ -	$ -
Administration		$ -	$ -	$ -	$ -	$ -
TOTALS		**$ 772,850.00**	**$ -**	**$ -**	**$ 1,522,850.00**	**$ 1,522,850.00**

Submitted:
6/25/14

Personnel Report
FY2013 Budget (7/1/12-6/30/13)

Acct No	Initiatives by Goal	Role	Individual	FTE %	New/Existing	Salary	Fringe
3049024113	**Clinical Trials**	Physician Scientist-Principal Investigator	Mullet, Timothy Dr.	1.00%	Existing	$ 15,625.00	$ 4,472.19
		Director for Clinical Studies	Damon, Kris	100.00%	Existing	$ 63,194.58	$ 20,202.04
		Res. Admin. Coord/Clin	TBN	100.00%	Existing	$ 45,387.86	$ 17,811.10
		Res. Admin. Coord/Clin	Hughes, Michelle	100.00%	Existing	$ 46,158.75	$ 18,113.62
		Admn Support Associate I	Alexander, Joseph	100.00%	Existing	$ 33,242.56	$ 13,045.05
			Total			**$ 203,608.75**	**$ 73,644.00**
3049024114	**NCI -Designation**	Regular Faculty Pharaceutical Sciences	Leggas, Mark	24.00%	Existing	$ 24,206.94	$ 6,928.51
		Regular Faculty Pharaceutical Sciences	Black, Penni	18.00%	Existing	$ 15,677.92	$ 4,487.33
		Regular Faculty Markey Cancer Center Core Support	Weiss, Heidi	42.11%	Existing	$ 89,404.50	$ 25,589.36
		Regular Faculty Markey Cancer Center Core Support	Kohler, Heinz	96.99%	Existing	$ 140,886.84	$ 40,324.63
		Regular Faculty Markey Cancer Center Core Support	Shelton, Brent	42.76%	Existing	$ 71,978.63	$ 20,601.72
		Regular Faculty Markey Cancer Center Core Support	Jones, Dennie	50.00%	Existing	$ 180,250.00	$ 51,591.16
		Regular Faculty Markey Cancer Center Core Support	Wang, Chi	100.00%	Existing	$ 106,893.36	$ 30,595.02
		Research Analyst Core Support	Lu, Xin	100.00%	Existing	$ 35,649.62	$ 13,989.62
		Facilities Specialist Core Support	Epperly, Garretson	100.00%	Existing	$ 46,040.00	$ 18,067.02

			Total			**$ 710,987.81**	**$ 212,174.37**
3049024115	**Administration**						
		Administrative Core Support	Vanderford, Nathan	100.00%	Existing	$ 69,974.00	$ 22,369.29
		Computer Support Sepcialist II Markey Cancer Center Core Support	Huey, Terry	50.00%	Existing	$ 22,602.00	$ 8,869.48
		Admin Services Assistant Markey Cancer Center Core Support	Matthews, Wanda	100.00%	Existing	$ 39,506.00	$ 15,502.94
			Total			**$ 132,084.50**	**$ 46,741.71**
3049024117	**Marty Dreisler**						
		Regular Faculty Internal Medicine	Arnold, Susanne	1.00%	Existing	$ 28,114.33	$ 8,046.88
		Regular Faculty Radiology	Brooks, Michael	4.00%	Existing	$ 11,848.67	$ 3,391.33
		Research Admin Coordinator/Clinical Markey Cancer Center Core Support	Sutherland, Lara	50.00%	Existing	$ 23,138.00	$ 9,079.81
			Total			**$ 63,101.00**	**$ 20,518.02**
3049024116	**BCP**						
			Total			**$ 275,220.00**	**$ -**
				TOTALS		**$ 1,385,002.06**	**$ 353,078.10**
				Annual Total		**$ 1,738,080.16**	

