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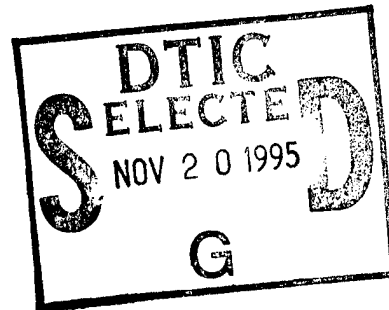
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Appendix 1: Organizational Structure of the SCCC

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(5) INTRODUCTION

A. Statement of the Problem

A diagnosis of breast cancer and subsequent treatment are known to bring about significant distress, disruption and sexual dysfunction in the lives of women who experience them. Factors such as socioeconomic status, treatment modality, patient perceptions, coping strategies and social support have all been shown to influence the ways in which women adjust to these events. Behavioral interventions developed on the basis of the results of systematic studies of this adjustment process have the potential to foster positive expectancies about the future, can alter patient's coping responses and health maintenance behaviors, increase their sense of support from others, and facilitate an attitude of re-engagement with life. While studies of ethnic minority women have been conducted on breast cancer incidence and survival rates and on tendencies to use or avoid mammography virtually no data exist on the predictors of psychosocial sequelae of breast cancer in these groups. This represents a serious limitation in our ability to develop effective behavioral interventions to facilitate the adjustment process in these populations.

These research agenda, central to ongoing collaborative work between the Division of Health Psychology and the University of Miami School of Medicine, intersect with at least two fundamental questions included in the framework for basic, clinical and public health research projects put forth in the September 15, 1993 announcement of the U.S. Army Medical Research and Development Command. These fundamental research issues include:

- (1) Studying the impact of risk, disease, treatment and ongoing care on the psychosocial and clinical outcomes of breast cancer patients and their families;
- (2) Defining and identifying (intervention) techniques for delivering effective and cost-effective health care to all women to prevent, detect, diagnose, treat and facilitate recovery from breast cancer.

In order to address these research agenda it is necessary to bring together a multidisciplinary team of talented investigators with expertise in social psychology, behavioral medicine, clinical health psychology, biostatistics/epidemiology, psychiatry and oncology. Traditionally, however, lack of communication among scientists in different disciplines and limited competence in the methodologies of different disciplines have been major obstacles to successful integrative research.

B. Background of Previous Work

At the University of Miami we have overcome many of the obstacles noted above. First, an NIMH Center for the Biopsychosocial Study of AIDS under the direction of Carl Eisdorfer, M.D., Ph.D. brought together a large number of research scientists from

different disciplines and taught them to work together on multidisciplinary research problems related to this other major health problem. These included several talented behavioral scientists, biomedical researchers and biostatisticians, and internists interested in the influence of behavior on health status in AIDS. At the same time our Division of Health Psychology was conducting an NHLBI Program Project on hypertension led by Neil Schneiderman, Ph.D. (Director of Health Psychology Division). This program project brought together behavioral scientists, physiologists, biochemists, and internists to conduct several interrelated studies exploring the influence of behavior, ethnicity and gender on the pathophysiology of cardiovascular disease and hypertension. Many of the scientists from the NIMH center and the NHLBI Program Project are now conducting research together and co-supervising graduate students and post-doctoral fellows in our associated training programs.

Over the past five years, two large training programs (NHLBI training program: HL07426-15; NIMH training program: MH18917-01) have facilitated the training of several pre-doctoral graduate students and post-doctoral fellows in our division of Health Psychology. Each of these training programs brought together multidisciplinary faculty to train our students and fellows through the development of coursework, weekly research meetings, exposure to major scientists in the field who served as consultants, laboratory rotations, and closely supervised research and clinical experiences. Our present roster of research activities includes, but is not limited to two 5-year funded program projects (P01), individual investigator awards focused upon breast cancer (ACS-funded) and cervical cancer (NCI-funded), and a series of pilot studies used to develop and test experimental interventions with breast cancer patients.

A unique feature of the proposed training program is the fact that it exists within the context of ongoing research studies (R01), program projects (P01) and co-existing training grants all centered around the examination of the effects of behavior and ethnicity on adjustment to and progression of chronic diseases. Specifically, the NHLBI training grant and program project are focused upon examining the influence of behavior, ethnicity and gender on stress responsivity, hypertension and diabetes. The NIMH training grant and program project are both dedicated to exploring the effects of behavior and ethnicity on adjustment to and management of HIV-1 infection. Two ongoing psycho-oncology programs led by Dr. Antoni focus on the influence of behavior on health outcomes in minority women recently diagnosed with early-stage breast cancer or pre-clinical cervical neoplastic changes. One of these, an NCI-funded project (NCI 5 P30CA14395) examines the role of stressors, coping and social support upon cervical neoplasia and related immune measures in African American women who carry multiple viral risk factors for cervical carcinoma. A second study funded by the American Cancer Society (ACS #PBR-82) explores the role of coping and social support as predictors of adjustment to mastectomy among African American and Hispanic American breast cancer patients. The

latter study recruits patients through the Breast Health Center (Director: Neil Love, M.D.) within the NCI-funded Sylvester Comprehensive Cancer Center.

In addition to the two psycho-oncology projects just described, several additional programs led or co-led by Dr. Antoni or Dr. Weiss and training program faculty were funded and commenced in YR 1 of the present training program. These included (1) an NCI-funded R01 project (1R01CA64710-01) entitled "Coping with Breast Cancer in Younger Women" (P.I. : C. Carver, co-P.I.: M. Antoni); (2) an NCI-supplemental project (1R01CA64710-01) entitled "Lifestyle and Breast Cancer in Cultural and Sexual Minorities" (P.I.: C. Carver, co-P.I.: M. Antoni); (3) an NCI-funded project entitled "PDQ/PIF Evaluation in Multiethnic Populations" (P.I.: S.Weiss); and (4) a developmental grant funded by the Sylvester Cancer Center entitled " Stress Management Intervention for Women with Breast Cancer"(P.I. : G. Ironson). It is noteworthy that each of these last four projects involves the examination of the efficacy of psychosocial interventions thus providing a key training opportunity for the trainees. Each trainee is involved in research activities on at least one of these breast cancer projects.

In sum, we are in a unique position to provide rich training in psycho-oncology and breast cancer. First, we have available for study a large multiethnic population of breast cancer patients. Second, our medical complex, including the newly constructed NCI-core funded Sylvester Comprehensive Cancer Center, is the major treatment center for breast cancer patients in South Florida and is actively involved in ongoing clinical trials and basic biomedical research protocols.. Third, we have a substantial number of extramurally funded research projects that are investigating relationships among psychosocial variables, health, adjustment and behavioral management of chronic diseases such as breast cancer, cervical cancer, HIV-1 infection, hypertension and diabetes. Fourth, we have a collegial, interactive faculty with demonstrated expertise in social psychology, behavioral medicine/clinical health psychology, epidemiology and biostatistics, psychiatry and oncology as these disciplines relate to the study of breast cancer. Fifth, we have a large pool of trainee applicants who are both qualified and interested in entering our training program and developing research careers. Sixth, our faculty is experienced in the intricacies of conducting collaborative research and training and has already worked together in administering two other health-related training grants.

C. Purpose of the Present Work

This program was designed to provide multidisciplinary research training in biopsychosocial aspects of breast cancer in the context of predoctoral training in Clinical Health Psychology leading to the terminal degree of Ph.D..

D. Methods of Approach

This program provides multidisciplinary research training in biopsychosocial aspects of breast cancer. Training is closely coordinated with ongoing research projects in breast cancer being conducted by Training Program faculty. The Training Program makes use of the faculty, resources, and experiences that are readily available at the Sylvester Comprehensive Cancer Center (SCCC) and those that we have secured from our ongoing NIMH and NHLBI training grants and parallel NIMH and NHLBI program projects (P01) that are focused on other chronic disease processes. Trainees are graduate students in Psychology (Health Psychology/Behavioral Medicine) and have offices in the Behavioral Medicine Research Center on the campus of the University of Miami School of Medicine Complex or at the Behavioral Medicine Research Building on the Coral Gables campus. The program was designed to offer the trainees the complete APA-approved academic program in Clinical Health Psychology in addition to participating in academic (didactic), research, and clinical activities specific to the biopsychosocial aspects of breast cancer. To accomplish these training goals, in addition to coursework, each trainee participates in our regularly scheduled psycho-oncology and breast cancer seminar/workshops held at the SCCC; and undergoes rotations in the psychosocial assessment, behavioral interventions, and statistics core laboratories at our Behavioral Medicine Research Center (BMRC) and at the SCCC. In addition each trainee is given the opportunity to complete other rotations in the immunology and biochemistry assay core laboratories at the University of Miami School of Medicine. They gain direct research experience working on federally-funded research projects with several training faculty members who are actively working in research on breast cancer. One faculty member from the Health Psychology faculty is designated as primary preceptor and one faculty member from the Departments of Medicine, Oncology, Psychiatry or Epidemiology will serve as the secondary preceptor for each trainee. All trainees are exposed through coursework to experimental design and statistics as well as psychosocial, biobehavioral and pathophysiologic perspectives on breast carcinoma that are provided by way of didactic research seminars and clinical workshops.

(6) BODY

A. Execution of Training Program Design

Training throughout YR 1 was closely coordinated with ongoing biopsychosocial breast cancer research projects including an ACS-funded and NCI-funded projects examining factors predictive women's adjustment to surgical mastectomy for primary disease. The training program was also able to make use of the faculty, resources, and experiences that we have secured from our ongoing NIMH and NHLBI training grants and parallel NIMH and NHLBI program projects (P01) that are focused on other chronic disease processes. All four of the trainees enrolled are graduate students in Psychology (Health Psychology/Behavioral Medicine) and have offices in the Behavioral Medicine

Research Center and affiliated buildings on the campuses of the University of Miami including the School of Medicine Complex and SCCC.

In the current program each trainee participates in regular (weekly and monthly) psycho-oncology and breast cancer didactic seminars, workshops, grand rounds and tumor boards; undergoes rotations in the psychosocial assessment, behavioral interventions, and statistics core laboratories; and has the opportunity to complete other rotations in the clinical immunology and biochemistry assay core laboratories within the University's School of Medicine. During the 01 year each trainee gained experience working on research projects with several training faculty members who were actively working in research on breast cancer. All trainees were exposed through coursework to experimental design and statistics as well as psychosocial, biobehavioral and pathophysiologic perspectives on breast carcinoma and other chronic diseases. The latter focus was extended by their attendance at the weekly Psycho-Oncology Clinical Workshop, weekly Breast Cancer Team Research Meeting, monthly Psycho-Oncology Research Seminar (which included presentations by Training Program faculty and Visiting faculty from major cancer research centers in the U.S. and abroad) and the monthly Psychoneuroimmunology Journal Club meeting.

Trainee selection . In September 1994 at the inception of the program, three (3) trainees were admitted by unanimous vote of the Executive Committee (C. Wynings, J. Lehman, R. Perczek). These students were recruited directly through the existing ranks of Clinical Psychology students who had been admitted at an earlier point. Christina Wynings was transferred from an NIMH training grant in Behavioral Immunology and AIDS and Jessica Lehman was transferred from a Research Assistantship on an NIMH-funded project on AIDS. Ruben Perczek was an entering (first-year) graduate student who had already secured a Research Assistantship in an NIMH Minority Health project but was transferred to the present program prior to the commencement of the academic semester. All of the positions vacated by these trainees were immediately filled by other graduate students. All three trainees expressed a strong interest in focusing their Clinical Health Psychology training in psycho-oncology in general and breast cancer and women's health issues in particular. The Executive Committee was unanimous in recommending all three of these candidates for positions on the present program. Their preceptors were as follows: J. Lehman-M. Antoni; C. Wynings-G. Ironson/M. Antoni; and R. Perczek-C. Carver. It was decided to delay the admission of the fourth trainee until the annual Health Psychology admissions meeting (2/95) for the 1995-96 class so as to provide the opportunity to recruit an additional first-year graduate student.

After receiving over 100 applications for the Clinical Health Psychology program, Dr. Antoni culled a set of five applicants who had the most outstanding files based upon Graduate Record Exam scores, grade-point average, excellence demonstrated in prior research experiences, strong letters of recommendation, and an expressed interest in

pursuing breast cancer and psycho-oncology as their chief focus during graduate studies in health psychology. Dr. Antoni then presented the candidates to the Executive Committee and a first choice and first alternate were selected. During this period one of the initially appointed trainees, R. Perczek, expressed a strong interest in moving his research focus into a related area within psycho-oncology--biopsychosocial factors in prostate cancer--and secured a position as a Research Assistant on VAMC-funded research project that ultimately commenced in 8/95. Although he retained Dr. Carver as his primary supervisor his focus of study no longer coincided with this training program and the Executive Committee was unanimous in their decision to allow him to transfer. Based upon this information, in 3/95 the Executive Committee decided to offer trainee positions to both the first choice and first alternate candidates, one for the position to be vacated by R. Perczek and one for the fourth trainee slot that was held open. After traveling to Miami and completing two days of intensive interviews each candidate accepted our offer and each joined the program in 8/95. These trainees are Bonnie McGregor and Amy Eisenberg. The progress of each trainee is detailed in a latter section of this report.

Training structure. A considerable amount of coursework and didactic training was available for trainees, though the major emphasis of the training program is upon direct involvement in research and focused clinical practica. All trainees (as well as other Health Psychology graduate students) spent a substantial portion of their time (approximately 20 hrs per week) conducting research throughout the calendar year. To facilitate this, Health Psychology students were restricted to 10 credits of coursework per semester. In addition to research and coursework the more senior trainees, J. Lehman and C. Wynings completed clinical practica ranging from 7 - 10 hrs/week during the Fall, Spring and Summer semesters during YR 1. The balance of their time was spent attending various didactic experiences (detailed below) as part of the Training Program. The newly admitted trainees, A. Eisenberg and B. McGregor will be engaged in coursework and research for Fall 1995 and Spring 1996 semesters before beginning their clinical practica in the Summer of 1996. They will also attend the didactic experiences detailed below.

Coursework. Through courses offered in the Health (Clinical) Psychology Program all trainees receive combined training in behavioral medicine research and the development of closely related skills useful for research in health clinical psychology. All graduate students in Health Psychology are required to take a rigorous three semester experimental design and statistics sequence taught by Drs. Gail Ironson and Maria Llabre. Dr. Ironson is the Leader of the Statistics Core Laboratory on our NIMH Program Project and Dr. Llabre serves as an experimental design and statistics expert on the NIH Behavioral Medicine study section. The first semester of the experimental design and statistics sequence reviews introductory statistics, principles of experimental design, basic computer applications and data management. Subsequently, predoctoral students take courses in Advanced Psychological Statistics and in Multiple Regression Statistics. Trainees must also complete *Core* courses in Psychobiology, Psychopathology, Social

Psychology, and Developmental Psychology. In addition to *Core* courses each trainee will complete three courses in Assessment, two additional courses in Pathology, and three courses in Intervention. The illustrative program for Clinical Health Psychology students applies to most trainees and includes some combination of the following: *Assessment* (general psychological assessment and two advanced specialty courses such as Psychological Assessment of Physical Disorders and Neuropsychological Assessment, Advanced Projective Assessment), *Pathology* (Fundamentals in Behavioral Medicine, Advanced Behavioral Medicine, Psychoneuroimmunology, Psychophysiology, Psychopharmacology, Advanced Experimental Psychopathology and Psychosomatics), and *Intervention* (Introduction to Psychological Intervention, Cognitive Behavioral Intervention, Psychological Intervention in Physical Disorders, Group Therapy, Family Therapy). At the time of pre-registration each trainee reviews their academic progress and chooses their coursework for the subsequent semester during a face-to-face meeting with their primary preceptor. Because many of the specific activities relating to breast cancer have evolved over YR 1 we include these within the next section: Program Development and Growth.

B. Program Development and Growth

This section focuses specifically on those experiences and facilities central to the focus of this training program: the biopsychosocial aspects of breast cancer. This section is divided into Symposia/Didactic Experiences, New Ongoing and Pending Breast Cancer Research Protocols, and Cancer Center Facilities and Resources, Trainee Progress, and Publications and Presentations of Training Program Faculty and Trainees.

