
The Clinical Research Center of Hawaii: A Nine Year Progress Report

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Abstract

The UH-CRC is an NIH minority funded infrastructure program at the University of Hawaii in partnership with Hawaii Pacific Health, now in its ninth year. The main purpose of the UH-CRC is to foster clinical research at UH in order to improve the health of the citizens of Hawaii, particularly those who suffer disproportionately from disorders affecting these communities. This status report documents the continued success and progress of the Center. Manuscripts published or in press have increased from an average of 43 in years 1-3 to 54 in years 4-6 to 84 for years 7-9. Actual dollars received per year ranged from 1-7 million dollars the first 6 years, but reached 8-22 million dollars the last three years. This status report also documents the mandate for this clinical research infrastructure program to compete successfully for mainstream funding status by 2010.

Introduction

This is a progress report of the University of Hawaii Clinical Research Center (UH-CRC) over the last three years. It is the third written report since the UH-CRC was funded in 1995. The first report¹ described the origins of the UH-CRC, and the second was a six year progress report.² Since 2001, progress has continued and as a result, the UH-CRC is closer to competing for mainstream funding for a General Clinical Research Center (GCRC). In contrast to the minority funded status of the present UH-CRC, a GCRC (both are funded by the National Center for Research Resources [NCRRR]) is a competitive mainstream clinical research infrastructure program that provides for a much higher funding limit, and greater resources and opportunities for research development which include core laboratory facilities. Reaching this goal will not only demonstrate that this JABSOM program is capable of attaining this higher level of success, but it will also indicate the potential for a long-term commitment from the NCRRR to clinical research development at UH.

To summarize, the UH-CRC, with its outpatient clinic located at Kapiolani Medical Center for Women and Children (KMCWC) and its administrative office located at the Gold Bond Building, both in Honolulu, was initially developed as a collaborative program between the Pacific Biomedical Research

Center (PBRC), John A. Burns School of Medicine (JABSOM), and Kapiolani Health (now called Hawaii Pacific Health). For the past nine years, the UH-CRC has been nationally funded by two, consecutive five year grants awarded by the Research Centers in Minority Institutions (RCMI) program of the NCRRR, one of 25 research institutes of the National Institutes of Health (NIH). This year, year ten, the focus of attention is the renewal application to fund the Center for the next five years to 2010. It is within the timing of this next cycle that the Center will be expected to transition into a successful GCRC.

The overall objectives of the UH-CRC have remained unchanged. It is to promote and conduct clinical research at UH to meet the health needs of Hawaii's diverse population. Acknowledging the diversity of ethnic groups throughout the state and the disproportionate burden of disease upon particular groups, the UH-CRC strives to foster clinical research that reduces disparities between and amongst such peoples. This objective is accomplished through the provision of infrastructure support of junior and minority investigators as they forge their clinical research careers, thereby increasing the quality and quantity of meritorious research projects, and by facilitating educational opportunities for students and established healthcare providers throughout the state.

UH-CRC infrastructure support is offered on a priority basis to investigators with R01-level funded studies (NIH funding for established investigators), and secondarily to investigators supported by career development awards and other programs of research that support junior faculty development. The UH-CRC also supports pilot projects, especially those that demonstrate strong potential for extramural funding. Finally, the UH-CRC supports junior faculty whose clinical research studies are a component requirement in the Masters in Clinical Research Program. This clinical research training and education program is part of JABSOM's overall strategy to expand the pool of competent clinical investigators with independent funding (See Fig. 1). The UH-CRC provides qualified investigators access to clinical and laboratory facilities, support in protocol design, epidemiological and biostatistical analysis, data analysis, specimen collection

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and analysis, and administrative and clerical support along with funding for study related expenses.

While emphasizing the last 3 years, the data presented below represents the cumulative activity of nine years of UH-CRC activity, as reflected in the graphs and tables.

Methods

Data utilized in this report was compiled from written and computer generated reports collected as part of the Annual Report, which in turn is submitted to the NIH. These reports were collected by UH-CRC research staff and UH-CRC investigators. The UH-CRC study coordinators collect demographic and research data such as target and actual enrollment (by ethnicity and gender) from specific science and administrative databases that have layered security at the file/group/domain levels. These data were reviewed by the authors of this report, and tables and figures were generated from the raw data. No statistical analysis was required for this study.