University of Louisville, Brown Cancer Center, KLCRP

Projected FY 2015 Budget

	Personnel	Travel	Operation		Total Budget
Goal 1: Investigator Initiated Research Program					$ 750,000.00
Goal 2: Early Detction Program	$ 125,000.00				$ 125,000.00
Goal 3: Lung Cancer Clinical Trials Network	$ 127,947.00		$ 1,269.00		$ 129,216.00
Goal 4: NCI Designation (Cancer Center Support Grant)	$ 479,256.00	$ 10,500.00	$ 240,000.00		$ 729,756.00
Administrataion	$ 128,978.00		$ 20,000.00		$ - $ 148,978.00
Totals	$ 861,181.00	$ 10,500.00	$ 261,269.00		$ 1,882,950.00

Projected FY 2016 Budget

	Personnel	Travel	Operation		Total Budget
Goal 1: Investigator Initiated Research Program					$ 750,000.00
Goal 2: Early Detction Program	$ 62,500.00				$ 62,500.00
Goal 3: Lung Cancer Clinical Trials Network	$ 100,000.00				$ 100,000.00
Goal 4: NCI Designation (Cancer Center Support Grant)	$ 250,000.00		$ 47,150.00		$ 297,150.00
Administrataion	$ 100,000.00				$ 100,000.00
Totals	$ 512,500.00	$ -	$ 47,150.00		$ 1,309,650.00

Submitted: 6/25/14

Projected FY 2015 Budget

	Personnel	Travel	Operation		Total Budget
Goal 1: Investigator Initiated					$ 750,000.00
Goal 2: Early Detction Program	$ 125,000.00				$ 125,000.00
Goal 3: Lung Cancer Clinical	$ 127,947.00		$ 1,269.00		$ 129,216.00
Goal 4: NCI Designation (Cancer	$ 479,256.00	$ 10,500.00	$ 240,000.00		$ 729,756.00
Administrataion	$ 128,978.00		$ 20,000.00		$ - $ 148,978.00
Totals	$ 861,181.00	$ 10,500.00	$ 261,269.00		$ 1,882,950.00

Projected FY 2016 Budget

	Personnel	Travel	Operation		Total Budget
Goal 1: Investigator Initiated Research Program					$ 750,000.00
Goal 2: Early Detction Program	$ 62,500.00				$ 62,500.00
Goal 3: Lung Cancer Clinical Trials Network	$ 100,000.00				$ 100,000.00
Goal 4: NCI Designation (Cancer Center Support Grant)	$ 250,000.00		$ 47,150.00		$ 297,150.00
Administrataion	$ 100,000.00				$ 100,000.00
Totals	$ 512,500.00	$ -	$ 47,150.00		$ 1,309,650.00

Kentucky Lung Cancer Research Program

2012 Strategic Plan Update

Approved by the KLCR Program Governance Board

October 31, 2012

KLCR Program Strategic Plan

Table of Contents

Kentucky Lung Cancer Research Program (KLCR Program)

Strategic Plan
January 2012

Introduction

In 2000, the Kentucky General Assembly passed enabling legislation that created the Lung Cancer Research Fund, a partnership of the Cancer Centers at the University of Kentucky and University of Louisville under the leadership of a Governance Board of the Lung Cancer Research Fund. This legislation required development of research expertise in lung cancer at each Cancer Center, innovative clinical trials to test new lung cancer treatments throughout the Commonwealth, and leveraging this support to lead the centers toward designation as National Cancer Institute recognized Cancer Centers.

The enabling legislation focuses on lung cancer research and complements the mission of the Commonwealth's two medical research universities in helping Kentuckians gain or retain their good health. To accomplish this mission, each university strives to meet the educational, research, and patient care needs of our citizens working cooperatively together as well as with similarly focused organizations throughout the Commonwealth.

The Governance Board set initial strategies and goals for the program. The following Strategic Plan Update for 2012 delineates specific goals, objectives, strategies and measurable outcomes and provides a blueprint for the two universities to follow as they continue to build the nation's centerpiece of lung cancer research in Kentucky.

GOAL 1: Investigator-Initiated Research

"164.476(5)(a) Develop an expertise in the area of lung cancer research."