1. Symposia/Didactic Experiences

The following activities constitute the present symposia/didactic experiences that are made available to trainees for the purpose of providing specific exposure to the biopsychosocial aspects of breast cancer. Some of these activities have mandatory attendance for trainees while others are optional:

- a. Ongoing Monthly Psycho-Oncology Research Seminar
- b. Weekly Clinical Psycho-Oncology Workshop (new)
- c. Weekly Breast Cancer (NCI) Research Meeting
- d. Other Training-Related Activities
 - Weekly Multidisciplinary Breast Cancer Tumor Board Meeting
 - Weekly SCCC Grand Rounds
 - Monthly PNI Journal Club
 - Weekly Stress Management Group Clinical Supervision
- e. Clinical Rotations
- f. Research Rotations

a. Psycho-Oncology Research in Breast Cancer Seminar. At the outset of the training grant period we instituted a regular Seminar on Psycho-Oncology Research in Breast Cancer. This seminar was coordinated by Drs. Antoni, Weiss, and Scheiderman. The seminar met in the conference room of the SCCC for approximately 1 - 1.5 hours and was attended by surgical oncologists, psychiatrists, clinical psychologists, social case workers, and nurses who staffed the SCCC, VAMC and the University of Miami School of Medicine. In addition the seminars were attended by trainees, clinical psychology interns and psychiatric residents. The seminar series included the following modules presented by Training Program faculty:

DR Carver	Psychosocial factors predicting adjustment to surgical mastectomy
Dr. Antoni	Behavioral interventions in psycho-oncology
Dr. Ironson	Methodological issues in evaluating the efficacy of behavioral interventions
Dr. Richman	Clinical trials research in breast cancer
Dr. Weiss	Intervention to improve sexual functioning in breast cancer patients
Dr. Brickman	Psychosocial and psychiatric assessment in breast cancer patients
Dr. Reynolds	Consultation/Liaison psychiatry issues in oncology and breast cancer

In addition to these presentations by Training Program Faculty the following presentations were also made by visiting faculty from national and international cancer centers:

- Dr. B. Garssen, Ph.D., Director of Research, Helen Dowling Institute for Biopsychosocial Medicine, Rotterdam, NTH
"The Assessment of Fatigue in Cancer Patients"
- Dr. P. Jacobson, Ph.D. Director of Psychosocial Oncology Program, E.F. Moffitt Cancer Center, Tampa, FL
"Conditioned Responses to Chemotherapeutic Regimens in Cancer Patients"
- Dr. D. Bovjberg, Ph.D., Director of Psychoneuroimmunology Laboratory, Memorial Sloan-Kettering Cancer Center, N.Y.
"Psychoneuroimmunology and Breast Cancer"
- Dr. A. Visser, Ph.D., Helen Dowling Institute for Biopsychosocial Medicine, Rotterdam, NTH
"The Role of Patient Education in Cancer Control"
- Dr. M Andrykowski, Ph.D., Bone Marrow Transplant Program, University of Kentucky School of Medicine, Lexington, Ky
"Quality of Life Considerations in Cancer Patients"

Attendance was mandatory for all trainees.

b. Weekly Breast Cancer (NCI) Research Meeting- Each week all trainees attend a one hour research meeting conducted by Drs. Antoni, Carver and Ironson in the Behavioral Medicine Research Building on the Coral Gables campus. Here issues related to the day-to-day conduct of the ongoing ACS and NCI protocols are discussed. Specific topics center around subject recruitment, assessment, randomized intervention methods, tracking and retention of subjects, data management and analytic strategies, preparation of

reports for publication and presentations for scientific conferences. In addition to faculty and trainees this meeting is attended Dr. Love and his staff and post-doctoral fellows who are working on the NCI protocols. In most cases each trainee receives their day-to-day supervision from one of these post-doctoral fellows.

c. (New) Weekly psycho-oncology clinical workshop.

This workshop commenced in July 1995 and is directed by Alicia Capitaine-Ceballos, Ph.D., the Director of Clinical Services in the Psychosocial Oncology program housed at the newly constructed Courtelis Center for Research and Treatment in Psychosocial Oncology at the SCCC. This weekly seminar uses a small group format to discuss clinical issues relevant to the psychological treatment of cancer patients. The workshop series is offered twice a year and the curriculum is as follows:

<u>DATE</u>	<u>TOPIC</u>
7/26/95	Stresses on Mental Health Professionals in Psycho-oncology
8/2/95	Behavior Techniques: Relaxation and Guided Imagery
8/9/95	Psychological Adjustment to Cancer: Intrapersonal Resources
8/16/95	Psychological Adjustment to Cancer: Interpersonal Resources
8/23/95	Medical Factors and Adaptation: Clinical Course of Cancer I (S. Weiss)
8/30/95	Medical Factors and Adaptation: Clinical Course of Cancer II (S. Weiss)
9/6/95	Medical Status Assessment in Oncology (C. Sandoval)
9/13/95	Role of the Family in Oncology
9/20/95	Oncology Social Work (L. Grenier)
9/27/95	Spirituality in Oncology (B. Black)
10/4/95	Treatment-Specific Psychological Issues: Bone Marrow Transplantation (S. Yount)
10/11/95	Treatment-Specific Psychological Issues: Radiation Treatment (A. Bernstein)
10/18/95	Psychotherapeutic Interventions in Oncology: Cognitive-Behavioral Therapy
10/25/95	Cancer Survivors: Psychological Sequelae
11/1/95	CNS Complications: Delirium, Dementia, Endocrine-related Psychiatric Disorders (S. Crawford)
11/8/95	Psychopharmacological Management of Cancer Patients (C. Sandoval)
11/15/95	Treatment-Specific Psychological Management: Chemotherapy and Surgery
11/22/95	Treatment-Specific Psychological Management: Cancer Pain
11/29/95	Death and Dying Issues

12/6/95	Self-Help and Mutual Support Programs (D. DeMontmollin)
12/13/95	Alternative/Complimentary Cancer Therapies (C. West)

d. Other training-related activities. In addition to these regular activities related to research and clinical training each trainee is invited to attend other Cancer Center activities including the weekly Multidisciplinary Tumor Board meeting and selected SCCC Grand Rounds where they can gain knowledge into the medical aspects of diagnosis and treatment procedures for breast cancer patients at various stages of disease. Trainees are also invited to attend two other regular activities at the Behavioral Medicine Research Center on the Coral Gables campus. One of these is the monthly *Psychoneuroimmunology (PNI) Journal Club* wherein health psychology faculty (M. Antoni, G. Ironson) meet with trainees and other health psychology graduate students and post-doctoral fellows to discuss recent articles and innovations in areas of design, assessment and intervention that are relevant to ongoing and planned research in immunologic-related diseases and neoplasias. Cross fertilization of ideas from graduate students and fellows working in different disease areas (e.g., AIDS, cardiovascular disease, and cervical and breast carcinoma) is especially encouraged in this informal format. Theoretical and practical issues involved in setting up independent research projects that supplement ongoing protocols are discussed and trainees are encouraged to propose small pilot protocols that can be supported by Training Program funds. All pilot projects that are deemed by the faculty to be worthy of further discussion are brought to the attention of other Training faculty with special expertise in the technical aspects of these lines of inquiry (e.g., Dr. M. Fletcher, Director of the Clinical Immunology Laboratory at the University of Miami School of Medicine). In any cases where these ideas lead to changes or embellishments in ongoing protocols, of course all of the procedures prescribed by the University's Institutional Review Board are strictly followed. In general the *PNI Journal Club* is designed to provide a regular source of research updates and to stimulate independent thinking and expansion of ongoing hypothesis testing in a supportive collegial atmosphere. In addition to accessing the Journal Club for research updates each trainee is furnished with an internet account that allows them to access large research information databases and services including the PNI research networks, MEDLINE and PSY ABSTRACTS.

A second regular training-related activity that occurs at the Behavioral Medicine Research Center is the *weekly Clinical Supervision for the Stress Management Group Intervention* that is used in two ongoing breast cancer protocols. Any trainees who are actively co-leading or in training for running an intervention group on one of the breast cancer research protocols is required to attend these supervisory sessions which are grouped into two parts: an initial 10-wk training program and a continuing supervision of ongoing groups. The 10-wk training program uses a detailed treatment manual that contains didactic materials, in-session exercises (role-playing stress management

techniques and relaxation exercises) , and homework assignments for each of 10 modules that make up the intervention used in the ongoing NCI intervention study led by Drs. Antoni, Carver and Ironson. After training is completed, advanced (2nd - 4th year in program) trainees will co-lead an intervention group with an experienced post-doctoral fellow or faculty member, will audiotape each session and will be supervised by Drs. Antoni and Ironson on a weekly basis. This activity is viewed as an important clinical experience that supplements the formal general and specialized health-related clinical practica that students must complete as part of our APA-approved clinical program.

e. Clinical rotations. In addition to research and coursework all trainees are given the opportunity to take one or more clinical practicum rotations in Clinical Health Psychology that are currently available through our collaboration with the Division of Biobehavioral Medicine in the Department of Psychiatry, and the Veterans Administration Medical Center's Psychology Service. For instance, our clinical health psychology graduate students who rotate through the Division of Biobehavioral Medicine's Chronic Medical Disease practicum are given the opportunity to focus on a psycho-oncology specialization in addition to other opportunities in Organ Transplant, Chronic Fatigue Syndrome, AIDS, and Diabetes. The psycho-oncology specialization involves consultation-liaison work with the Department of Oncology and is coordinated through the Sylvester Comprehensive Cancer Center. At the VAMC, students may choose among rotations in Oncology, AIDS, Alcohol and Drug Rehabilitation, or Inpatient and Outpatient Psychiatry.

f. Research rotations. An important part of our program is the opportunity it offers trainees to participate in multiple *Research Rotations*. Trainees are encouraged to participate in more than one project and to work in more than one Core facility before becoming fully committed to research in a particular laboratory. In terms of Core Rotations, students are exposed to the Psychosocial/Psychiatric Assessment (Dr. Antoni), Statistics (Dr. Ironson), and Behavioral Intervention (Drs. Antoni and Ironson) laboratories concerned with ongoing projects involving other chronic disease populations. In addition to the initial Core rotations, trainees are expected to maintain continuing interactive collaboration between their selected research project and the Cores.

2. Active Biopsychosocial Breast Cancer Research Protocols

One essential feature of the training program experience is the ability to offer trainees the opportunity to work on large-scale research projects focused on the biopsychosocial aspects of breast cancer. As stated previously, based upon grants existing at the commencement of the training program and those obtained during YR 1 trainees have the opportunity to work on one of five different projects:

(1) an ACS-funded study (ACS #PBR-82; "Coping With Breast Cancer Among Low SES Blacks and Hispanics") exploring the role of coping and social support as predictors of adjustment to mastectomy among African American and Hispanic American breast cancer patients (P.I.: M. Antoni). This study recruits patients through the Breast Health Center within the NCI-funded Sylvester Comprehensive Cancer Center;

(2) an NCI-funded R01 project (1R01CA64710-01) entitled "Coping with Breast Cancer in Younger Women" (P.I. : C. Carver, co-P.I.: M. Antoni). This is a 2-part project. Part 1 identifies the major concerns of breast cancer patients in the months following mastectomy and examines the psychosocial predictors of affective, interpersonal and psychosexual adjustment over this period. The chief variables under investigation include vulnerability/resilience, mediating variables of coping, perceptions of partner reactions to surgery, and quality of life. Part 2 applies information on patients' concerns and predictors of adjustment post-mastectomy to formulate and evaluate the efficacy of a group-based cognitive behavioral stress management intervention on an independent cohort of post-mastectomy patients. The major outcomes in this study are affective, interpersonal and psychosexual functioning. This study recruits patients from the SCCC as well as from a network of surgical oncologists practicing throughout Dade and Broward counties;

(3) an NCI-supplemental project (1R01CA64710-01) entitled "Lifestyle and Breast Cancer in Cultural and Sexual Minorities" (P.I.: C. Carver, co-P.I.: M. Antoni). This study as a supplement to the parent project just described, examines the special needs of lesbian breast cancer survivors, their concerns and their psychosocial adjustment. Based upon the results of this phase of the study a pilot study will develop and test the effectiveness of a CBSM intervention designed to meet the special needs and concerns of this specific sub-population of breast cancer patients;

(4) an NCI-funded project entitled "PDQ/PIF Evaluation in Multiethnic Populations" (P.I.: S. Weiss). This study examines the usefulness of patient information files of the PDQ/PIF database for identifying new approaches to presenting information to patients in order to assist them with decision making and impact on their adherence to treatment regimens. This study focuses on ethnic-specific beliefs about health care and cancer, health care delivery, information types and sources, uses of traditional medicines or healers and types of health services utilized;

(5) an SCCC Developmental grant entitled "Stress Management Intervention for Women with Breast Cancer" (P.I. : G. Ironson). This project tests the effects of a 10-week cognitive behavioral stress management intervention on the quality of life, distress, coping and immunologic status of women with early-stage breast cancer in a randomized experimental design. Women complete a comprehensive biopsychosocial

assessment battery (including psychosocial interviews and questionnaires and blood draws for immunologic assays) at pre-intervention, post-intervention and at follow-up.

It is noteworthy that each of projects (2) - (5) involves the examination of the efficacy of psychosocial interventions thus providing a key training opportunity for the trainees. Each trainee is involved in research activities on at least one of these breast cancer projects. At least two additional biopsychosocial projects have been designed and are under review at the present time. These projects deal with evaluating the concerns of older breast cancer patients and the efficacy of psychosocial interventions with this group. Our ultimate goal would be to have a comprehensive program of research that addresses the major concerns of breast cancer patients from different ethnic groups, SES groups and age groups at multiple stages of disease through the use of prospective natural history studies whose results lead directly to the development of theoretically-driven and empirically-validated psychosocial interventions specifically tailored to the chief concerns and to modulating the mediators of psychosocial adjustment and physical health for each group. Our goal is to couch all of these activities in the context of a joint collaboration between the Department of Psychology, the SCCC and the Departments of Medicine and Psychiatry. This collaborative arrangement not only facilitates the conduct of this research but also provides a state of the art training environment. The next section describes developments in the SCCC that occurred during the 01 year of the training grant which are particularly important for the evolution of the training program.

3. SCCC Programs, Facilities and Resources

The SCCC is located on and functions as a matrix center within the campus of the University of Miami School of Medicine. The SCCC was actually the first of six centers established by the School of Medicine and has been in operation since 1974. The Center is made up of a coordinated network of research and clinical facilities. The research facilities include the Fox Cancer Research Complex (including the Papanicolaou Building and the Louis Fox Building), Rosenstiel and Glaser Medical Science Buildings, R. Bun Gautier Molecular Biology Building, the McKnight Vision Research Building, the Behavioral Medicine Research Center, and the Mailman Center for Child Development. The clinical facilities include the Sylvester Clinical Facility, the University of Miami Hospital and Clinics, Jackson Memorial Hospital, Profession Arts Building, Cedars of Lebanon Hospital, Veterans Administration Medical Center, and the Hope Lodge facility for cancer patients. All of these research and clinical facilities are housed on the Medical School campus consortium. In addition to these sites, the SCCC is affiliated with the Department of Psychology on the Coral Gables campus and multiple primary Health Care Centers in the Greater Miami Metropolitan Area. The organizational structure of the SCCC is detailed in Appendix 1. There are three major advances in the SCCC that occurred during YR 1 of the training program which are especially relevant to the program: the creation of the Courtelis Center for Research and Treatment in Psychosocial

Oncology, the expansion of the SCCC Breast Cancer Research Program, and the formation of the SCCC Biopsychosocial Oncology Program.

Courtelis Center for Research and Treatment in Psychosocial Oncology

In September, 1995 the Courtelis Center for Research and Treatment in Psychosocial Oncology was formally opened. This Center, created in part from a donation of \$1.2 million from the Alec Courtelis Corporation, is housed on the second floor of the SCCC and has been designed to offer state of the art multi-specialty services to cancer patients, their families and the medical staff who treat them.

The central missions of the Center are:

- (1) to organize current knowledge of the interactions of biological, environmental, psychological, behavioral and social variables related to the prevention and control of disease and the promotion of health;
- (2) to develop effective treatment interventions to reduce the impact of environmental, physical, psychological and social stressors on health and well being that emerge in the context of dealing with chronic disease;
- (3) to explore at the individual, social and environmental levels as creative means to promote health and to protect individuals against the deleterious effects of stress.

In addition to these general missions the Center' specific objectives are to *develop effective treatment interventions* for cancer patients to enable them to develop and enrich their social support networks, improve their quality of life, and gain illness-related coping skills; *to support a combined research, clinical, and training program* devoted to mind-body interactions and their effects on health and well being; *to conduct working consensus conferences, seminars, and workshops* to translate research findings into practical guidelines for clinicians; and to *train students in the health profession and established health researchers* in the methodological issues related to the study of biopsychosocial factors and health and in the clinical issues related to healing and recovery.

The Center provides: psychiatric, psychological and social work consultation; individual, family and group counseling; stress reduction techniques such biofeedback, relaxation, and imagery techniques and massage; acupuncture; nutritional counseling; pastoral counseling; a patient education library; and a community outreach program made up of seminars, workshops and retreats which integrate physical, psychological and spiritual dimensions of healing. The Center is staffed by a multidisciplinary team of clinical psychologists, psychiatrists, clinical social workers, nurses, and post-doctoral fellows and provides a training site for psychology interns and pre-doctoral health psychology graduate students. The Centers' facilities are also the site for breast cancer research protocols being conducted by training program faculty and their trainees. This

Center is truly one of the first of its kind in this country and will provide unique research and clinical training opportunities for trainees in the program.

SCCC Breast Cancer Research Program

Although the SCCC Breast Cancer Research Program has been in existence since 1993, it was expanded and restructured during 1994 to take on its present form. The overall aim of this program is to expand multidisciplinary and interprogrammatic studies of breast cancer by coordinating a framework for a variety of breast cancer-related research activities. Some of this coordination was accomplished by *convening regular meetings of the P.I.s of relevant research projects; establishing a comprehensive breast cancer database* that links conventional clinical and laboratory parameters of disease with epidemiologic and biomarker studies for clinical research and correlation with laboratory studies of tumor cell biology; *recruiting new clinical and basic science investigators* to the center, and *promoting research that allows rapid translation* of basic science and epidemiologic observations into preclinical and clinical applications. The Breast Cancer Research Program is organized into three project areas--*Basic Science Program, Clinical Research Program, and Cancer Control Program*--and a central core facility, the multidisciplinary Breast Cancer Evaluation Center whose director is Sharlene Weiss, Ph.D., the co-P.I. of this training program. The *Basic Science Program* is made up of components in Regulation of Growth and Progression, Tumor Immunology, and Hormonal Regulation. The *Clinical Research Program* is made up of components in Experimental Therapeutics, Biomarkers, and Clinical Trials. The *Cancer Control Program* is made up of components in Early Detection and Community Outreach, Cancer Etiology, and Biopsychosocial Studies. For a detailed description of the themes, resources, faculty, projects and current funding for the activities composing each of these programs and their components see Appendix 2.