Results

Over the first nine years, a total of 188 applications for research funding have been submitted to the UH-CRC. The UH-CRC requires that applications include research hypotheses, background and significance, preliminary results, the research design and methods, a description of data-producing instruments, and a statistical analysis. Submission rates have risen steadily over the first six years, largely a reflection of the number of investigators who needed first-time support. New submission rates have declined somewhat in the latter years due to the UH-CRC's increased concentration and focus on extramurally funded investigators and their complex and infrastructure consuming studies. As evidenced below, the UH-CRC has offered support in diverse research areas (See Fig. 2).

UH-CRC support has contributed to consistent publication rates, as shown in Figure 3. Table 1 offers examples of recent publications. Grants submitted and awarded by UH-CRC investigators have also continued to increase, particularly since UH-CRC investigators have focused their efforts upon health disparities research (See Fig. 4 showing the total dollars awarded, including the amount awarded for all years of multi-year grants). Indeed, yearly funding received from research grants has climbed steadily over the last three years (See Fig. 5). The underlying number of grants has varied from 9, 19, and 27 in years 1-3 to 35, 23, and 23 in years 4-6 to 18, 3, and 19 in years 7-9. Examples of recent grants (and investigators) include A Study of Oral Health Disparities in Adult Asian & Pacific Islanders (Easa and Harrigan), Collaborative Alcohol Research Development and Planning (Goebert), Female Puberty – A Multiethnic Cohort Study (Novotny), Mechanical and Infection

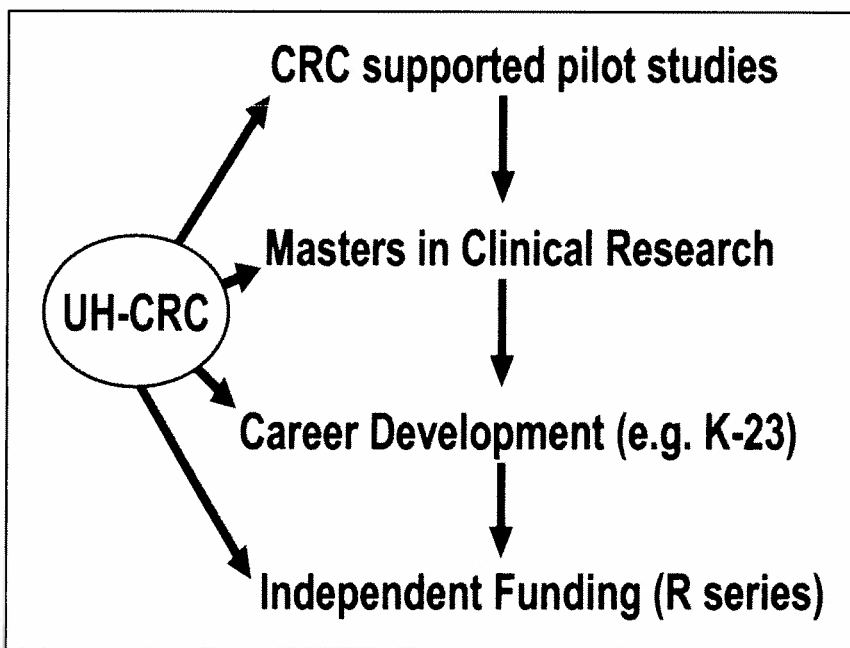


Figure 1.— Clinical Research Faculty Development: This diagram shows the clinical research faculty development process at UH. Pilot studies lead to interest in the Master's in Clinical Research Program Curriculum. This provides junior faculty with the tools to become successful investigators in clinical research, allowing them to compete for career development grants and eventually become independent investigators. The CRC supports this process at all levels. CRC= Clinical Research Center.