The conduct of investigator-initiated, hypothesis-driven research – i.e., independently conceived research approaches and projects developed by scientists from all relevant disciplines - is the primary means by which biomedical research is advanced. Driven by state of the art knowledge and creative synergism present at medical schools, hospitals, universities, research centers, and corporations they represent, these highly trained investigators:

- Review current scientific knowledge and identify critical gaps
- Develop new hypotheses
- Design the most direct pathways to test those hypotheses
- Utilize and develop novel molecular, genetic and cellular approaches in lung cancer research
- Develop and utilize animal models in the analysis of lung cancer
- "Translate" new findings and technologies into innovative clinical applications
- Test the most promising new prevention and treatment strategies in clinical trials

The KLCR Program's Investigator-Initiated Research Initiative continues to provide valuable financial resources to develop novel concepts and identify new avenues of research in lung cancer. These innovative research projects are by nature the most high-risk/high-reward research approaches generating proof-of-concept/proof-of-principle data that will lead to stronger scientific programs, increased publication s and additional extramural funding.

Objectives

1. Recruit existing faculty at the front-lines of cancer research to focus on problems in lung cancer.
2. Recruit new faculty both with interests and expertise in cancer that may be applied specifically to lung cancer problems.
3. Develop, mentor and focus early stage career investigators and graduate students on lung cancer.
4. Continue to support a robust research portfolio for lung cancer at each university.
5. Develop intra-programmatic linkages within and between both Cancer Centers.
6. Conduct annual scientists' seminars to share research results among lung cancer scientists funded by the KLCR Program.

Priorities for 2012-2014

- Recruit additional scientists into the lung cancer research program.

- Develop more integrated research programs at each Cancer Center, as well as links between universities.
- Utilize KLCR investigator-initiated grants to leverage current and future cancer research into the area of lung cancer.

Endpoints 2014

- Publications of lung cancer research at each university continue to break new ground in understanding and intervening in the incidence and mortality from lung cancer.
- Research portfolios mature into well-rounded representations of lung cancer study, with progressive increases in extramural funding.
- Annual professional meetings for KLCR scientists result in additional collaborative studies.
- The Markey Cancer Center and the Brown Cancer Center are identified as increasingly prominent lung cancer research and treatment centers.

GOAL 2: Research in Early Detection & Prevention

"164.476(5)(a) Develop an expertise in the area of lung cancer research with an immediate focus on early detection and epidemiology and with an ultimate goal of eradication of lung cancer."

Despite the direct link between tobacco and lung cancer, only 15% of smokers develop the disease. Thus, a fundamental goal is to discover risk factors that predispose a person to lung cancer. Defining high-risk individuals and development of an effective screening methodology will allow earlier detection, when a malignant tumor is small and asymptomatic, when treatment produces a higher cure rate.

Recent technological advances and new tools for screening have led to renewed trials for detecting early stage lung cancers. Correlative explorations of smoking history, compromised lung function, and biomarkers in serum or exhalant are proposed to help pre-define lung cancer risk in otherwise asymptomatic individuals. Establishment of a biospecimen repository is a key resource to facilitate such studies.

Objectives

1. Conduct screening and early detection research using available and applicable tools in key geographic areas of the state.
2. Expand and refine methodologies for risk-factor delineation.
3. Validate the use of methodologies for lung cancer screening.
4. Identify and develop methodologies for lung cancer prevention.
5. Maintain and expand the biospecimen repository for use by lung cancer

researchers.
6. Capitalize on partnerships with regional and local hospitals and clinics to build an early detection network where research is integral to the relationship.
7. Link prevention and early detection studies.

Priorities for 2012-2014

- Develop an evidence-based algorithm for lung cancer risk assessment.
- Continue the development of biomarker correlates of lung cancer and/or lung cancer risk through advanced molecular surveillance studies.
- Through CME programs for Kentucky physicians, articulate current standards of surveillance for lung cancer.

Endpoints 2014

- Updated templates for early detection are available in each administrative development district.
- The biomarker repositories at the universities are effectively serving advanced early detection investigations.
- Further development of candidate molecular markers identified for lung cancer susceptibility and/or early diagnosis.
- Further development of lung cancer preventative measures.

GOAL 3: Kentucky Clinical Trials Network

"164.476(5)(b) Establish a statewide clinical trial network to make university-based clinical trials available to the community physician in order to bring the most innovative cancer treatments to all Kentuckians in need of these treatments."