SCCC Biopsychosocial Oncology Program

The Psychosocial Oncology Program is the newest program to be developed at the SCCC having just been established in the past year through the efforts of its director, Sharlene Weiss, Ph.D., the co-P.I. of this training program. The overall aim of the program is to expand multidisciplinary studies of the interactions between biological, psychological and behavioral aspects of cancer with a special focus on multiethnic populations. This research program encompasses the Multidisciplinary Breast Cancer Center, the Psycho-Oncology component of the Cancer Control Program, and the Courtelis Center for Research and Treatment in Psychosocial Oncology. This program achieves its aims *by providing core resources for pilot studies* to develop and/or integrate common data elements for cross-study comparisons of different populations; *establishing collaborative relationships with ongoing programs in other departments* (e.g., psychology, psychiatry) and laboratories to foster multidisciplinary research; *convening*

regular seminars and research meetings between P.I.s of ongoing projects and potential new investigators and others in training to facilitate communication between laboratory and clinical investigators; and by *establishing a comprehensive psycho-oncology database* for all clinical oncology patients. The SCCC has provided Clinical Research Service shared resources (e.g., data managers, biostatisticians, programmers), laboratory space, space for clinical activities, and financial support to facilitate the rapid development of this program. For a detailed description of the rationale, facilities, faculty, projects, and funding for the activities of this program see Appendix 3.

Special Events During YR 1 of the Training Program. In addition to the regular seminars, workshops and coursework that trainees completed there were assorted all-day symposia dedicated to the topic of Psycho-Oncology and Breast Cancer. These included the annual *Symposium on Stress and Coping*, the *Symposium on Psycho-Oncology*, and the *Scientific Program for the Opening of the Courtelis Center for Research and Treatment in Psychosocial Oncology*. The *symposium on Stress and Coping* sponsored by the Department of Psychology and the School of Medicine focused this year on Stress, Coping and Cardiovascular Disease and Hypertension. This event was a 2-day Symposium attended by training faculty and trainees and involved empirically-based presentations by national and international behavioral medicine researchers. Although the topics of these talks did not involve Psycho-Oncology many generic issues relevant to the conduct of behavioral medicine research (statistical analytic models, stress-coping theoretical models, and methodological issues involved in the assessment of coping). The *Symposium on Psycho-Oncology* was sponsored by the VAMC Psychology Service and held in July, 1995. This symposium was attended by oncologists, clinical psychologists, psychiatrists, post-doctoral fellows, psychology interns, trainees and other graduate students. Several of the training program faculty presented summaries of their research along with several invited speakers from other cancer centers across the country. The *Scientific Program of the Opening of the Courtelis Center* featured empirically-based presentations (e.g., psychoneuroimmunology in psycho-oncology; a review of clinical and research issues in psycho-oncology; a review of the role of psychosocial, social and spiritual factors in remarkable recoveries) that are central to the training program. Training faculty and trainees submitted a number of abstract and symposia proposals for consideration for the scientific program of the Society of Behavioral Medicine meeting to be held in March 1996.

4. Progress of Trainees

Christina Wynings

GRE: 1440

G.P.A.: N/A Yale/Stanford

Ms. Wynings was transferred from an NIMH traineeship in behavioral Immunology and AIDS in September, 1994. During her prior traineeship she co-managed an NIMH-funded psychoneuroimmunologic study examining the effects of Hurricane Andrew upon affect, intrusive thoughts and immunologic function among 180 citizens sampled from the

neighborhoods that were in the path of the storm in Dade County, Miami, Florida. During The YR 1 period of the present training grant she successfully defended her M.S. Thesis examining the influence of social support and social networks as buffers of the stress of the hurricane and its associated losses. Ms Wynings has presented papers based upon the results of this study at several major national conferences including the Society of Behavioral Medicine, American Psychosomatic Society, and the American Psychological Association. Since transferring to the Breast Cancer Training Program Ms. Wynings has dedicated the bulk of her research time to working on the NCI-funded project on " Adjustment to Breast Cancer Among Younger Women". She has co-authored one abstract based upon this study that is being considered for presentation at the 1996 Society of Behavioral Medicine conference. During the 01 year she has attended weekly breast cancer research meetings, the monthly seminar on Psycho-oncology Research in Breast Cancer, and has served 15 -20 hrs per week collecting data on the NCI project. During this period she has gained specific knowledge in recruitment strategies, psychosocial assessment, data management and statistical analysis. She has developed a focused interest in examining the role or social support as a predictor of adjustment to surgery.

Ms. Wynings has also completed the training portion of the protocol for stress management intervention being used in a second NCI study examining the efficacy of cognitive behavioral stress management intervention in this population and is slated to co-lead her first group within the YR 2 period. During YR 1 she also completed advanced coursework in Clinical Health Psychology, taught an undergraduate course in Introduction to Psychology (as part of her Ph.D. program requirements) and successfully passed her Clinical Qualifying examinations. She is in the process of preparing a dissertation proposal. In addition to her coursework and research, Ms. Wynnings completed one clinical practicum at the Psychological Services Center, one practicum in Pediatric Oncology at the Division of Pediatric Hematology/Oncology at the University of Miami School of Medicine, and is in the process of completing a third practicum in Chronic Disease Assessment and Intervention at the Department of Clinical Biobehavioral Medicine within the Department of Psychiatry at the University of Miami School of Medicine. This trainee is making excellent progress in academic coursework, teaching, research training and clinical training.

Jessica Lehman

GRE: 1340

G.P.A.: 3.87 Goshen College

Ms. Lehman was transferred from an NIMH-funded research project in September, 1994. In her work on that project Ms. Lehman conducted extensive psychiatric interviews, psychosocial and neuropsychological assessments in the context of a clinical randomized trial examining the effects of group bereavement counseling on affective status, immune function and health in bereaved HIV+ and HIV- gay men. She received training in the conduct of these interventions and functioned as an independent

rater of therapist adherence to protocol and group process based upon videotaped therapy sessions. Thus she came to the present training program with extensive patient interview and assessment experience and wishing to focus her training specifically in the area of breast cancer.

Since joining the training program Ms. Lehman has completed advanced pre-doctoral coursework in family therapy, neuroanatomy, psychological intervention in physical disorders, and social psychology. As part of our graduate program requirement she also taught an undergraduate course in the Psychology of Women. During the 01 year she defended her M.S. Thesis entitled "Coping with Chronic Illness and Hurricane Andrew and Its Relationship to Symptoms, Immune Function and Illness Burden in Chronic Fatigue Syndrome". This project is based upon data that she collected in the period 1992-93. This work examines how individual patient's coping strategies can moderate the impact of external stressors on their adjustment to and health course of their medical condition.

During the YR 1 period Ms. Lehman was also extensively involved in both the ACS and NCI projects of Drs. Antoni and Carver. She has been able to extend her interest in coping strategies from chronic fatigue syndrome to the context of adjustment to mastectomy in breast cancer patients. She worked 15 -20 hrs /week in various project activities including: recruiting subjects, conducting psychosocial interviews, training new students, maintaining liaison with the surgical oncology offices, managing the project database, and entering data from the interviews. During the 01 year Ms. Lehman also participated in the preparation of an empirical abstract based on her work on the NCI project to be presented at the Society of Behavioral Medicine in 1996. She is in the process of completing training in the 10-week stress management intervention for breast cancer patients and will co-lead a group as part of the NCI protocol during YR 2. In addition to these activities Ms. Lehman completed one clinical practicum rotation at the Division of Clinical Behavioral Medicine at the Department of Psychiatry where she gained extensive experience in psychosocial evaluation and intervention for pre and post kidney and liver transplant patients with end-stage on both an in- and out- patient basis. She has also begun a rotation at the VAMC working with terminally ill patients and geriatric patients where she is gaining experience in working with issues related to death and dying. This trainee is making excellent progress in academic coursework, teaching, research training and clinical training.

Bonnie McGregor

GRE Total: 1250

GPA:3.28 Pacific Lutheran

Ms. McGregor completed her B.S. degree from Pacific Lutheran University in 1984 and before completing two years in a histocompatibility lab conducting tissue typing and cross matching for bone marrow, kidney and heart transplants. This post-graduate experience led her to the research she has been conducting for the past 7 years on examining B-lymphocyte defects and cytokine regulation abnormalities in bone marrow transplant patients at the Fred Hutchinson Cancer Center at the University of

Washington School of Medicine. This work led to the preparation of three empirical manuscripts. During this period Ms. McGregor also managed the clinical immunology laboratory service for the cancer center and was responsible for tracking changes in immune function over the one-year post-transplant period and acquiring, organizing, and analyzing patient data for both research and clinical purposes. Ms. McGregor expressed a particular interest in focusing her graduate training in Health Clinical Psychology in the area of psychosocial intervention and psychoneuroimmunologic aspects of psycho-oncology with a special emphasis on breast cancer. Her commitment to a career in clinical oncology research in general and in the area of psycho-oncology in particular along with her years of research experience made Ms. McGregor an outstanding candidate for the this training program and she began with the program in August, 1995. Since joining the training program Ms. McGregor has enrolled for the full academic load of core courses and has been working 15 -20 hrs/wk on research-related activities. Specifically she has participated on the NCI project on a cross-sectional study examining major concerns of breast cancer patients post-mastectomy and factors associated with adjustment in the months following surgery. She has also participated in the development of Part 2 of this NCI project which examines the effects of a cognitive behavioral stress management intervention on patients adjustment following mastectomy. As part of her work on this project, Ms. McGregor is developing a sub-project to assess immunologic changes that occur over the intervention period in a subgroup of women who receive either surgical treatment or a combination of surgery and Tamoxifen. Once this trainee and training grant faculty prepare a protocol the Executive Committee will review it before forwarding a revised version to the University's IRB for approval. Once approved the project would commence as a pilot study largely managed by the trainee. In so doing this trainee will be able to gain specific experience in biopsychosocial applications of psychotherapeutic interventions and psychoneuroimmunology to breast cancer--her primary interest area. Plans are also underway to utilize funds from the newly opened Courtelis Center for Research and Treatment in Psychosocial Oncology to subsidize some of the costs of these types of pilot studies which will open up further training opportunities for other interested trainees. During her first month in the training program Ms. McGregor also attended weekly meetings of the Breast Cancer research team and two monthly PNI Journal Club meetings and has already established a working relationship with the Research Assistants and Post-Doctoral Fellows working in breast cancer psycho-oncology research.

Amy Eisenberg

GRE Total: 1320

G.P.A: 3.51 U. Penn.

Ms. Eisenberg was admitted to the program in August, 1995. Before coming to the program she completed her undergraduate training at the University of Pennsylvania where she worked in the laboratory of Dr. Martin Seligman conducting studies on the correlates of attributional style. After completing her degree she worked at the Memorial Sloan-Kettering Cancer Center as a full-time research assistant with Sharon Manne, Ph.D. Specifically she worked on an NCI-funded longitudinal study examining how couples

cope with breast and colon cancer and chemotherapy treatment over a 4-month period. Her responsibilities included recruiting subjects and their spouses, coordinating with medical staff to acquire medical information, maintaining rapport with participants through the 4-month period, and managing the database. Since joining the training program Ms. Eisenberg has enrolled for the full academic load of core courses and has been working 15 -20 hrs/wk on research-related activities. Specifically she has participated on the NCI Project on a cross-sectional study examining major concerns post-mastectomy and factors associated with adjustment in the months following surgery. On this team she has gained experience in patient contact and recruitment, telephone administration of questionnaire packets, coordinating with the network of surgical oncology offices involved in the study, and database management. She attended weekly meetings of the Breast Cancer research team and two monthly PNI Journal Club meetings during her first month in the program and has already established a working relationship with the Research Assistants and post-doctoral fellows working in breast cancer psycho-oncology research.

5. Publications and Presentations of Training Faculty and Trainees During YR 1

PUBLICATIONS IN REFEREED JOURNALS

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Witherspoon, R., McGregor*, B., Danyu, L., Mori, M. & Storb, R. Recombinant human Interleukin-4 proliferation of B lymphocytes from chronic GVHD patients. (under review)

Ironson, G., Wynings*, C., Schneiderman, N., Baum, A., Rodriquez, M., Greenwood, D., Benight, C., Antoni, M., LaPerriere, A., Huang, H., Klimas, N., & Fletcher, M.A. Post-traumatic stress symptoms, intrusive thoughts, loss and immune function after Hurricane Andrew (under review)

Burnett, K, Ironson, G., Benight, C., Wynings, C*, Kumar, M., Greenwood, D., Carver, C., Baum, A., Schneiderman, N. Chronic stress and mental health during rebuilding following Hurricane Andrew: The secondary disaster. (under review)

Mulder, N., Antoni, M.H., Duivenvoorden, H., Kauffman, R., & Goodkin, K. (in press) Active confrontational coping predicts decreased clinical progression over a one-year period in HIV-infected homosexual men. *Journal of Psychosomatic Research.* .

Lutgendorf, S., Antoni, MH., Ironson, G., Fletcher, MA., Penedo, F., VanRiel, F., Baum, A., Schneiderman, N., & Klimas, N.(1995) Physical symptoms of chronic fatigue syndrome are exacerbated by the stress of Hurricane Andrew.

Psychosomatic Medicine, 57, 310-323.

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Hinkle, Y., & Antoni, M.H. (in press) Pregnancy and HIV-1 : Bidirectional effects. In E. Johnson et al (Eds.), *AIDS in African-Americans and Hispanics: The role of behavioral and psychosocial factors*. Praeger Press.

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PAPER PRESENTATIONS

1996

Spencer, S., Wynings*, C., Lehman*, J., Antoni, M., Love, N., & Carver, C. *What are the salient concerns of breast cancer patients?* (March, 1996) To be presented at the Annual Meeting of the International Society of Behavioral Medicine/Society of Behavioral Medicine, Wash. D.C.

Wynings*, C., Ironson, G., Antoni, M., Burnett, K., Fletcher, M.A., Baum, A., & Schneiderman, N. (March, 1996) *Loss, social support and depression in recovery from Hurricane Andrew*. To be presented at the Annual Meeting of the International Society of Behavioral Medicine/Society of Behavioral Medicine, Wash. D.C.

1995

Ironson, G., Wynings*, C., Burnett, K., Greenwood, D., Rodriguez, M., Carver, C., Baum, A., Fletcher, M.A., & Schneiderman, N. (April, 1995) *Predictors of recovery from Hurricane Andrew (2-year follow-up)* Paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.

Burnett, K., Ironson, G., Wynings*, C., Benight, C., Carver, C., Baum, A., & Schneiderman, N. (April, 1995) *Chronic disruption and family strain following Hurricane Andrew: The secondary disaster*. Paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.

Cruess, D., Ironson, G., Kumar, M., Wynings*, C., Benight, C., Greenwood, D., Steffen, P., Baum, A., Fletcher, M.A., & Schneiderman, N. (April, 1995). *Intrusive and avoidant thoughts and cortisol at two time points after Hurricane Andrew*. Paper presented at the Annual Meeting of the American Psychosomatic Medicine Society, New Orleans, LA.

Steffen, P., Ironson, G., Burnett, K., Wynings*, C., Greenwood, D., Rodriguez, M., Cruess, D., Carver, C., Baum, A., Fletcher, M.A., & Schneiderman, N. (April, 1995) *Hostility correlates*

with distress, coping, immune and health measures following Hurricane Andrew. Paper presented at the Annual Meeting of the American Psychosomatic Medicine Society, New Orleans, LA.

Carver, C. S., Pozo-Kaderman, C., Harris, S. D., Noriega, V., & Price, A. A. *Personal investment in body image: Influences on adjustment to early stage breast cancer.* Presented at the annual meeting of the Society of Behavioral Medicine. San Diego, 1995.

Carver, C. S. *Psychosocial predictors of adjustment to early stage breast cancer.* Invited presentation, American Society of Psychiatric Oncology/AIDS. Miami Beach, 1995.

Carver, C. S. *Some psychosocial predictors of adjustment to early stage breast cancer.* Invited presentation, Psycho-Oncology '95: Issues in Treatment and Clinical Research, Miami VA Medical Center, 1995.

Price, A. A., Carver, C. S., & Pozo-Kaderman, C., *Thought suppression predicts negative thought intrusion during breast cancer treatment.* American Psychological Association. New York, 1995.

Harris, S. D., Carver, C. S., Pozo-Kaderman, C., & Durel, L. *Expectancy concerning cancer recurrence predicts postsurgical distress in women.* American Psychological Association. New York, 1995.

Carver, C. S. *Dispositional optimism as a source of resilience.* American Psychological Association. New York, 1995.

Lollis, C., Antoni, M.H., Chitwood, D., Johnson, E.H. (March, 1995) *Differences in the health beliefs of injection drug users and university women who vary in their practice of health preventative behaviors.* Paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.

Quillian, R., Antoni, M.H., Brickman, A., Rey, G., Ironson, G., McCabe, P., Imia-Fins, A., Klimas, N. (March, 1995) *Neuropsychological deficits covary with lymphocyte activation markers in chronic fatigue syndrome.* Paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.

Quillian, R., Brickman, A., Antoni, M.H., Rey, G., Ironson, G., McCabe, P., Imia-Fins, A., Klimas, N., & Mirsky, A. (March, 1995) *Neuropsychological functioning in chronic fatigue syndrome patients.* Citation paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.

Wagner, S., Kilbourn, K., Antoni, M.H., Costello, N., Ironson, G., Baum, A.,

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- Penedo, F., Costello, N., Ironson, G., Antoni, M., DiLillo, V., Starr, K., Fletcher, M.A., Baum, A., & Schneiderman, N. (March, 1995) *Emotional expression, psychosocial distress, and immune functioning following Hurricane Andrew*. Paper presented at the annual meeting of the Society of Behavioral Medicine, San Diego, CA.
- Antoni, M.H. (March, 1995) *Emotional expression and immune function in people dealing with major stressors and traumas*. Symposium presented at the annual meeting of the American Psychosomatic Society. New Orleans, LA.
- Costello, N., Antoni, M.H., Ironson, G., Klimas, N., Fletcher, M.A., Klimas, N., Kumar, M., & Schneiderman, N. (March, 1995) *Emotional expression, HPA axis and immune functioning in victims of Hurricane Andrew*. Paper presented at the annual meeting of the American Psychosomatic Society. New Orleans, LA.
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Premorbid pessimism as related to style of cognitive processing, sexual behavior, and HHV-6 antibody titers among HIV-1 seropositive symptomatic gay men. Presented at the annual meeting of the American Psychosomatic Society. New Orleans, LA.