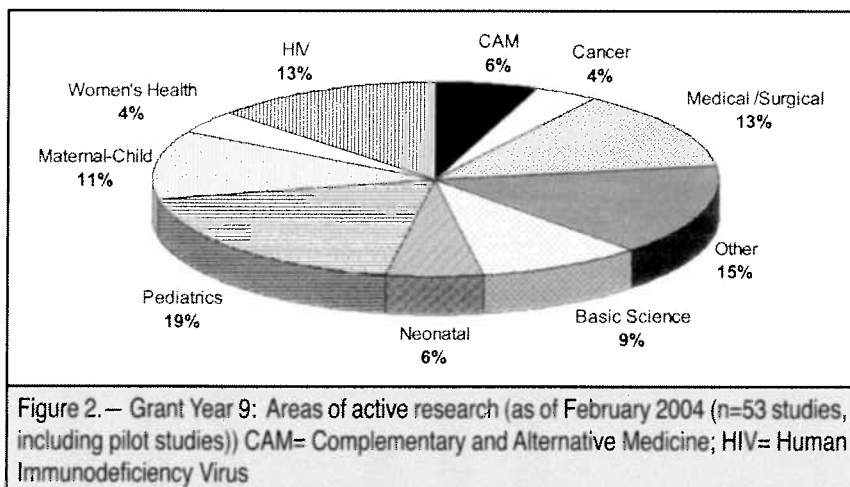


Figure 2.— Grant Year 9: Areas of active research (as of February 2004 (n=53 studies, including pilot studies)) CAM= Complementary and Alternative Medicine; HIV= Human Immunodeficiency Virus

Pathways to Preterm Birth (Bryant-Greenwood), Multiethnic Cohort Study of Diet and Cancer (Le Marchand), Periodontal Disease in Diabetic Women with Preterm Birth (Millar), Study of Cellular Mechanisms of Lung Growth: Effect of NKCC Cotransporter Inhibition on Lung Cell Proliferation (Iwamoto), Mobile Access Resource Project (MARP) (Jacobs), Development of Gene Transfer Approaches for NeuroAIDS (Lu), and the Masters of Science in Clinical Research (Harrigan and Easa – this is a clinical research training and education award).

Other achievements include an increased number of scientific seminars and colloquia, along with an increased number of visiting scientists. In year 9, for example, UH-CRC sponsored two workshops, a short course, and a seminar series; no more than 1 or 2 such activities were sponsored in previous years. Distinguished scientists visiting in year 9, and helping UH-CRC to expand its clinical capacity,