Improvements in the effectiveness of cancer treatments are accomplished through a series of phased clinical trials: Phase I – identify maximum tolerated doses of new drugs and dose-limiting toxicities; Phase II – test the study drug's effectiveness in specific cancers; Phase III – compare new treatments or new use of a treatment with approved treatments. All current approved drugs and treatment guidelines are based on clinical trials before they became generally available. Despite that record of success, many people do not know that cancer clinical trials are the means by which cancer research becomes cancer treatment.

Thousands of cancer clinical trials underway in the United States. The National Cancer Institute, cooperative groups, academic medical centers, community hospitals, physician private practices, and pharmaceutical companies sponsor cancer clinical trials. Of the 1.3 million people who will be diagnosed with cancer this year, only three to five percent will participate in cancer clinical trials.

The University of Kentucky and University of Louisville have worked together to establish the Kentucky Clinical Trials Network (KCTN) to facilitate collaborative participation in trials, to educate patients and physicians about the benefits of clinical trials, and trial availability and to assist physicians with planning and implementing trials.

Objectives:

1. Increase number of Kentuckians with access to and participating in lung cancer clinical trials.
2. Develop and maintain a critical mass of trained professional staff to support multi-site clinical trials.
3. Offer and manage industry-sponsored lung cancer clinical trials through the Network.
4. Identify and develop investigator-initiated clinical trials at both universities that can be offered to patients in diverse settings.
5. Continually improve the Network's services with input from practicing Kentucky physicians

Priorities for 2012 – 2014:

- Efficiently and effectively manages clinical trials for the Network. Expand technologies utilized to engage, manage and conduct network activities.
- Increase number of industry sponsored trials and number of therapeutic trials.
- Obtain access to or assist sites to gain access to cooperative group trials.
- Expansion of investigator-initiated clinical trials from both Institutions.
- Improve process and number of trials referred from both universities.
- Continue and expand training sessions with site investigators and site coordinators
- Increase number of patient accrual to network trials.

Endpoints in 2014:

- The Network has a continuing stream of novel therapeutic trials and non-therapeutic trials available to patients, partnering physicians and sites.
- The network has increasing patient accrual.
- The Kentucky Clinical Trials Network provides training and information to physicians and citizens throughout the Commonwealth, including updated clinical trial results and new standards of care.
- Clinical trials are accessible for Kentuckians.

GOAL 4: NCI-Designation as Cancer Centers

"164.476(5)(c) Leverage the resources earmarked for the Lung Cancer Research Project toward the certification of the cancer program at the University of Kentucky and the University of Louisville by the National Cancer Institute as a cancer center[.]"

The Cancer Centers Program of the NCI supports major academic and research institutions throughout the United States to sustain broad based, coordinated, interdisciplinary programs in cancer research. These institutions demonstrate scientific excellence and the ability to integrate a diversity of research approaches to focus on cancer. The NCI and its Cancer Centers Program are dedicated to advancing cancer research to ultimately reduce cancer incidence, morbidity, and mortality.

Designated Cancer Centers receive funds from NCI for scientific infrastructure of the center, including such elements as scientific leadership and administration; shared/core research resources that give ready access to state-of-the-art technologies; and flexible program development funds that help the center and its associated faculty pursue its planned objectives and take immediate advantage of new research opportunities.

The University of Kentucky and the University of Louisville are each pursuing NCI designation as cancer centers to provide Kentuckians and the nation advanced understandings of and improved interventions in our fight against cancer. Support from the KLCR Program has provided vital financial resources to both institutions during a critical stage of development. The goal of NCI Designation requires a continued investment in scientific expertise, equipment, space and financial resources.

Objectives

1. Expand the base of cancer research expertise, particularly in translational research, with the recruitment of both promising young scientists and established investigators working at the front lines of cancer research.
2. Develop diverse cancer research programs with a high degree of inter- and intra-team collaboration.
3. Provide and promote interactive research opportunities.
4. Offer expanded innovative clinical trials, building on combined research underpinnings of the two centers.

Priorities for 2012-2014

- Continue to expand the overall research bases at each institution, particularly in Translational and Clinical Research.