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Starr, K., Antoni, M.H., Costello, N., Lutgendorf, S., Penedo, F., Zuckerman, M., Lehman*, J., Ironson, G., & Schneiderman, N. (March, 1995) *The effects of group cognitive behavioral stress management (CBSM) intervention on intrusive thoughts and high-risk sexual behavior in HIV+ symptomatic gay men.* Presented at the annual meeting of the American Psychosomatic Society. New Orleans, LA.

van der Pompe, G., Antoni, M.H., Heijnen, C., & deVries, M. (March, 1995) *The influence of laboratory stress on immunologic reactivity in breast cancer patients.* Presented at the annual meeting of the American Psychosomatic Society. New Orleans, LA.

1994

Ironson, G., Greenwood, D., Wynings*, C., Baum, A., Rodriguez, M., Fletcher, M.A., Baum, A., & Schneiderman, N. (Nov., 1994) *Predictors of recovery from Hurricane Andrew.* Paper presented at the annual scientific meeting of the Psychoneuroimmunology Research Society. Key Biscayne, FL.

Antoni, M.H. (August, 1994) *Effects of group stress management on psychological adjustment in asymptomatic and symptomatic HIV-infected gay men.* Paper presented at the annual meeting of the American Psychological Association. Los Angeles, CA.

Antoni, M.H. (August, 1994) *A psychoneuroimmunologic model for chronic fatigue syndrome.* Paper presented at the annual meeting of the American Psychological Association. Los Angeles, CA.

Ironson, G., Wynings*, C., Burnett, K., Greenwood, D., Benight, C., Rodriguez, M., Carver, C., Baum, A., Fletcher, M.A., & Schneiderman, N. (August, 1994) *Coping and social support in recovery in a community sample.* Paper presented as part of a symposium on Models of Social Support and Coping in Hurricane Andrew.

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Los Angeles, CA.

Burnett, K., Ironson, G., Wynings*, C., Greenwood, D., Benight, C., Carver, C.,
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disruption during recovery from Hurricane Andrew*. Paper presented at the annual
meeting of the American Psychological Association. Los Angeles, CA.

Ironson, G., Wynings*, C., Burnett, K., Greenwood, D., Carver, C., Benight, C.,
Baum, A., Fletcher, M.A., & Schneiderman, N. (July, 1994) Predictors of
recovery from Hurricane Andrew (10 month follow up). Paper presented at the
Third International Congress of Behavioral Medicine, Amsterdam, NTH.

Carver, C. S. (August, 1994) *Effects of optimism and pessimism in responses to major surgery*.
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Price, A. A., Carver, C. S., & Pozo-Kaderman, C. (April, 1994) *Thought suppression at time of
surgery as a predictor of subsequent thought intrusion and distress among women
undergoing breast cancer treatment*. Paper presented at the annual meeting of the Society of
Behavioral Medicine. Boston, Massachusetts.

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Carver, C. S., Pozo-Kaderman, C., Harris, S. D., & Price, A. A. (1994) *Optimism, coping, and
adjustment to early stage breast cancer*. APA Conference on Psychosocial and Behavioral
Factors in Women's Health, Washington, DC.

Carver, C. S. (1994) *The power of positive thinking: How optimists and pessimists face adversity*.
(Keynote address) Midwest Conference on Health Psychology. Terre Haute, Indiana.

Carver, C. S. (1994) *Optimism, pessimism, and coping with surgery*. Colloquium presented at
the University of Texas. Austin, Texas.

Wynings*, C., Ironson, G., Greenwood, D., Burnett, K., Fletcher, M.A., Baum, A., &
Schneiderman, N. (April, 1994) *The role of social support and marital status on
the impact of Hurricane Andrew*. Paper presented at the annual meeting of the
Society of Behavioral Medicine, Boston, MA.

Benight, C., Ironson, G., Wynings*, C., Greenwood, D., Rodriguez, M., Burnett, K.,
Carver, C., Baum, A., & Schneiderman, N. (April, 1994) *The effect of perceived
competence on psychological adjustment and health following Hurricane Andrew*.

Paper presented at the annual meeting of the Society of Behavioral Medicine, Boston, MA.

Burnett, K., Ironson, G., Wynings*, C., Greenwood, D., Benight, C., Carver, C., Baum, A., & Schneiderman, N. (April, 1994) *Disruption as a predictor of mental health status during rebuilding after Hurricane Andrew*. Paper presented at the annual meeting of the Society of Behavioral Medicine, Boston, MA.

Lehman*, J., Kilbourn, K., Antoni, M.H., Costello, N., Ironson, G. & Klimas, N. (August, 1994) *Coping with Hurricane Andrew and chronic fatigue--Illness burden effects*. Paper presented at the annual meeting of the American Psychological Association. Los Angeles, CA.

Antoni, M.H. (July, 1994) *Effects of cognitive behavioral stress management intervention in asymptomatic and symptomatic HIV+ gay men*. Paper presented at the III International Congress on Behavioral Medicine. Amsterdam, Netherlands.

van der Pompe, G., Antni, M.H., & Heijnen, C. (July, 1994) *Immune reactivity in metastatic and non-metatstatic breast cancer patients*. Paper presented at the III International Congress on Behavioral Medicine. Amsterdam, Netherlands.

Lutgendorf, S., Antoni, M. H., Ironson, G., Starr, K., Klimas, N., Kumar, M., Cleven, K., Penedo, F., Schneiderman, N., & Fletcher, M. A. (April, 1994). *Impact of avoidant thoughts on immune functioning in symptomatic HIV positive men*. Paper presented at the annual scientific meeting of the American Psychosomatic Society, Boston, MA.

Kilbourn, K., Costello, N., Antoni, M. H., Ironson, G, Fletcher, M. A., Baum, A., Schneiderman, N. (April, 1994). *How are coping strategies that people use to handle major challenges related to their immune and neuroendocrine responses?* Paper presented at the annual scientific meeting of the American Psychosomatic Society, Boston, MA.

Benight, C., Antoni, M. H., Kilbourn, K., Ironson, G., Costello, N., Fletcher, M. A., Scheiderman, N. (April, 1994). *The effect of perceived competence and responsiveness of the environment on psychological and physical health in HIV+ men following Hurricane Andrew*. Paper presented at the annual scientific meeting of the American Psychosomatic Society, Boston, MA.

van der Pompe, G., Antoni, M. H., Garssen, B., Heijnen, C. (April, 1994). *Does psychosocial intervention modulate immunologic reactivity in breast cancer patients?* Paper presented at the annual scientific meeting of the American

Psychosomatic Society, Boston, MA.

Mertz, T., Antoni, M. H., Ironson, G., & Brickman, A. (April, 1994). *Chronic fatigue syndrome and depression: Development of empirically-derived factors for differential diagnosis*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Imia-Fins, A., Antoni, M. H., Brickman, A., Klimas, N., Lutgendorf, S., Ironson, G., Quillian, R., Fletcher, M. A. (April, 1994). *Stressful life events, cognitive appraisals, coping strategies and illness burden in chronic fatigue syndrome*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Costello, N., Kilbourn, K., Antoni, M. H., Ironson, G., Fletcher, M. A., Schneiderman, N. (April, 1994). *Social provisions, optimism, and distress levels in HIV+ gay men dealing with the aftermath of Hurricane Andrew*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Kilbourn, K., Antoni, M. H., Costello, N., Ironson, G., Schneiderman, N. (April, 1994). *Are coping strategies people use to handle major stressors consistent? Hurricanes and HIV*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Hinkle, Y., Antoni, M. H., Schneiderman, N., Ironson, G., Schneiderman, N., & Efantis, J. (April, 1994). *Psychosocial correlates of stress and anxiety among African American women who are HIV-positive and HIV-negative*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Ackerman, M., & Antoni, M. H. (April, 1994). *Unhappy wives do not corroborate details of their husband's erectile difficulties: Disparities in attributions of symptoms?* Citation paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Kilbourn, K., Costello, N., Antoni, M. H., Ironson, G., Fletcher, M. A., & Schneiderman, N. (April, 1994). *The physiological and psychological impact of Hurricane Andrew on an HIV positive population as compared to other stressed populations*. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

van der Pompe, G., Antoni, M. H., Garssen, B., & Heijnen, C. (April, 1994).

Immunologic reactivity in breast cancer patients. Paper presented at the annual scientific meeting of the Society of Behavioral Medicine, Boston, MA.

Summary of Ongoing Funded Breast Cancer Psycho-Oncology Projects
(see also Appendix 2 and 3)

<u>P.I.</u>	<u>Source</u>	<u>Grant #</u>	<u>Dates</u>	<u>Title</u>
C. Carver	NCI	1R01CA64710-01	10/1/94 - 8/30/96	Lifestyle and Breast cancer in Cultural and Sexual Minorities
C. Carver	NCI	1R01CA64710-01	7/1/94- 6/30/98	Adjustemnt to Breast Cancer among Younger Women
S. Weiss	NCI	not available	9/30/94- 6/30/95	PDQ/PIF Evaluation in Multiethnic Populations
M. Antoni	ACS	PBR-82	7/1/93- 6/30/95	Coping with breast cancer among low SES Blacks and Hispanics
G. Ironson	NCI-Dev	—	1/1/95 - 12/31/95	Stress Management Intervention for Women with Breast Cancer

(7) CONCLUSIONS

YR 1 of the training program was quite successful in accomplishing the general mission of providing multidisciplinary research training in biopsychosocial aspects of breast cancer in the context of predoctoral training in Clinical Health Psychology. Four trainees were enrolled in the training program in YR 1. Training was closely coordinated with 5 ongoing ACS-funded and NCI-funded biopsychosocial breast cancer research projects. All trainees were exposed through coursework to experimental design and statistics as well as psychosocial, biobehavioral and pathophysiologic perspectives on breast carcinoma and other chronic diseases. The latter focus was extended through the program's weekly Psycho-Oncology Clinical Workshop, weekly Breast Cancer Team Research Meeting, monthly Psycho-Oncology Research Seminar and the monthly Psychoneuroimmunology Journal Club meeting. There was a significant amount of development and growth in the training program across the following areas: Symposia/Didactic Experiences; Active Biopsychosocial Breast Cancer Research Protocols; Cancer Center Programs, Facilities and Resources; Trainee Progress; and Publications and Presentations of Training Program Faculty and Trainees. Advances in the Sylvester Comprehensive Cancer Center (SCCC) that occurred during YR 1 which are highly relevant for the training program included the creation of the Courtelis Center for Research and Treatment in

Psychosocial Oncology, expansion of the SCCC Breast Cancer Research Program, and formation of the SCCC Biopsychosocial Oncology Program. All four trainees appear to be making excellent progress in coursework, research training and clinical training.

At least two additional biopsychosocial projects have been designed and are under review at the present time. These projects deal with evaluating the concerns of older breast cancer patients and the efficacy of psychosocial interventions with this group. Our ultimate goal is to have a comprehensive program of training and research that addresses the major concerns of breast cancer patients from different ethnic groups, SES groups and age groups at multiple stages of disease through the use of prospective natural history studies whose results lead directly to the development of theoretically-driven and empirically-validated psychosocial interventions specifically tailored to the chief concerns and to modulating the mediators of psychosocial adjustment and physical health for each group. Our goal is to couch all of these activities in the context of a joint collaboration between the Department of Psychology, the SCCC and the Departments of Medicine and Psychiatry. This collaborative arrangement not only facilitates the conduct of this research but also provides a state of the art training environment.

APPENDIX 1

Organizational Structure of the Sylvester Comprehensive Cancer Center

F. ESSENTIAL CHARACTERISTICS OF THE CANCER CENTER

I. Institutional Commitment

Since the inception of the Cancer Center in June 1974, the University of Miami School of Medicine has maintained a high level of commitment to the success of the Sylvester Comprehensive Cancer Center (SCCC) evidenced in the development of the Fox and Papanicolaou Cancer Research Buildings, the Sylvester Clinical Facility, and UMHC Cancer Hospital and the provision of financial support for operations. As was planned, during the previous funding period (9/91-10/94), this commitment substantially increased. This is apparent in the successful efforts to enhance SCCC physical facilities, recruit 21 new faculty with strong interests in cancer research, increase fund raising by \$2,200,000, and promote the Center within the entire University community, the general South Florida community, and especially the Hispanic and African-American community of South Florida.

A. Organization of the Cancer Center

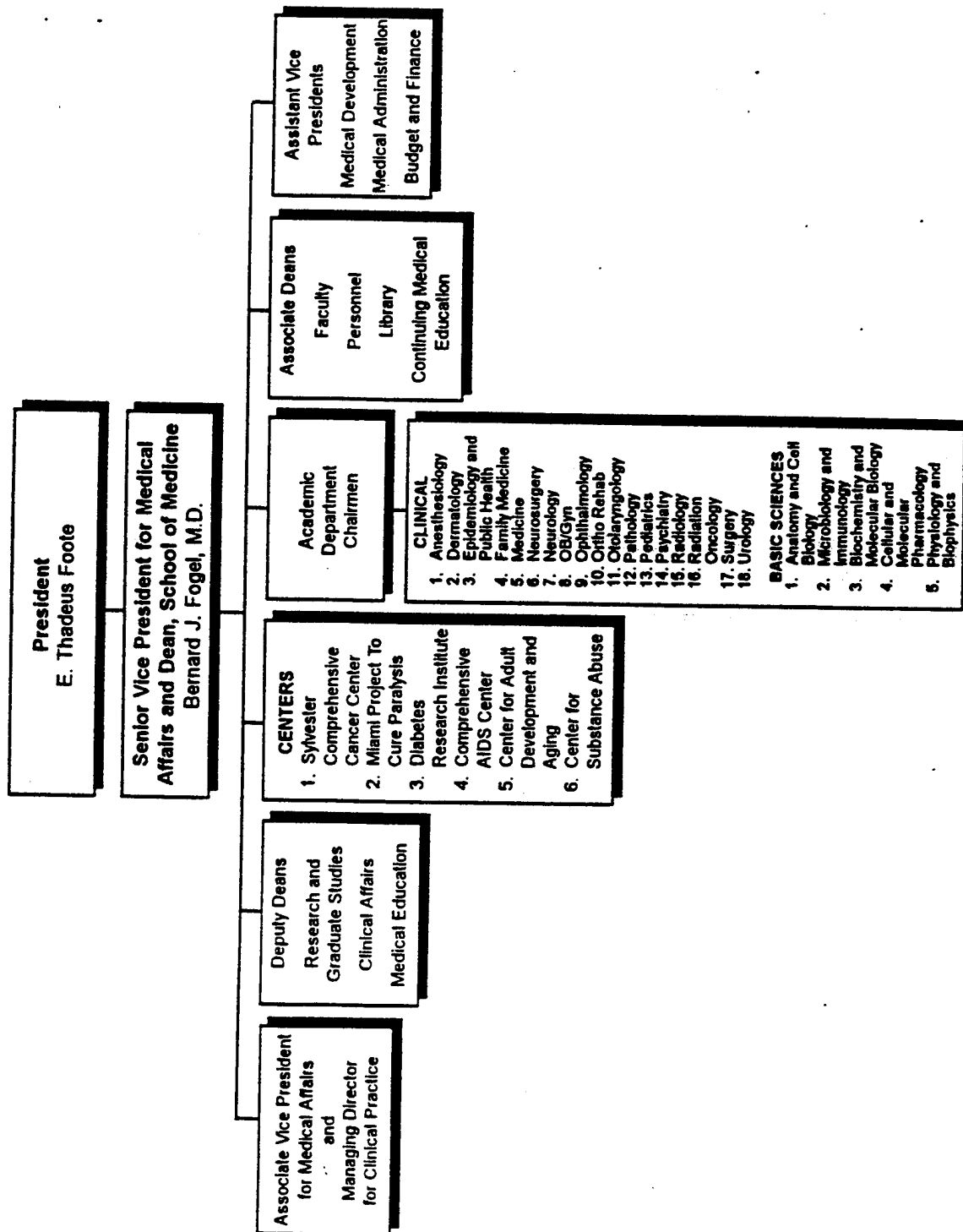
The SCCC functions as a matrix cancer center in the School of Medicine. SCCC was the first multidisciplinary center established at the School of Medicine and this model has been used to develop five other centers, including AIDS, Diabetes, Aging, Spinal Cord Injury (Miami Project), and Drug Abuse. Directors of these Centers meet quarterly as a group with the Senior Vice President for Medical Affairs (Bernard J. Fogel, M.D.) to discuss operational issues unique to Centers.

Dr. Fogel is the Senior Vice-President for Medical Affairs and Dean of the University of Miami School of Medicine. The Sylvester Cancer Center Director is appointed by Dr. Fogel and reports directly to him. In addition to serving as a member of the Council of Center Directors, the SCCC Director is also a member of the Executive Advisory Committee of the School of Medicine. The Director meets with the Senior Vice-President for Medical Affairs at least twice monthly to discuss and consult on programmatic issues, and annually as part of a formal process to review the progress of the Center, its budget, and to negotiate institutional support, infrastructure, program development, and space.

The Cancer Center Director has the authority and responsibility for managing all budgetary allocations from the School of Medicine and the University of Miami, Cancer Center grant funds, and all funds donated to the Cancer Center including endowments. The Center has its own fund raising staff (located in part in Center facilities and reporting to the Center Director) who work in concert with the School of Medicine Development office. The Center Director has responsibility for the management and allocation of Cancer Center space and equipment.