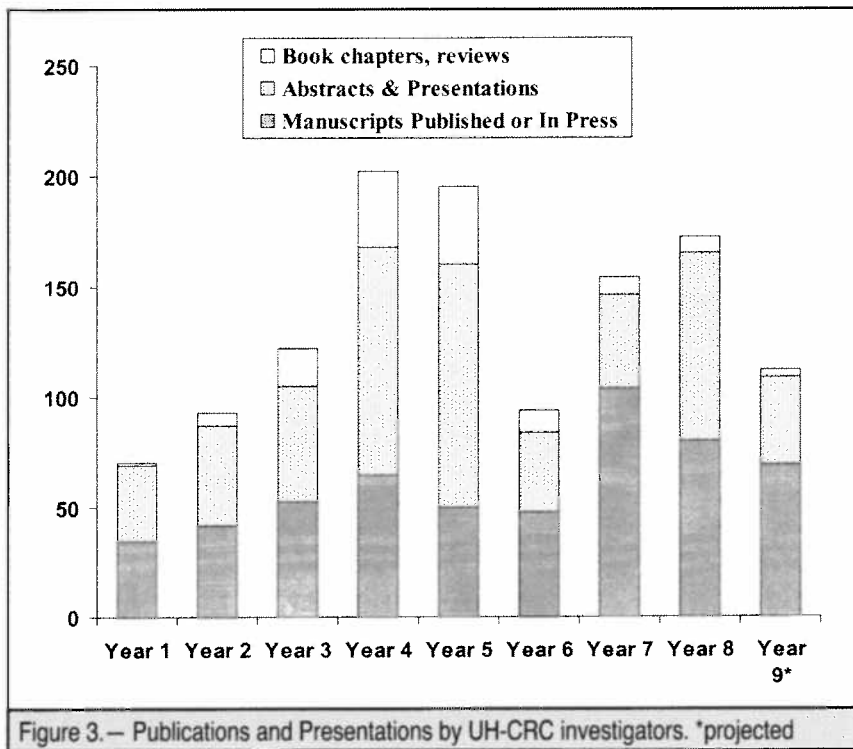


Figure 3.— Publications and Presentations by UH-CRC investigators. *projected

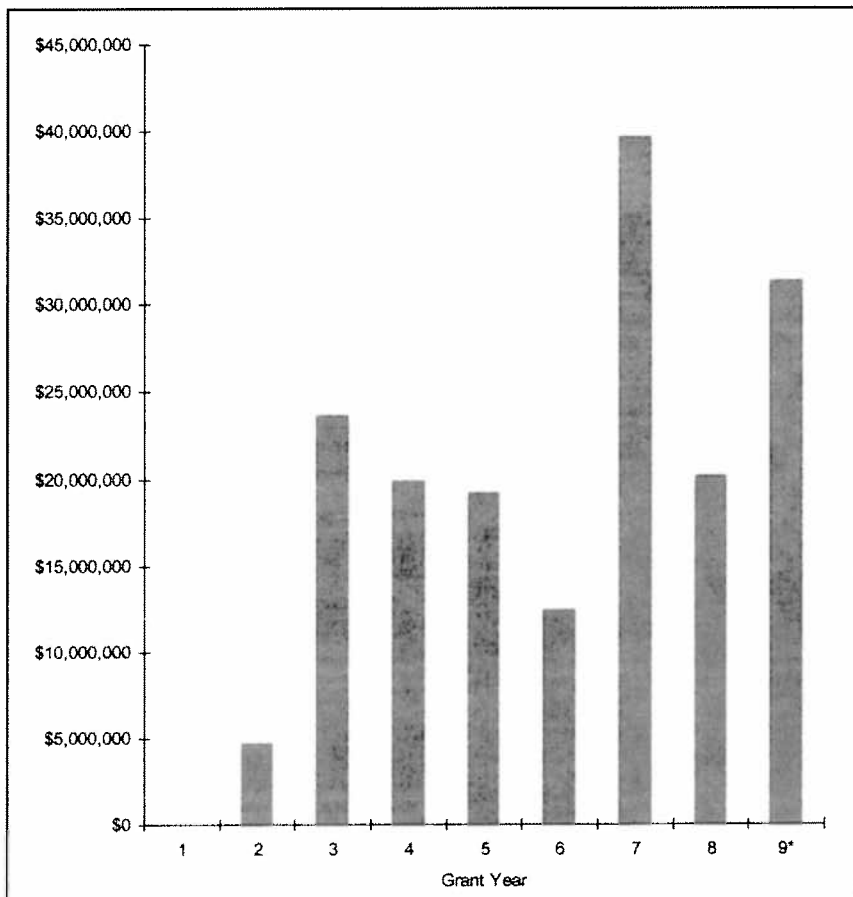


Figure 4.— Total Value of Grant Awards including the amounts awarded for all years of multi-year grants (as of February 2004)

include Drs. Diane Wara and Steven Hulley from the University of California at San Francisco, and Dr. Richard Galbraith from the University of Vermont. Along with these achievements, the UH-CRC has hired skilled technical personnel, two of whom were Research Subjects Advocates (RSA) filling newly created positions. Venkataraman Balaraman, MD, and Kari Kim, a nationally certified Institutional Review Board (IRB) Professional, were appointed as the UH-CRC's RSAs in 2001. The RSA position is separate from the IRB and the RSAs are not IRB employees. Their primary purpose is to ensure that every UH-CRC supported research project protects the rights of human subjects in clinical research. They also report any problems with research procedures, review IRB documents, help with consent forms, review SAC (Scientific Advisory Committee) documents, and assist with data safety monitoring plans. RSAs are the link between the UH-CRC and the IRB. Finally, the UH-CRC's clinical research environment has new creative opportunities for expansion. Queens' Medical Center, Leahi Hospital, the University of Hawaii at Manoa and Kapiolani Community College are all potential sites for clinical research activity.

The UH-CRC has improved its infrastructure, as measured by increased proficiency for grants and contracts management. Indeed, JABSOM has created a newly structured Grants Development Office to facilitate research proposal development for the UH-CRC and JABSOM's clinical investigators. The Grants Development office provides the following services: budget preparation, preparation of biographical sketches, grants writing, completion of University forms (i.e., Conflict of Interest, ORS-5), assistance with letters of support, review and consultation related to proposal narrative, proposal packaging, duplication and mailing of proposal, and institutional review of proposal.

Although the UH-CRC has improved its infrastructure, there continue to be challenges, including accommodating for the dramatic increase in clinical research activity during the past year. Indeed, the volume of research participant visits conducted during Grant Year 9 represents a 69% increase and Grant Year 8 a 49% increase over Grant Year 7. These participant visits all represent substantial increases from year 1; in absolute numbers, visits increased from 486 in year 1 to 3,092 in year 9. However, staffing and space have not entirely kept pace with demands. In addition, housing of clinical and administrative staff in separate locations continues to pose operational challenges. This has been further exacerbated by the move of UH-CRC administrative staff to the Gold Bond Building (January, 2004) which is now 3½ miles away from the clinical unit at KMCWC. Indeed, travel time for meetings detracts from other duties such as implementation of studies. Operating from separate

facilities has also resulted in inefficiencies related to duplication of files, records, and administrative processes. However, the strategic benefit of relocation to the Gold Bond Building is to position JABSOM research programs and departments, including the UH-CRC, to be located near the new medical school building, the completion of which is anticipated in Summer 2005.