- Increase extramural funding with emphasis on funding from the NCI.
- Increase NCI multi-project grants including program projects, SPORE grants and NCI cooperative grants.
- Expansion of research laboratory space.
- Develop a more broadly inclusive smoking-related cancer program that involves lung, head & neck, pancreas, cervix and bladder cancers.
- Provide all support necessary to process and support submissions for the Markey Cancer Center and James Graham Brown Cancer Center for NCI designation.
- Continue to develop multidisciplinary clinics for lung cancer patients.

Endpoints 2014

- Document 3-5 firmly established NCI-designable cancer research programs at each institution, with an emphasis on translational and clinical research.
- Growth of NCI funding at both institutions in the range of $12-$15 million.
- Meet with, receive and respond to recommendations of an External Advisory Committee.
- Meet with, receive and respond to recommendations of the NCI Centers Branch Director.
- Submit P30 application for NCI-designation.

Timeline - Due Dates for Reporting/Activities of Kentucky Lung Cancer Research Program

	FY 2012			FY 2012-2013												
	May	June		July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	
Purchase Order's Prepared	Biennially															REPEAT THROUGH 2020
Reviewed, Authorization Signatures	Biannually															
Budget Request for Following Year	31-May													By May 10		
CPE Disbursement to Centers		By 6/15													by 6/15	
Annaul Reports Due						15-Sep										
Investigator Initiated Grants Proposed/Reviewed			New FY		Request for I-I Proposals - Submissions - Peer Review											
Governane Board Meeting							GB Meets - Review Annual Reports				Review mid-year fund expenditures/ balances, review I-I grant recommendations, *Approve revisions to Strategic Plan (only in even years)*			GB Meets - post May 10 to review budget requests		
Review Strategic Plan Annually/Revise Strategic Plan Biennially							Review Stratgic Plan									
Invoice CPE for funding												Centers invoice for I-I amd programmatic funding, prior to 6/1				

Responsibility of GB

Responsibility of Centers

Disbursement made by 6/15 IF funds received, all Center Reporting received

KLCRP AGENDA

Review of Minutes
Center Reports/Updates per Goals
> Research
> Prevention/Early Detection
> Clinical Trials Network
> NCI Designation

October 2012 - Agenda Actions
> Determinants of Full Program Review
> Project recommendation from Mullett with regard to screening
> Centers inclusion of Success Stories from KLCRP

February 2013 - Agenda Actions
> Strategic Plan Revisions

May 2013 - Agenda Actions
> Incorporated revisions ito Strategic Plan into budget requests

PLEASE INCLUDE THE FOLLOWING ON ALL DOCUMENTS:
INSTITUTION: _____
SUBMITTED BY: _____
DATE: _____

Kentucky Lung Cancer Research Program
Reporting-Activity Timeline FY 2014-2015

			FY 2014-2015											
	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June
Purchase Order's Prepared	Biennially													
Reviewed, Authorization Signatures	Biannually													
Budget Request for Following Year	31-May												By May 10	
CPE Disbursement to Centers		By 6/15												by 6/15
Annaul Reports Due					15-Sep									
Investigator Initiated Grants Proposed/Reviewed				Request for I-I Proposals - Submissions - Peer Review										
Governane Board Meeting						GB Meets - Review Annual Reports				Review mid-year fund expenditures/ balances, review I-I			GB Meets - post May 10 to review budget requests	
Review Strategic Plan Annually/Revise Strategic Plan Biennially			Review Stratgic Plan											
Invoice CPE for funding								Centers invoice for I-I amd programmatic funding, prior to 6/1						

Responsibility of GB
Responsibility of Centers
Disbursement made by 6/15 IF funds received, all Center Reporting received

PLEASE INCLUDE THE FOLLOWING ON ALL DOCUMENTS:
INSTITUTION: _____
SUBMITTED BY: _____
DATE: _____

KLCRP AGENDA

Review of Minutes
Center Reports/Updates per Goals
> Research
> Prevention/Early Detection
> Clinical Trials Network
> NCI Designation

October - Agenda Actions

February - Agenda Actions
> Strategic Plan Revisions
> Grant Funding Review

May Agenda Actions -