University of Miami School of Medicine

Table of Organization



Although the Center Director appoints members in the Cancer Center, faculty appointments follow a joint appointment process in conjunction with Department Chairmen similar to that used by most matrix centers. The Center provides support (salary and space) for faculty positions as needed, and the recruitment, selection, and appointment process is shared with the academic departments.

B. History of Institutional Commitment to the Cancer Center

The history of institutional commitment to the Cancer Center has been demonstrated by the recruitment of faculty to strengthen Cancer Center programs, the development of new research and clinical facilities and the renovation of existing ones, and financial support for both developmental and for recurring expenses.

To help the Cancer Center achieve its scientific goals, the medical school invested in major faculty recruitments that strengthened the Center's Basic Science and Clinical Research Programs. The faculty recruitments in the previous funding period are outlined below.

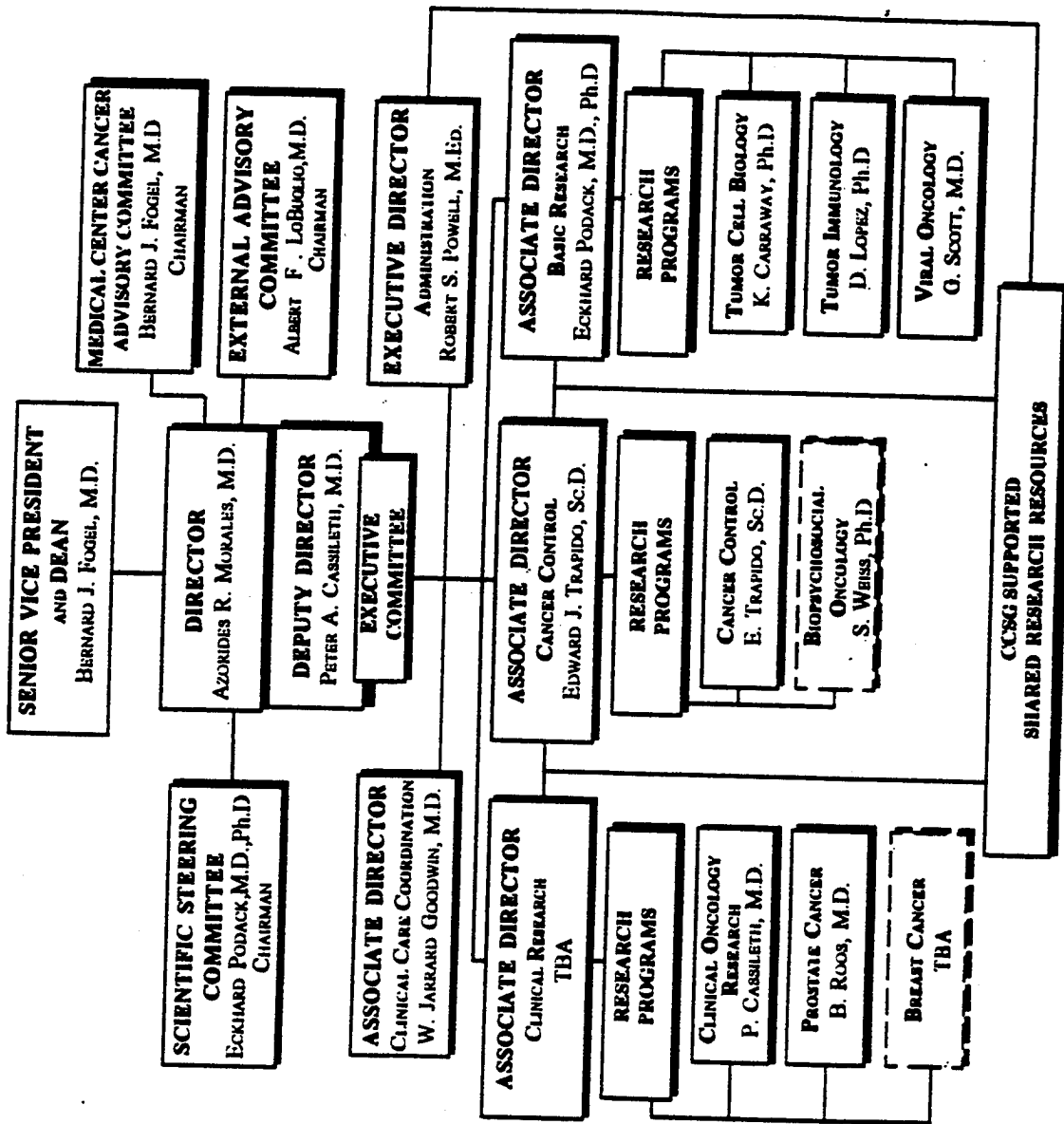
INVESTIGATOR	DEGREE	UM RANK	ACADEMIC APPOINTMENT	RECRUITED FROM	START DATE UM
Assoian, Richard	Ph.D	Associate Professor	Cell Biology & Anatomy	Columbia University	1992
Bai, Ge	M.D., Ph.D.	Assistant Professor	Urology	University of Miami	1993
Balkan, Wayne	Ph.D.	Assistant Professor	Medicine	Duke University	1992
Burnstein, Kerry	Ph.D.	Assistant Professor	Molecular and Cellular Pharmacology	University of North Carolina, Chapel Hill	1992
Cassileth, Peter	M.D.	Professor	Medicine	University of Pennsylvania	1992
Civantos, Francisco	M.D.	Assistant Professor	Otolaryngology	Vanderbilt University	1992
Fernandez, Hugo	M.D.	Assistant Professor	Medicine	University of Miami	1994
Francheschi, Dido	M.D.	Assistant Professor	Surgery	Memorial Sloan-Kettering	1994
Goodman, Mark	M.D.	Assistant Professor	Medicine	University of Miami	1994

INVESTIGATOR	DEGREE	UM RANK	ACADEMIC APPOINTMENT	RECRUITED FROM	START DATE UM
Grotendorst, Gary	Ph.D.	Associate Professor	Cell Biology & Anatomy	University of South Florida	1991
Krongrad, Arnon	M.D.	Assistant Professor	Urology	Southwestern Medical Center, Dallas	1992
Mehta, Parmender	Ph.D.	Assistant Professor	Medicine	University of Miami	1994
Perez-Stable, Carlos	Ph.D.	Assistant Professor	Medicine	Columbia University	1992
Salas, Pedro	M.D., Ph.D.	Assistant Professor	Cell Biology & Anatomy	Buenos Aires, Argentina	1992
Schwartz, Gary	Ph.D., Ph.D.	Associate Professor	Epidemiology & Public Health	University of Pittsburgh	1994
Smith, Selina	Ph.D.	Assistant Professor	Epidemiology & Public Health	ACS National	1993
Soloway, Mark	M.D.	Professor & Chair	Urology	University of Tennessee, Memphis	1991
Spector, Neil	M.D.	Assistant Professor	Medicine	Dana Farber Cancer Institute	1993
Vega-Salas, Dora	M.D., Ph.D.	Assistant Professor	Cell Biology & Anatomy	Buenos Aires, Argentina	1992
Weiss, Sharlene	R.N., Ph.D.	Associate Professor	Medicine	NIH	1994
Wood, Charles	Ph.D.	Associate Professor	Neurology	University of Kansas	1992

The Chairman of the Department of Cell Biology and Anatomy, Kermit Carraway Ph.D., who was originally recruited with a major commitment from the Cancer Center, recruited four new faculty members, Richard Assoian, Ph.D., Gary Grotendorst, Ph.D., Pedro Salas, Ph.D., and Dora Vega-Salas, Ph.D., each with major research interests in cancer cell biology. Additionally, he encouraged one of the program's eminent investigators, Lilly Bourguignon, Ph.D. to refocus her research efforts in breast cancer research.

Jarrard Goodwin, M.D., Chairman, Department of Otolaryngology and a Head and Neck Cancer surgeon with an NIH supported chemoprevention grant, was appointed CEO for the Sylvester Clinical Facility in June 1993. The appointment of a Center

SYLVESTER COMPREHENSIVE CANCER CENTER



III. Facilities - See Map of the Medical Center Campus on the Next Page)

A. Research Facilities

1. Fox Cancer Research Complex - This complex is under the control of the Center Director and consists of two five story buildings (the Papanicolaou and Louis Fox Research buildings) connected at two levels, with a total of 100,000 ft² of laboratory, non-laboratory, and administrative space. The distribution of the space is as follows:

Papanicolaou Building (built in 1989)

<u>Floor</u>	<u>Programs</u>
First -	Clinical Oncology Research, Tumor Immunology, & Prostate Cancer
Second -	Viral Oncology, Tumor Immunology
Third -	Tumor Cell Biology
Fourth -	Breast Cancer
Fifth -	Clinical Oncology Research

Louis Fox Building (built in 1984, laboratories renovated in 1988)

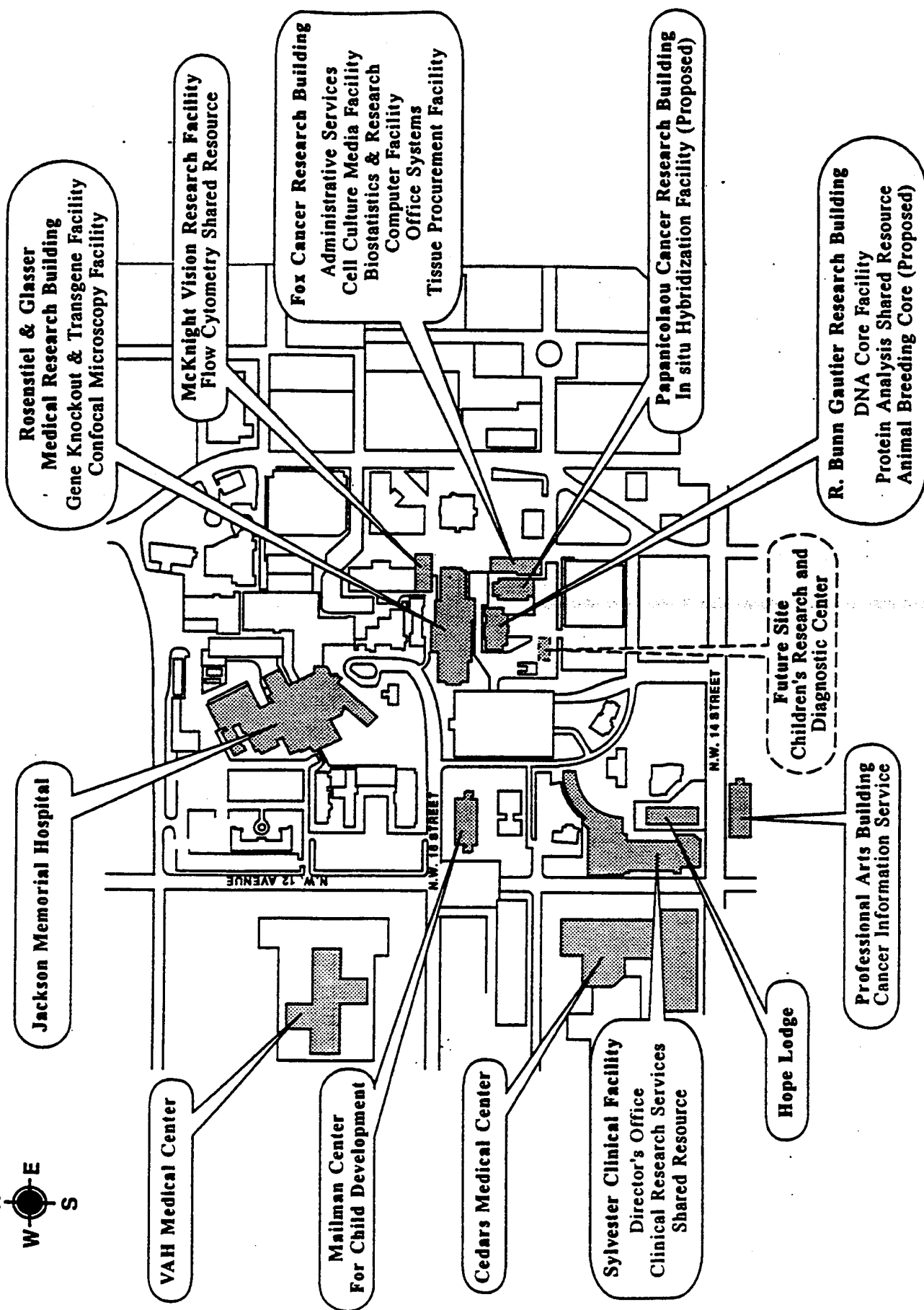
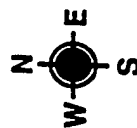
<u>Floor</u>	<u>Programs</u>
First -	Clinical Oncology Research, Viral Oncology, Cell Culture Media shared resource, Tissue Procurement
Second -	Viral Oncology Program
Third -	Cancer Control Research, Biostatistics and Research Computing shared resource, Cancer Center Administration.
Fourth -	Prostate Cancer, Clinical Oncology Research, Cell Culture Media Shared resource
Fifth -	Viral Oncology, Clinical Oncology Research

The Cancer Center has full control of the space and has established a review mechanism for space utilization. This permits the generation of space for new programs by reallocating and compressing space currently in use depending on SCCC priorities and investigator productivity. In addition to the Papanicolaou and Fox Buildings, Cancer Center member investigators and some of the Center's shared resources are housed in the Medical School. A brief description of these facilities follows.

2. Rosenstiel and Glaser Medical Science Buildings - These two adjoining buildings totaling 850,000 ft² house the School of Medicine's administrative offices, the pre-clinical departments, animal housing, and other physical plant and facilities services.

UNIVERSITY OF MIAMI/JACKSON MEMORIAL MEDICAL CENTER

SCCC Shared Resource Facilities



Several laboratories used by Cancer Center members are also located in these buildings. For example, the Center's Confocal Microscopy shared resource is located in 300 ft² on the 4th floor, and the Gene Knockout and Transgene Facility shared resource is located in 660 ft² on the 6th floor of the Rosenstiel Building. The research laboratories of Immunology and Microbiology are on the 3rd floor and the 7th floor houses Hematology/Oncology laboratories.

3. R. Bunn Gautier Molecular Biology Building - This seven story 77,000 ft² research building housing the Department of Biochemistry and Molecular Biology is connected by elevated enclosed walkways to both the PAP Cancer Research Building and the Rosenstiel Medical Science Building. The upper two floors of this building have P3 containment facilities and animal housing for virus free rodents and transgenic mice. It is the proposed site for the new Animal Breeding Core Facility. The DNA Core Laboratory shared resource of the Center is located in 415 ft² on the 3rd floor of this building.

4. McKnight Vision Research Building - This is an eight story 75,000 ft² laboratory building for research on eye diseases. Several Center Member investigator laboratories from the Tumor Immunology Program are located in this building. The Center's Flow Cytometry shared resource is located in 313 ft² on the 7th floor.

5. Mailman Center - This is a nine story 100,000 ft² office, clinical treatment, and research laboratory building for Pediatrics. Cancer Center members conducting research in the genetics of familial cancer are housed here.

B. Clinical Facilities

1. Sylvester Clinical Facility - The building is a four story 117,000 ft² multi-disciplinary outpatient cancer treatment facility for adult cancer. The facilities include:

- Ambulatory care facility for Surgical and Gynecologic Oncology, Hematology/Oncology, Otolaryngology, and disease-site specific cancer groups.
- Radiation Oncology Department including three linear accelerators, two treatment planning simulators, and facilities for hyperthermia and high dose brachytherapy.
- Ambulatory Surgical Facility with four operating rooms
- Day hospital and Pharmacy for experimental drugs
- Diagnostic Radiology and Clinical Pathology

- Social Services and Community Education
- Faculty Offices for the Department of Radiation Oncology, and the Divisions of Hematology/Oncology, and of Surgical and Gynecologic Oncology
- The Cancer Center Administrative offices and the SCCC Clinical Research Services Shared Resource are located on the same floor (third) as the faculty offices for the clinical cancer disciplines.

2. University of Miami Hospital and Clinics (UMHC) - The hospital is a five story hospital owned by the University. It is physically connected to the Sylvester Clinical Facility and, together with Sylvester, operates as a unit within the medical school. It contains outpatient facilities for several of the clinical departments, medicine, surgery, urology, orthopedics, and laboratories and other support services for patients. Although licensed for 80 beds, currently 40 beds are in service, primarily occupied by cancer patients. Plans are underway to upgrade and reconfigure the existing beds. The hospital has applied for American College of Surgeons recognition as a cancer hospital, and maintains its own tumor registry.

3. Jackson Memorial Hospital - Jackson Memorial Hospital is the public hospital for Dade County with 1,250 beds serving a population of almost two million citizens including increasing numbers of recent refugees. In the past fiscal year, Jackson Memorial Hospital had 49,510 admissions, 256,639 outpatient visits and 125,274 emergency room visits. Hematology/Oncology operates a 30 bed-inpatient unit on West Wing 12th floor at Jackson Hospital. Immediately adjacent to the WW12 unit, six beds were renovated August 1992 to establish a sealed infection-controlled environment used for a Bone Marrow Transplantation unit. Gynecologic Oncology has 30 beds in Maternity and Child Care East Tower. Including Surgical Oncology on West Wing (40 beds), a total of 106 beds are dedicated to cancer patient care and research at Jackson Memorial Hospital. Additionally, there are another 80-90 cancer inpatients hospitalized at any one time in scattered beds, bringing the daily census of cancer patients to approximately 200. Adult cancer outpatient clinics are held on the third floor of Ambulatory Care Center West and the first floor Ambulatory Care Center East. Pediatric cancer outpatient clinics are held on the fifth floor of the Ambulatory Care Center West.

4. Professional Arts Building - This is a seven story, 81,500 ft² building with physician's offices and outpatient treatment facilities. The Center's Cancer Information Services is located on the 2nd floor in 3,000 ft².