As for training and education programs designed to increase the critical mass of qualified clinical investigators, Dr. Easa, Dr. Rosanne Harrigan and the UH-CRC prepared a successful NIH application to establish a Master of Science in Clinical Research at JABSOM. The Masters Program provides the necessary tools to junior and minority faculty through a specific curriculum and a required research study in order to prepare them for careers in clinical research.

Health disparities research continues to be a major focus for the UH-CRC. For example, the Program Director of the UH-CRC, Dr. David Easa, along with co-investigators including Dr. Harrigan, were successful in an R-21 application, an application for exploratory and developmental research, entitled, "A Study of Oral Health Disparities in Adult Asian & Pacific Islanders, the objective of which was to apply a state-of-the-art, molecular and epidemiological approach to examining oral health disparities in Adult Asian and Pacific Islanders. In addition, Dr. Easa and the UH-CRC, who assisted with the successful Hawaii EXPORT Center application, are now supporting the program by fulfilling biostatistical and computer specialist needs. The Hawaii EXPORT Program is led by Dr. Marjorie Mau, and is a community based research program in diabetes targeted to Native Hawaiian and Pacific peoples. The UH-CRC has demonstrated its commitment to collaborative health disparities research through continued interaction with several Community Health Centers and other University of Hawaii research institutes.

Discussion

The UH-CRC has continued to make progress over its nine year history as evidenced by the data presented here. The current renewal application in preparation will fund the UH-CRC for the next five years. The four specific aims include: 1) Increasing the number of R01-level investigators at the UH-CRC; 2) Expanding career development programs to increase the number of clinical investigators at UH; 3) Improving UH-CRC infrastructure in order to better support innovative research; and 4) Strengthening collaborations designed to benefit Hawaii's diverse communities. Included in the competitive renewal application will be a proposal to include a Core Laboratory at Queen's Medical Center. This will incorporate Dr. Linda Chang's Magnetic Resonance (MR) facility and research program. Dr. Linda Chang's area of

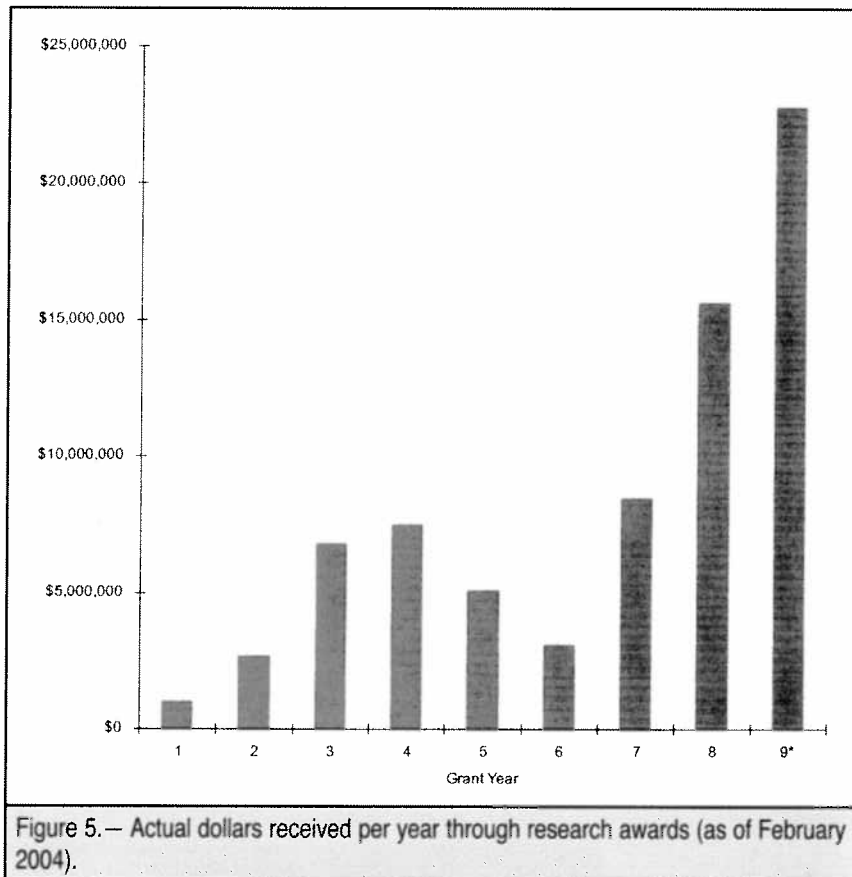


Table 1.— Examples of year 9 publications supported by the University of Hawaii Clinical Research Center