5. Cedars of Lebanon Hospital - This is a 500 bed private hospital adjacent to the Medical Center, and owned and operated by Columbia Hospitals. Through an

affiliation agreement with the School of Medicine, access to 90 beds has been provided. It serves as the location for inpatient Urologic and Orthopedic Oncology services.

6. Veterans Administration Medical Center - The Veterans Administration Medical Center (VAMC) is a 750 bed hospital adjacent to the medical campus. This is a Dean's committee hospital in which most staff positions are held by full time faculty members. It had 12,000 admissions in 1993, and approximately 400,000 outpatient visits. The VAMC has a Tumor Registry and independent Radiation Therapy facility. Cancer admissions were 2,010 and cancer outpatient visits totaled 11,550 in 1993.

7. Hope Lodge - The Hope Lodge facility for cancer patients and their families is across the courtyard from the Sylvester Clinical Facility. This facility, a 30 room patient/family residence and education center, opened on October 1, 1992. The land was provided by the School of Medicine and funds for construction were raised by the American Cancer Society and the Winn Dixie super market chain. The American Cancer Society continues to provide funds for the general operation of the Lodge.

8. Primary Health Care Centers - There are seven primary health care centers affiliated with Jackson Memorial Hospital that are networked in the Center's Breast Cancer Early Detection Program throughout the Dade County community.

- Coconut Grove Family Health Center
- Family Health Center, Liberty City
- Dade County Health Department, 14th Street Center
- Liberty City Health Center
- Martin Luther King, Homestead
- Stanley Myers Community Health Center, Miami Beach
- North Dade Health Center, Carol City

9. Department of Psychology - Located at the University of Miami's Coral Gables Campus. The psychologists who participate in the Biopsychosocial Oncology program are housed here. The Behavioral Medicine Research building has approximately 12,000 ft² of research space specifically designed for biobehavioral research, including a vivarium, shared equipment facility, and faculty offices.

The Behavioral Medicine Research Center (BMRC) consists of 10,000 ft² of research space in the Jackson Medical Towers on the Medical Center complex.

10. Research Affiliates - SCCC Research Affiliates are established by a formal agreement between the Cancer Center and a Hospital or physician group that wishes to improve the care of cancer patients by furthering research in cancer treatment and control by increased education and interchange. The affiliated groups are expected to participate in research protocols sponsored by the Center either through patient referrals or the use of Cancer Center protocols and data collection at their own sites. Each affiliate has an annual targeted accrual goal, on which continuation of the agreement depends. This program is described in further detail in the Clinical Protocol Monitoring section. The current affiliates that have a formal agreement with the Cancer Center that allows them to use the SCCC Affiliate designation are:

- Boca Raton Community Hospital - Boca Raton
- University Hospital - Broward
- Radiation Therapy Regional Center - Ft. Myers
- W Memorial Hospital - Ft. Myers
- Southwest Regional Hospital - Ft. Myers
- Baptist Cancer Treatment Center - Miami
- Winter Park Cancer Care Center - Winter Park
- Sacred Heart Hospital - Pensacola

The map on the following page shows the location of these affiliates.

APPENDIX 2

Description of the Breast Cancer Research Program Sylvester Comprehensive Cancer Center

University of Miami School of Medicine

DEVELOPING PROGRAMS

PROGRAM CODE: #7

BREAST CANCER RESEARCH PROGRAM

Acting Program Leader: Peter A. Cassileth, M.D.

Project Leader, Basic Science: Eckhard Podack, M.D., Ph.D.

Project Leader, Clinical Research: Peter A. Cassileth, M.D.

Project Leader, Cancer Control: Edward Trapido, Sc.D.

Project Leader, Breast Cancer Evaluation Center: Sharlene Weiss, R.N., Ph.D.

I. PROGRAM PARTICIPANTS

Name	Department	Title
Michael Antoni, Ph.D.	Psychology & Psychiatry	Assoc. Professor
Fernando Arena, M.D., Ph.D.	Pediatrics	Asst. Professor
Richard Assoian, Ph.D.	Cell Biology & Anatomy	Assoc. Professor
Marianna Baum, Ph.D.	Epidemiology & Public Health	Asst. Professor
Lilly Bourguignon, Ph.D.	Cell Biology & Anatomy	Professor
Coralie Carraway, Ph.D.	Biochem. & Molecular Biology	Assoc. Professor
Kermit Carraway, Ph.D.	Cell Biology & Anatomy	Professor & Chair
Charles Carver, Ph.D.	Psychology & Psychiatry	Professor
Peter Cassileth, M.D.	Medicine	Professor
Gregory Conner, Ph.D.	Cell Biology & Anatomy	Asst. Professor
Lora Fleming, M.D.	Epidemiology & Public Health	Asst. Professor
Oskar Frankfurt, Ph.D.	Pathology	Assoc. Professor
Nevis Fregien, Ph.D.	Cell Biology & Anatomy	Asst. Professor
Zeenat Gunja-Smith, Ph.D.	Medicine	
Awtar Krishan, Ph.D.	Assoc. Professor	
Theodore Lampidis, Ph.D.	Radiation Oncology	Professor
Diana Lopez, Ph.D.	Cell Biology & Anatomy	Assoc. Professor
Clyde McCoy, Ph.D.	Microbiology and Immunology	Professor
Carolyn Mies, M.D.	Epidemiology & Public Health	Professor
Frederick Moffat, M.D.	Pathology	Asst. Professor
Azorides Morales, M.D.	Surgery	Assoc. Professor
Louise Morrell, M.D.	Pathology	Professor & Chair
Eckhard Podack, M.D., Ph.D.	Medicine	Asst. Professor
Stephen Richman, M.D.	Microbiology & Immunology	Professor & Chair
Pedro Salas, M.D., Ph.D.	Medicine	Professor
Gary Schwartz, M.D.	Cell Biology & Anatomy	Asst. Professor
	Epidemiology & Public Health	Asst. Professor

Selina Smith, Ph.D.	Epidemiology & Public Health	Asst. Professor
Kasi Sridhar, M.D.	Medicine	Professor
Edward Trapido, Sc.D.	Epidemiology & Public Health	Assoc. Professor
Dora Vega-Salas, M.D., Ph.D.	Cell Biology & Anatomy	Asst. Professor
Sharlene Weiss, R.N., Ph.D.	Medicine & Psychiatry	Assoc. Professor

No CCSG support is requested for this developing program.

II. PROGRAM DESCRIPTION

A. Rationale and Need for Developing the Program

Breast cancer was identified as a major disease focus for program development as a result of a series of strategic planning meetings of the Cancer Center's Executive and Scientific Steering Committees and a Cancer Center retreat. This program was initiated in response to the magnitude of the breast cancer problem, and the opportunity to improve outcomes for women affected by this disease. The program at the Cancer Center is being organized with special regard for the minority populations the Cancer Center serves and draws upon existing clinical and laboratory strengths on campus. The evolving program enhances the opportunity for translational research, which is a core function of the Cancer Center.

The high proportion of minorities in the Dade County population gives us the potential for investigation of breast cancer's impact on minority and high-risk populations. The Breast Cancer Program, in part, is directed at determining whether differences in tumor cell biology among ethnic groups and/or socioeconomic and cultural factors contribute to differences in clinical outcomes. The aim is to develop interventional strategies to alter adverse outcomes, which is especially relevant to minority populations.

Dade County has 1,937,094 persons, comprising 17% of the total population of Florida. The population of Dade County is composed predominantly of Hispanics (49%), Non-Hispanic Whites (30%), and Non Hispanic Blacks (21%). Dade's Black population is among the most rapidly growing Black populations in the United States. The largest segment of the county's Black, non-Hispanic population are U.S. born African Americans, as opposed to Blacks from the Caribbean, although the latter are an increasingly large component of Dade's population. Caribbean Blacks primarily come from Haiti, Jamaica, and the Bahamas, with smaller groups from Trinidad and the Virgin Islands. Considering all women in Dade County 40-64 years old, breast cancer rates rise with age, and are highest for White, non-Hispanic women. However, Blacks have the highest rates among those 60-64 years old, whereas Hispanics have the highest rates among those ages 45-49. In the <40 year old age group, the incidence of breast cancer among Black women has risen more rapidly than in White women, and the mortality rate for Blacks has disproportionately increased.

Black and Hispanic patients are more heavily represented in the indigent patient population, and they tend to present at diagnosis with more advanced breast cancer than do white patients.

Socioeconomic factors and stage at presentation may account for some differences in outcome between race and ethnic groups. Recent studies controlling for anatomic stage, however, have shown significant biologic differences in Blacks that may bear on survival. Specifically, a large percentage of poorly differentiated carcinomas and estrogen receptor negative tumors are seen in Black women. Racial and ethnic differences in the molecular genetics of breast cancer are an important focus for study because of their implications for understanding mammary carcinogenesis and because they bear on efforts to screen, diagnose, and treat breast cancer in our heterogeneous population.

B. How Long Has this Activity Been under Development?

In 1992, the leadership of the Cancer Center identified research programs in Breast Cancer, Prostate Cancer and Cancer Control as high priority areas for development. The Center's efforts and resources were first focused on the Prostate Cancer research program, which reached "established" status this year. The Breast Cancer Program began in 1993, with support from the Sylvester Cancer Facility and Cancer Center resources.

The initial approach was to induce capable investigators on campus to direct their energies toward breast cancer research and to develop the resources and space necessary for the recruitment of additional breast cancer clinicians and scientists to the campus. The incentives, including a Cancer Center-sponsored competition for seed money development funds, have created a nexus of clinical and laboratory-based researchers focused on breast cancer research. These early efforts have been successful, resulting in newly obtained competitive funding of NCI and DOD breast cancer research grants totalling approximately \$700,000 in annual direct costs, of which \$330,000 is attributable to the Breast Cancer Program as shown in Summary 2. Moreover, Dr. Peter Cassileth, Deputy Director of the Cancer Center, undertook to organize the program and submitted a breast cancer planning grant application to the NCI, which was awarded funding of \$260,000 in annual direct costs. This award provides seed money for pilot projects, retreats and symposia, and the recruitment of additional scientists that will help the Cancer Center establish a competitively funded collaborative Breast Cancer program.

C. How Does It Fit In With Overall Plan For The Cancer Center?

Among the criteria used by the Center to determine foci for new programmatic initiatives are the following: cancers of national importance because of the number of patients affected and the potential to reduce adverse outcomes; unique opportunities to obtain information about cancer cell biology through molecular biology, immunology and molecular genetics, especially those that provide insights potentially broadly applicable to cancers in

general; circumstances in which research quality will be enhanced by increasing the bidirectional flow between clinic and bench research; and the potential applicability and utility to the minority population in our area.

Consideration of new programs also involves assessment of available strengths on campus that can be brought to bear on the problem, the extent of additional required resources, and the likelihood of success. The Breast Cancer Program met all the above criteria, and the Cancer Center determined to commit its resources toward its development.

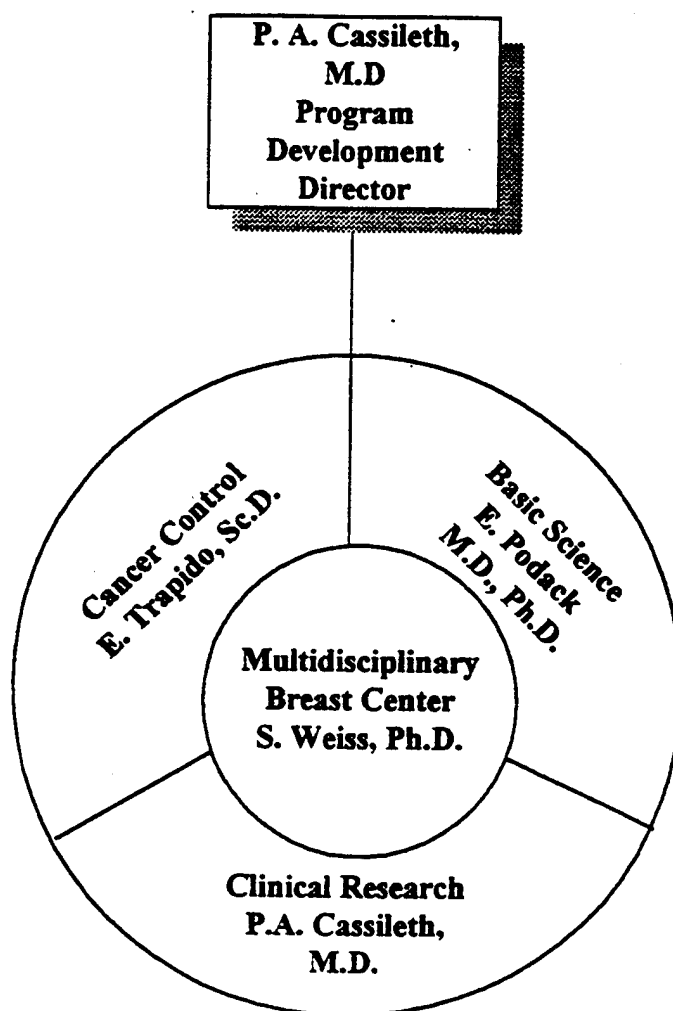
D. Plans for Building the Program

The overall aim of the breast cancer research program is to expand multidisciplinary and interprogrammatic studies of breast cancer by providing a coordinated framework for a variety of breast cancer-related research activities. This will be accomplished by:

- Convening regular research meetings with principal investigators of relevant research projects, potential new investigators, and extramural scientists to share information, stimulate cross-project collaboration, and facilitate communication between laboratory and clinical investigators.
- Establishing a comprehensive breast cancer database that links conventional clinical and laboratory parameters of disease with epidemiologic and biomarker studies for clinical research and correlation with laboratory studies of tumor cell biology.
- Recruiting new clinical and basic science investigators to the campus.
- Conducting pilot epidemiologic studies to compare different ethnic groups and to permit cross-study comparisons.
- Developing innovative clinical research studies in early and advanced breast cancer using bone marrow transplantation, gene transfer therapy, and immunologic modulation.
- Promoting research that allows rapid translation of basic science and epidemiologic observations into preclinical and clinical applications.
- Expanding breast cancer control research to promulgate improved early detection, follow-up, and treatment programs for minority and underserved populations.

The Breast Cancer Research Program has been organized to include three project areas led by Senior Cancer Center members, namely Basic Science (Podack), Clinical Research (Cassileth), and Cancer Control (Trapido), and a central core facility, the multidisciplinary Breast Cancer Evaluation Center. The structure of the program and the relationships among the components is diagrammed below.

Sylvester Comprehensive Cancer Center Breast Cancer Research Program



E. Projected Time

The projected time for the development of the program is four years (94-98), during which the new clinical and basic scientists will be recruited, integrated with other Center members and research activities, and compete for peer-reviewed funding.

Projected Time Line

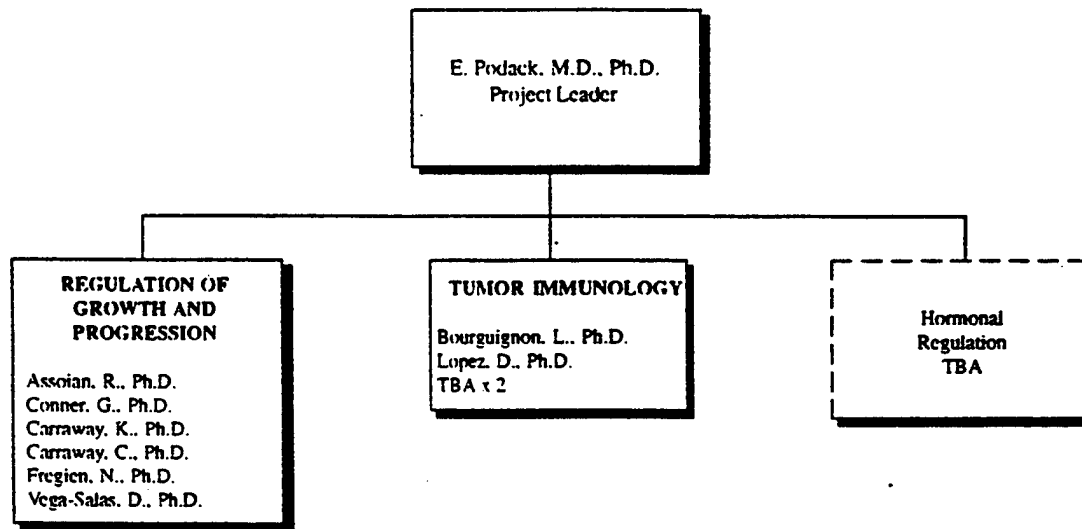
Timeline	Year 1	Year 2	Year 3	Year 4
Hold Planning Retreat	x	x	x	x
Recruitment	x	x	x	x
Establish Sylvester Breast Cancer Evaluation Center	x			
Develop Preliminary Data	x	x	x	
Create Laboratory and Clinical Relational Database	x	x		
Pilot Studies/Applications	x	x	x	
Full Grant Applications		x	x	x
Develop/Refine Laboratory and Clinical Collaboration	x	x	x	

F. Focus and Breadth of the Program

The research components of the Breast Cancer Program consist of Basic Science (Dr. Podack), Clinical Research (Dr. Cassileth), and Cancer Control, (Dr. Trapido) and a central core clinical activity, the multidisciplinary Breast Cancer Evaluation Center. These elements are described in detail below. Much of the current effort is derived from apportioning to the Program, breast cancer research activities of investigators from other Cancer Center Programs. These activities need to be expanded by recruitment and particularly by the development of an effort in the hormonal regulation of breast cancer, a critical pathway in the control of breast cancer growth and spread.

III. BASIC SCIENCE

The basic science effort in breast cancer is led by Dr. Podack who is the Cancer Center's Associate Director for Basic Science Research and the Principal Investigator of the Gene Transfer Immunotherapy Program Project. A small cadre of investigators from multiple departments are studying breast cancer biology (described below) and others have been drawn into this effort since the Center identified the development of a Breast Cancer Research Program as a high priority. The basic science program currently consists of two components: Regulation of Growth and Progression and Tumor Immunology. A third component in Hormonal Regulation is planned (see diagram below).



The overall theme of the basic science project is to determine what potentially manipulatable factors within the cancer cell and/or the host alter disease progression. For example, Regulation of Growth and Progression focuses on the genetic control of cell proliferation and metastatic potential. Studies are evaluating how oncogene products relate to cell surface expression of ligands for growth factors and cellular attachment, how signal transduction conveys information about replication to the nucleus, and how growth factors modulate cancer cell proliferation in the cyclin-dependent pathway. The Tumor Immunology effort focuses on the interplay of tumor antigens and the host's tumor specific immune recognition systems.

A. Regulation of Growth and Progression

Interprogrammatic Collaboration: *Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.*

NAME	PROJECT	FUNDING	PROGRAM
Carraway, K., Ph.D.	Ligand for <i>neu</i> Oncogene Encoded Receptor	ACS	Tumor Cell Biology
Carraway, K., Ph.D.	Structure/Biosynthesis of Tumor Sialomucin Complex	NCI	Tumor Cell Biology
Assoian, R., Ph.D.	Mutational Analysis of Anchorage-Independent Growth	NIH & ACS	Tumor Cell Biology

1. Ligand for *neu* Oncogene - Encoded Receptor. Dr. Kermit L. Carraway, (Department of Cell Biology and Anatomy)

This research examines the contribution to tumor progression of epidermal growth factor (EGF)-like factors and their receptors, such as p185^{neu}, the protein encoded by the *neu* (proto)oncogene, which has been implicated in breast cancer and other carcinomas. Dr. Carraway recently discovered a new ligand for this receptor in a cell surface sialomucin complex from rat mammary carcinoma. This complex is composed of two components, a large (approx. 700 kDa) highly glycosylated sialomucin ASGP-1 and a smaller (120 kDa), N-glycosylated, transmembrane glycoprotein ASGP-2. His studies suggest that ASGP-2 is a ligand for both p185^{neu} and the EGF receptor. Utilizing gene transfection and deletion studies and comparing binding characteristics of ASGP-2 to EGF receptor and p185, Dr. Carraway is pursuing a step-wise evaluation of the hypothesis that this transmembrane protein acts as a cellular autostimulatory factor in breast cancer cell lines.

2. Structure/Biosynthesis of Tumor Sialomucin Complex. Dr. Kermit L. Carraway, (Department of Cell Biology and Anatomy)

The overall goal of this research is to understand the role(s) of cell surface glycoproteins, particularly sialomucins, in mammary cancer. Sialomucins have been implicated in the escape of tumors from immune destruction and in metastasis and provide potentially important markers for immunological diagnosis, prognosis and therapy. The model system being studied is the cell surface sialomucin complex of metastatic 13762 rat mammary adenocarcinoma ascites cells. The compartments involved in

glycosylation/recycling of sialomucin, the role of processing in the localization of sialomucin antigens, and relationship to tumor progression are under study.

3. Mutational Analysis of Anchorage-Independent Growth. Dr. Richard K. Assoian, (Department of Cell Biology and Anatomy)

Loss of anchorage-dependent growth correlates with tumorigenicity. Dr. Assoian developed novel methodology that allows him to compare proliferation of adherent and non-adherent fibroblasts in a manner that avoids suspension of cells in soft agar or methylcellulose. His studies indicate that activation of G1/S transit is the key step in control of anchorage-independent growth. He is now identifying the genes that are responsible for regulating anchorage-dependent G1/S transit. These experiments should establish the anchorage dependency of some established G1/S gene products (e.g. retinoblastoma protein, cyclins and p34-like kinases) and also reveal a panel of new human genes that mediate the anchorage requirement for cell cycle progression. Dr. Assoian is now applying this approach to the study of murine and human breast cancer.

4. The Relationship of Oncogenes to Surface Glycoprotein Expression and Breast Cancer Metastases. Dr. Nevis Fregien, (Department of Cell Biology and Anatomy)

This research is based on the established correlation between the direct stimulation of N-acetylglucosaminyltransferase V (GlcNAc-T V) gene expression by oncogenes and subsequent changes in the cell surface glycoprotein structures which contribute to metastatic properties. The long range goal of this research is to understand the molecular mechanism by which oncogene expression, for example, activation of the neu(HER-2) oncogene in breast tumor cells and v-src expression in fibroblasts, promotes progression to metastatic potential by expression of the specific glycosyltransferase, (GlcNAc-T V). Dr. Fregien has begun to establish an association between neu(HER-2) expression and regulation of GlcNAc-T V expression, and has found that reduction in these oligosaccharide correlates with decreased metastatic potential.

5. A Cell Cycle-Related Nuclear Protein Absent in Breast Cancer. Drs. Dora E. Vega-Salas and Pedro J.I. Salas, (Department of Cell Biology and Anatomy)

This study focuses on a 58 kD nuclear protein, which is associated with the chromosomes during mitosis and differs chemically, quantitatively, and functionally from any of the known cell-cycle associated proteins. Because this 58 kD protein is absent in breast carcinoma cells, it may restrain the cell's malignant properties, suggesting a similarity with the products of anti-oncogenes like RB1 and p53. Moreover, the predicted encoded protein for p53 as with other anti-oncogenes, is a DNA-binding (Zn finger) protein that is phosphorylated by cdc2 protein kinase in cells entering the S phase. This study seeks to characterize and localize (structurally and biochemically) the 58 kD protein in tissue culture cell lines, sequence the 58 kD protein, suppress and over-express the 58 kD protein in tissue

culture epithelial cells, and evaluate the functional role of this protein in human breast carcinomas and normal tissues.

6. Signal Transduction Through HER2/Neu in Mammary Tumor Cells. Dr. Coralie A.C. Carraway, (Department of Biochemistry and Molecular Biology)

Cytoskeletal reorganization plays a role in cell-cell interactions and cell motility, factors that are important in tumor metastasis. P185^{neu} has been implicated in metastasis, however, little is known about how its activation is coupled to cellular changes. P185 also associates with a high M_r microfilament-associated glycoprotein complex, forming a complex involved in signal transduction. Dr. Carraway is analyzing the structure and function of transmembrane complex glycoproteins (TMC-gp) involved in signal transduction across breast cancer cells by examining their association with actin and p185, effect of activation of p185 in breast cancer cells on its association with the TMC-gp complex, and effects on the cytoskeleton, and their linkage to altered malignant cell biology.

7. The Role of Cathepsin D in Breast Tumor Growth and Invasion. Dr. Gregory E. Conner, (Department of Cell Biology and Anatomy)

Overexpression and secretion of the protease, cathepsin D, is associated with a subset of human breast tumors; however, overexpression of cathepsin D does not strongly correlate with clinical prognostic parameters. Dr. Conner is studying, using the hormone sensitive MCF-7 breast cancer cell line, whether cathepsin D secretion, by degrading extracellular material, allows tumor cells to invade surrounding tissue, inappropriately cleaves other protein(s) resulting in accelerated cell growth, or is intrinsically itself a component of growth regulation.

B. Tumor Immunology

Interprogrammatic Interactions: Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.

NAME	PROJECT	FUNDING	PROGRAM
Lopez, D., Ph.D.	Cell Mediated Immunity in Mammary Tumor Models	NCI	Tumor Immunology
Bourguignon, L., Ph.D.	The Structure and Function of Membrane Proteins in T-Lymphocyte Activation	NIH	Tumor Cell Biology
Lopez, D., Ph.D.	Tumor Factors and Immunity During Pre-Neoplasia/Neoplasms	NCI	Tumor Immunology

Program's new funded research efforts:

NAME	PROJECT	FUNDING
Bourguignon, L., Ph.D.	Role of CD44 & Variants in Membrane Cytoskeleton Interactions, Adhesion & Metastasis	DOD NCI

1. Cell Mediated Immunity in Mammary Tumor Models. Dr. Diana Lopez, (Department of Microbiology and Immunology)

The main thrust of this work, which continues studies initiated 16 years ago, is to analyze the role of cell-mediated immunity during mammary tumorigenesis, using murine viral and/or chemically mediated models. The long term goals of these studies are to elucidate the roles that viral and tumor antigens play in the cell mediated immune responses of mice bearing mammary tumors and the modulation of these reactions by tumor derived factors. Dr. Lopez showed that mice bearing large tumors present a series of phenotypic and functional alterations that suggest a major immunoregulatory imbalance. Her current work seeks to: investigate the molecular alterations leading to the constitutive production of TNF- α by B lymphocytes that parallels increasing tumor growth and the development of cachexia; elucidate the role played by exogenous mouse mammary tumor virus in the downregulation of immune responses that occurs during mammary tumor progression; determine the mechanisms

underlying the observed thymic involution; and analyze the reasons for altered cytokine expression in murine peripheral T cells.

2. The Structure and Function of Membrane Proteins in T-Lymphocyte Activation. Dr. Lilly Y. Bourguignon, (Department of Cell Biology and Anatomy)

T cell activation is a critical event in the generation not only of immune responses to pathogens, but also of a cytotoxic lymphocyte response to cancer. Specific binding between a surface receptor and ligand (e.g. mitogens, lymphokines, lectins, antibodies against specific surface molecules and antigens) initiates a cascade of biochemical events that produce a number of intracellular signals that modify biochemical processes within the cell and at the surface. This research tests the hypothesis that the T-lymphocyte transmembrane glycoprotein, CD45 (GP180), physically interacts with the T cell antigen receptor/CD3 complex (TCR/CD3 complex) and analyzes the linkage between CD45 and the cytoskeleton in the T-lymphocyte plasma membrane. Special emphasis is placed on the following: isolating the putative CD45 TCR/CD3 complex and identifying substrates of the CD45 (GP180)-tyrosine phosphatase in these receptor complexes; determining the protein sequences in CD45 (GP180) involved in cytoskeleton binding; and examining the possible regulatory role of the cytoskeleton on CD45 (GP180)-associated tyrosine phosphatase activity. A concomitant line of investigation seeks to explore the structural and functional relationships between the inositol triphosphate (IP_3) receptor and IP_3 -induced internal Ca^{2+} release.

3. Tumor Factors and Immunity During PreNeoplasia/Neoplasia. Dr. Diana Lopez, (Department of Microbiology and Immunology).

The progression of mammary cells from preneoplasia to neoplasia necessitates initial genetic changes and appropriate conditions that favor the further proliferation of the first transformed cells. Dr. Lopez documented that profound changes in the immune system correlate with increasing tumor burden. Some of the phenotypic and functional alterations are due, at least in part, to the production of immunomodulatory cytokines by the tumor. Dr. Lopez showed that GM-CSF is constitutively produced by benzanthracycline-induced (DMBA) tumors and that it promotes the appearance and/or expansion of a population of aberrant macrophages capable of downregulating the immune responses of tumor bearing mice. She is determining whether animals implanted with preneoplastic lesions also display altered parameters of immunity, and what alterations in the immune response occur after progression to established neoplasia.

4. CD44 Variant Isoforms (CD44v) and their Relationship to Tumor Metastases and Breast Cancer. Dr. Lilly Bourguignon, (Department of Cell Biology and Anatomy)

CD44 isoforms appear to play an essential role in the activation of lymphocytes into reactive cells in the lymph nodes. Most importantly, during metastasis tumor cells express CD44v structures which in effect mimic developing lymphocytes, allowing them to escape

immune surveillance. At the present time, very limited information is available regarding the factors responsible for the onset of breast cancer and the potential markers for detecting breast cancer metastasis. The facts that CD44v expression is closely associated with breast cancer metastasis and that these CD44v isoforms confer metastatic behavior in a spontaneous metastasis assay suggests that CD44v could be a very useful marker clinically for establishing the progression of breast cancer development. The ability to clone these breast cancer-specific variant exons into standard CD44 cDNA followed by expression of these constructs in non-metastatic human breast epithelial cells will provide us a good opportunity to analyze CD44v-related adhesion functions and metastatic behavior.

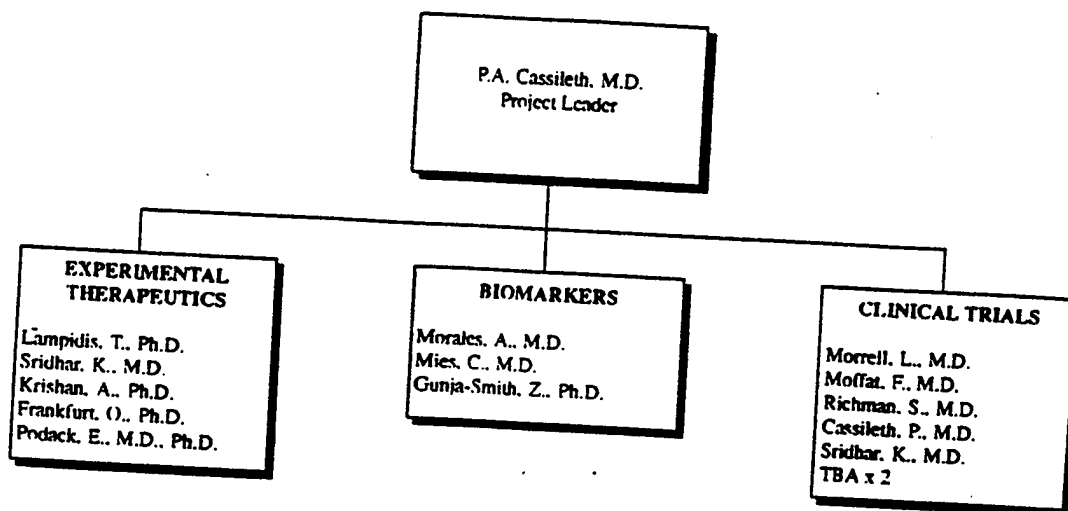
C. Hormonal Regulation

Breast tissue, both normal and malignant, responds to locally and systemically released growth factors by differentiation and proliferation. The Breast Cancer Program plans to recruit new investigators to develop a laboratory effort in Hormonal Regulation not only because of its growing importance, but also because it offers substantial opportunity for linkage with other basic science elements of the Program.

Molecular genetic studies show that a number of growth factor receptors are homologous to the protein products of cellular and viral proto-oncogenes that play a role in both abnormal and normal breast cell growth. Greater understanding of the interaction between growth factor ligands for cell surface receptors, the mechanisms of signal transduction across the membrane, and how these regulate gene function and activation are critical to an understanding of breast cancer biology and should open new directions in therapy.

IV. CLINICAL RESEARCH

The components of the current program in breast cancer clinical research consist of Biomarkers, Experimental Therapeutics, and Clinical Trials. Dr. Cassileth, the Cancer Center Deputy Director, leads this effort (see diagram below).



A. Biomarkers

Ongoing funded breast cancer research efforts:

NAME	PROJECT	FUNDING
Mies, C., M.D.	Cooperative Breast Cancer Tissue Registry	NCI
Morales, A., M.D.	Assessment of Markers of Tumor Behavior in Breast Cancer Patients in South Florida	Private Foundation
Mies, C., M.D.	DNA Sequence Analysis of the DNA Binding Domain of the Estrogen Receptor Gene in ER(+) Tamoxifen-Resistant Human Breast Cancer	Private Foundation
Mies, C., M.D.	Comparative Analysis of the Estrogen Receptor Gene in Breast Cancer in Blacks, Hispanics and Non-Hispanic Whites	Private Foundation

Program's new funded research efforts:

NAME	PROJECT	FUNDING
Gunja-Smith, Z., Ph.D.	Role of Matrix Metalloproteinases and their Tissue Inhibitors in Breast Cancer	DOD

In breast cancer, tumor size, the presence and extent of axillary lymph node involvement and the hormonal receptor status are the principal independent predictors of outcome. Other potential markers of tumor cell biology have been evaluated, such as oncogene expression, and DNA ploidy and DNA synthesis rates. How valuable these variables are as prognostic factors and whether they are independently predictive, differ in frequency or significance in minorities, and separable from the established factors, is unknown. Refining the ability to predict outcome has become increasingly important as attempts are made to intervene therapeutically early in the course of the disease. The intent of this component is to develop improved prognostic markers that will be used to guide the studies of the Clinical Research component and to provide cross-correlation of biologic aggressiveness (proliferation rate and metastatic potential) with the studies of the Basic Science component.

1. Cooperative Breast Cancer Tissue Registry. Dr. Carolyn Mies, (Department of Pathology)

The controversy about the prognostic significance of HER-2/neu amplification or overexpression of p¹⁸⁵ in breast cancer has served to highlight many of the problems of oncogene analysis. A careful examination of different approaches used to assess gene amplification and overexpression failed to explain differing conclusions on the basis of methodological problems. It is likely that these conflicting data are a result of a combination of factors including patient selection, sample size, lack of consistent pathologic analysis, and an absence of established uniform laboratory procedures with quality control.

To address these issues, Dr. Mies successfully competed for NCI funding of a Cooperative Breast Cancer Tissue Registry (CBCTR). The CBCTR systematically addresses one of the most vexing problems in biomarker research, namely, the need for breast cancer tissues from adequate numbers of patients in particular disease subcategories with a known outcome. Furthermore, it makes it possible to compare the utility of breast cancer markers in both women and men and among different racial and ethnic groups. The solutions to other problems such as feasibility, accessibility, cost, reproducibility, quality control and therapeutic utility should be integral to appropriate biomarker studies.