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| Brizzolara S, Pillai-Allen A. Risk of mesh erosion with sacral colpopexy and concurrent hysterectomy. <i>Obstetrics and Gynecology</i> . 2003 Aug;102(2):306-310. |
| Brown AC, Valiere A. Probiotics and Medical Nutrition Therapy. <i>Nutr Clin Care</i> Apr-June. 2004;7(2): 56-68. |
| Davis J, Busch J, Hammatt Z, Novotny R, Harrigan R, Grandinetti A, Easa D. The relationship between ethnicity and obesity in Asian and Pacific Islander populations: a literature review. <i>Ethnicity and Disease</i> . 2004;14:111-118. |
| Derauf C, Katz AR, Easa D. Agreement between maternal reported ethanol and tobacco use during pregnancy and meconium assays for fatty acid ethyl esters and cotinine. <i>American Journal of Epidemiology</i> . 2003;158(7):705-709. |
| Hernandez BY, McDuffie K, Wilkens LR, Kamamoto L, Goodman MT. Diet and premalignant lesions of the cervix: evidence of a protective role for folate, riboflavin, thiamin, vitamin B12. <i>Cancer Causes and Control</i> . 2003;14(9):859-870. |
| Huang TK, Uyehara CFT, Balaraman V, Miyasato CY, Haley TF, Egan E, Person DA, Easa D. Surfactant lavage with lidocaine improves pulmonary function in piglets after HCl induced acute lung injury. <i>Lung</i> . 2004;182(1):15-25. |
| Iwamoto LM, Fujiwara N, Nakamura KT, Wada RK. Na-K-2Cl cotransporter inhibition impairs human lung cellular proliferation. <i>Am J Physiol (Lung Cell Mol Physiol)</i> 287:L510-4, 2004. |
| Maskarinec G, Robbins C, Riola B, Kane-Sample L, Franke AA, Murphy S. Three measures show high compliance in a soy intervention among premenopausal women. <i>Journal of the American Dietetic Association</i> . 2003;103(7):861-866. |
| Sato RL, Wong JJ, Sumida SM, Marn RY, Enoki NR, Yamamoto LG. Efficacy of superactivated charcoal administered late (3 hours) after acetaminophen overdose. <i>American Journal of Emergency Medicine</i> . 2003;21(3):189-191. |
| Novotny R, Daida YG, Grove JS, Acharya S, Vogt TM. Formula feeding in infancy is associated with adolescent body fat and earlier menarche. <i>Cellular and Molecular Biology</i> . 2003;48(8):1289-1293. |

interest is the effect of substance abuse drugs on central nervous system function. The MR scanner is an outstanding and innovative tool to define functional defects resulting from drugs that are subject to abuse. The competitive renewal application also emphasizes areas of scientific focus including health disparities research, early human development, maternal child health, cancer, cardiovascular disease and related risks, neurosciences, oral health and emerging infectious disease.

The goal for the next five years of the UH-CRC is to resolve several key issues to make it competitive for GCRC status. For example, an R01 or comparably funded clinical investigator must be recruited to qualify as Program Director. The UH-CRC must also expand the strength and depth of clinical research activity with at least twenty studies that have extramural funding. In order to achieve this goal, more focus must be placed on R01 investigators. The UH-CRC also needs to identify and continue to broaden the base of clinical investigators to include those from other hospitals and healthcare organizations in Hawaii.

In sum, the RCMI-supported UH-CRC has demonstrated its ability to progress and prosper to increase clinical research capacity in the State of Hawaii. The number of UH-CRC-supported clinical investigators, research studies, publications, and research grants continues to increase. Given the UH-CRC's increasing capacity to support meritorious research studies and funded investigators, it is well positioned to compete for GCRC status sometime in the future. This will become a reality given the opportunity to do so with the funding of the UH-CRC renewal application for a final five year cycle.

Acknowledgement

The manuscript was supported by the Centers in Minority Institutions award, P20 RR11091, from the National Center for Research Resources, National Institutes of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCR/NIH.

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