2. Assessment of Markers of Tumor Behavior in Breast Cancer Patients in South Florida. Dr. Azorides Morales, (Department of Pathology)

Molecular events that result in tumor progression and metastasis can now be studied using cellular substances as markers of biology and behavior of breast cancer. This pilot project investigates the kinetics as well as phenotypic and genotypic properties of breast cancer among the ethnic populations (Blacks, Hispanics and non-Hispanic Whites) of South Florida as they relate to tumor aggressiveness. Dr. Morales will use three related strategies that include immunohistochemistry, molecular biologic techniques, and cytogenetics applied to archival breast cancer tissues from approximately 400 women who were treated at the Cancer Center from 1984 to 1987 and correlate the results with the patient's clinical histories and follow-up outcome information.

3. DNA Sequence Analysis of the DNA Binding Domain of the Estrogen Receptor Gene in ER (+), Tamoxifen-Resistant Human Breast Cancer. Dr. Carolyn Mies, (Department of Pathology)

The biochemical basis for the estrogen receptor (+), antiestrogen (tamoxifen) - resistant phenotype, which occurs in approximately 40% of women with breast cancer is unknown. The purpose of this study is to test the hypothesis that DNA sequence abnormalities occur in the DNA binding domain (DBD) of the estrogen receptor (ER) gene in such cases, producing a dysfunctional ER protein incapable of binding to estrogen response elements in DNA. Tumors harboring such mutations would register as ER (+) on ligand binding analysis but would be impervious to ligand binding with either estrogen or tamoxifen. ER (+) primary breast cancers from 12 women with metastatic disease who have unexpectedly failed tamoxifen therapy will be retrospectively studied using paraffin embedded tumors (PETs) archived in the Department of Pathology. Five ER (+) breast cancers from patients who appropriately respond to tamoxifen will be evaluated as controls. The genomic DNA sequence of exons 2 and 3 which encode the DBD of the ER will be determined using a combination of in vitro amplification and deoxynucleotide sequencing techniques.

4. Comparative Analysis of the Estrogen Receptor Gene in Breast Cancer in Blacks, Hispanics, and Non-Hispanics. Dr. Carolyn Mies (Department of Pathology)

Epidemiologic studies have shown that breast cancer incidence varies depending on socioeconomic class, parity, marital status, geographic region and ethnic and racial background. Estrogen receptors (ER) are a member of superfamily of nuclear receptors that act as ligand-inducible transcription factors that bind to regulatory DNA sequences associated with target genes. More than 200 women are treated for breast cancer at the SCCC every year and at least 20% of the patients are Black. This pilot study assays estrogen and progesterone receptor protein content as usual, and residual fresh-frozen breast cancer tissue is used for molecular analysis. Nucleic acids (DNA and RNA) will be extracted and restriction

enzyme digestion analysis using a cDNA probe for the ER gene will be performed to look for gene rearrangements and large deletions.

5. Role of Matrix Metalloproteinases and Their Tissue Inhibitors in Breast Cancer. Dr. Zeenat Gunja-Smith (Department of Medicine)

Excessive secretion of a group of matrix metalloproteinases (MMPs) or decreased production of their tissue inhibitors (TIMPs) has been implicated in tumor invasion and metastasis. This study examines the hypothesis that an imbalance favoring MMPs (collagenase, gelatinases, stromelysin, and matrilysin) over TIMPs contributes to the invasive and metastatic processes of human breast tumors. Human breast cancer tissue is examined by immunohistochemical analysis and by characterization and quantitation of the MMPs and TIMPs and their mRNAs from the same tissues. The results of these studies will then be correlated with clinical outcome measures, including relapse, time to recurrence and survival. This effort is made feasible by the availability of a unique repository of frozen (and adjacent fixed) blocks of tumor tissue dating back 5 years. These tissues are not only thoroughly characterized pathologically, but also the clinical history of the patient in the intervening years is available through the Florida Tumor Registry.

B. Experimental Therapeutics

Interprogrammatic Interactions: *Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.*

NAME	PROJECT	FUNDING	PROGRAM
Lampidis, T., Ph.D.	Drug Selectivity in Cardiac and MDR Cells	NCI	Clinical Oncology Research
Frankfurt, O., Ph.D.	Flow Cytometric Study of Anticancer Drug Effect on DNA	NCI	Clinical Oncology Research
Krishan, A., Ph.D.	Modulation of Doxorubicin Efflux in Human Solid Tumors	NCI	Clinical Oncology Research
Krishan, A., Ph.D.	Adriamycin Effects on Tumor Cell Proliferation	NCI	Clinical Oncology Research

This effort focuses on mechanisms of chemotherapy-mediated cell death and tumor cell resistance, with the intent to utilize the data in clinical trials that are directed at overcoming chemoresistance.

1. Drug Selectivity in Cardiac and Multi-Drug Resistant (MDR) Cells - Dr. Theodore Lampidis (Department of Cell Biology & Anatomy).

Dr. Lampidis has developed in vitro systems that permit cardiotoxic as well as tumoricidal and MDR-mediated drug handling to be studied, at the cellular and subcellular level. He has found fundamental differences in the electronegative membrane potentials of cells that may in part explain differential cellular attraction of, and sensitivity to, Adriamycin, which is positively-charged. Dr. Lampidis is studying how charge and lipophilicity of Adriamycin and related analogs affect their selective accumulation and toxicity in cardiac-muscle cells (MDR-) and in MDR- and MDR+ tumor cell lines. The overall goal is to understand the underlying mechanisms involved in both Adriamycin-induced cardiotoxicity and multi-drug resistance, which are important problems in breast cancer therapy.

2. Flow Cytometric Study of Anticancer Drug Effects and DNA. Dr. Oskar Frankfurt (Department of Pathology).

Dr. Frankfurt has developed a monoclonal antibody that binds to DNA epitopes at sites of alkylating agent-induced injury. By flow cytometry, the antibody provides a measure of DNA injury and, overtime, of DNA repair. In human cancers, and xenografts in murine models and cell cultures, he is studying DNA repair and its inhibition by chemotherapeutic agents to evaluate the effect of chemotherapeutic agents of different classes (antimetabolites, topoisomerase inhibitors, and anthracyclines) on the repair of DNA damage in order to develop a rational basis for combination chemotherapy. He is analyzing how inhibitors of the repair of DNA damage effect human tumor xenografts and cells in culture. Companion studies investigate the phenomenon of apoptosis and how chemotherapeutic agents kill cells, in part, by allowing programmed cell death to proceed.

3. Modulation of Doxorubicin Efflux and Effects on Tumor Cell Proliferation in Human Solid Tumors. Dr. Awtar Krishan (Department of Radiation Oncology)

Dr. Krishan demonstrated that phenothiazines could modulate doxorubicin efflux in vitro in concentrations that could be achieved in humans. Working with Dr. Sridhar of the Hematology/Oncology Division, Dr. Krishan completed a phase I study of prochlorperazine, establishing that at the maximally tolerated dose, the plasma concentration of the drug was sufficient to inhibit doxorubicin efflux. Moreover, analysis of tumor cells from patients with ascites or pleural effusions after therapy with prochlorperazine plus doxorubicin, showed enhanced doxorubicin retention. These investigators are now embarked on a phase II study in breast cancer and mesothelioma that seeks to document that doxorubicin efflux is in fact blocked in patients with solid tumors by prochlorperazine; demonstrate that clinical responses can be obtained with the addition of prochlorperazine in patients documented to be resistant to doxorubicin; determine that pharmacokinetics of doxorubicin are unaltered by prochlorperazine (in contrasts to other MDR-inhibiting drugs, prochlorperazine does not seem to alter doxorubicin metabolism); and analyze tumor cells pre- and post-therapy to detect changes in MDR1 gene expression and chemosensitivity with view to correlating these laboratory studies with response.

4. Gene Transfer Immunotherapy Program (planned development in Experimental Therapeutics). Drs. Eckhard Podack (Department of Immunology and Microbiology) and Peter Cassileth (Division of Hematology/Oncology)

Drs. Podack and Cassileth successfully competed for a gene transfer therapy program project involving the insertion of the IL-2 gene into tumor cells. Final approval from the RAC and the FDA for a clinical trial of this technology in patients with small cell lung cancer was obtained in May 1994.

Dr. Cassileth and Podack will expand this effort and the Cancer Center leadership will provide space and money for additional faculty recruitment. Space is available from additional divisional laboratory space committed to Dr. Cassileth (2,500 ft² and from reassignable Cancer Center space.) Drs. Cassileth and Podack are recruiting jointly for an

immunobiologist and retrovirologist for the gene transfer program. The intent is to extend gene manipulation to the treatment of breast cancer, and to establish this effort as a component of the Breast Cancer Clinical Research Program. Research will focus on altering immunologic response either by gene insertion into the patient's tumor cells or into their lymphocyte effector cells. Preliminary laboratory and clinical studies suggest that this approach is useful in breast cancer, and a range of cytokines such as IL-2 , IL-4 and the interferons are available for this purpose.

C. Clinical Trials

The clinical trials effort in breast cancer consists largely of the translational research described above under Experimental Therapeutics and funded participation in cooperative group breast cancer trials. We need to develop novel investigative studies, such as the one we are conducting in locally advanced breast cancers that is described below. Dr. Cassileth has the commitment and support to recruit two additional clinician scientists with expertise in breast cancer clinical research and experience in translational research. The ongoing clinical trials are briefly described below.

1. Locally Advanced Breast Cancer. Dr. Louise Morrell, (Division of Hematology/Oncology)

Because of the delays in obtaining medical attention, socioeconomically disadvantaged patients with breast cancer are frequently diagnosed with locally advanced (Stage III) disease. They represent a particular challenging problem in local and systemic disease control. Dr. Louise Morrell recently completed a study of 55 patients with advanced disease using a combined modality approach consisting of intensive courses of chemotherapy (M-VAC), surgery and radiation therapy. This approach led to a pathologic complete remission in 24% of patients at the time of surgery, and a two-year disease-free survival of 70%. Her successor protocol for this group of patients involves high-dose sequential chemotherapy, surgery, autologous bone marrow transplantation, and radiation therapy.

2. Phase I/II Trials. Dr. Stephen Richman, (Division of Hematology/Oncology)

Dr. Stephen Richman is conducting a CTEP-sponsored phase I/II study of topotecan and cyclophosphamide in the treatment of selected patients with advanced breast cancer and other neoplasms. Topotecan is one of an interesting class of investigational drugs with a unique mechanism of action, that is, inhibition of the DNA repair enzyme, topoisomerase-1. It appears to have a broad range of anti-tumor activity. Combination with an alkylating agent may well enhance the efficacy of both agents.

3. Cooperative Group Studies. Drs. Fred Moffat, (Division of Surgical Oncology, NSABP) and Peter Cassileth, (Division of Hematology/Oncology, ECOG)

Dr. Fred Moffat leads the Cancer Center's participation in NSABP trials, and he is PI of our participation in the national randomized tamoxifen prevention trial. The SCCC has been one of the most active centers in screening and entering patients and has contributed a substantial proportion of minority patients to this study.

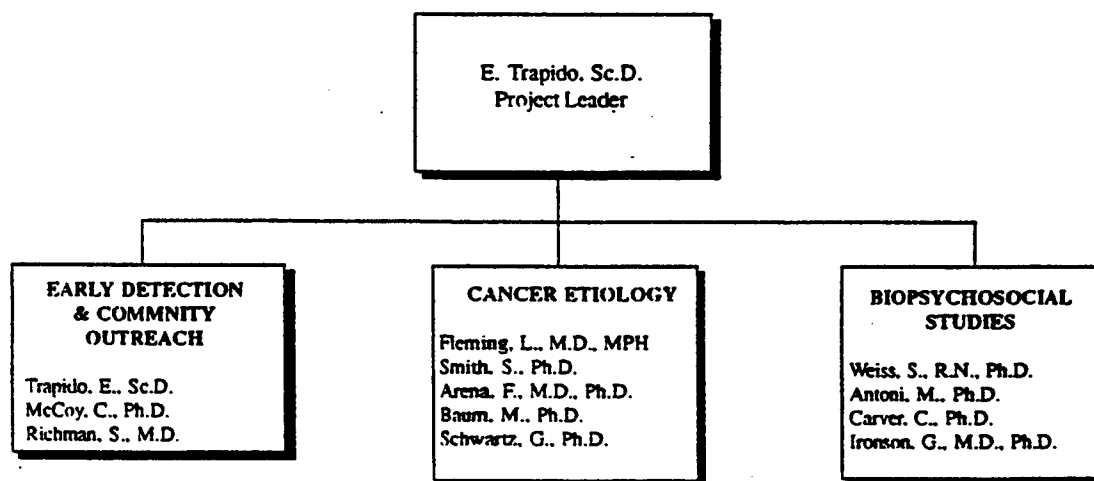
Dr. Cassileth is Co-Chair of the ECOG-led intergroup randomized trial that compares autologous bone marrow transplantation plus adjuvant chemotherapy to adjuvant chemotherapy alone in patients presenting with unfavorable stage II breast cancer. As PI of the University of Miami's newly established full membership in the ECOG, Dr. Cassileth has sponsored increased participation in a number of ECOG's clinical trials in breast cancer. He hired a research nurse/nurse practitioner, whose entire effort is focused on soliciting minority patients to enter intra- and extramural research protocols and ensure adherence to protocol design. This kind of special attention will continue to be necessary to make clinical research studies and new technology accessible to these patients, which is an important part of the Cancer Center's mission.

4. Bone Marrow Transplantation. Dr. Hugo Fernandez, (Division of Hematology/Oncology)

Dr. Cassileth began the autologous bone marrow transplantation, (BMT) program two years ago and thus far has treated 54 patients, including 30 patients with breast cancer. Dr. Fernandez recently assumed responsibility for directing this effort. Transplant protocols have been established for patients with metastatic breast cancer and for patients with unfavorable presentation of early disease. From its inception, the program has utilized peripheral stem cell mobilization and harvest for marrow reconstitution instead of bone marrow stem cells. The research thrusts of the program are aimed toward characterizing the hematopoietic precursors in the harvested product and on immunologic modulators of the host response to the tumor in the phase of recovery from transplant, in order to generate a host versus tumor cytotoxic lymphocyte effect. Bone marrow transplant will be a component of Dr. Louise Morrell's (a medical oncologist who is the clinician-leader of the Breast Cancer Working Group) new phase II study of the treatment of locally advanced, newly diagnosed breast cancer. Dr. Mark Goodman (a newly recruited faculty member charged with developing a clinical research effort in biologic response modifiers) is developing a study of interleukin-2 after BMT to enhance the host immune response to breast cancer during the phase of immunologic reconstruction. The basic science and clinical recruitments to the Breast Cancer Program will allow us to fully develop the clinical research potential of bone marrow transplant and its linkages with the gene therapy and immunobiology programs.

V. CANCER CONTROL

The Cancer Control project consists of three elements, Early Detection and Outreach, Cancer Etiology, and Biopsychosocial Studies. These are outlined below. This component of the Breast Cancer Program strives to capitalize on the remarkable population admixture of Florida. Research activities seek to identify subgroups with low rates of screening, high rates of breast cancer incidence or excessive late stage disease, develop culturally sensitive interventions, and evaluate their effectiveness. While continuing its strong program in early breast cancer detection among the medically underserved, the program is now directed toward assessment of risk factors in relation to tumor markers within this multiracial, multiethnic, and multicultural population. The opportunities for making substantial contributions to the understanding of the etiology and pathogenesis of breast cancer are enhanced in South Florida, by the availability of population-based databases, and uniquely heterogeneous populations who have experienced changes in their putative exposures, through emigration and acculturation. We recently recruited Dr. Gary Schwartz, a molecular epidemiologist from the University of Pittsburgh, who is interested in carcinogenesis and cancer prevention.



A biopsychosocial effort, under Dr. Sharlene Weiss' direction, began this year. Its focus is on studying the interactive effects of stress, behavior, and psychosocial components on neuroendocrine, hormonal, and immune function; the development and evaluation of psychosocial interventions; and investigation of suppression or enhancement of immune function in relationship to clinical outcomes.

A. Early Detection and Community Outreach

Interprogrammatic Collaborations: Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.

PI NAME	PROJECT	FUNDING	PROGRAM
McCoy, C., Ph.D.	Evaluation of the Early Detection Program	NCI-AHCPR	Cancer Control
Trapido, E., Sc.D.	South Florida National Hispanic Leadership Initiative in Cancer	NCI	Cancer Control
Trapido, E., Sc.D.	Increasing Breast Cancer Screening Among Older Hispanic Women in Dade County	Private Foundation	Cancer Control

Program's new funded research efforts:

PI NAME	PROJECT	FUNDING
Richman, S., M.D.	Evaluation of Peer Intervention to Increase Breast Cancer Screening Behavior	NCI

1. Evaluation of the Early Detection Program (Breast Cancer Screening) of the Sylvester Comprehensive Cancer Center. Dr. Clyde McCoy, (Department of Epidemiology and Public Health)

In an effort to increase the availability, accessibility and utilization of cancer screening examinations to medically underserved women, the SCCC developed a community based comprehensive Early Detection Program (EDP), involving ten Primary Healthcare Centers located in lower income neighborhoods of Dade County who are the main sources of primary health care for the socioeconomically disadvantaged. Dr. McCoy seeks to evaluate the EDP's activities and to determine factors which either contribute to or reduce the effectiveness of this innovative community-based program. Impact of the EDP will be measured relative to screening and biopsy rates, cancers detected, shifts in staging, survival and mortality.

2. South Florida National Hispanic Leadership Initiative in Cancer/En Accion Contra el Cancer. Dr. Edward Trapido, (Department of Epidemiology and Public Health)

This component of the National Hispanic Leadership Initiative in Cancer is designed to change risk behaviors among Cubans in Miami. This five year study includes a needs assessment and risk factor survey in two areas in South Florida. Based on these data, an educational intervention will be implemented in one of two areas with Dade County. Opinion leaders, educators, social workers, medical providers, and residents are being surveyed to help guide the educational intervention, which will be developed as the needs assessment and telephone surveys are analyzed. The intervention itself will rely heavily upon the identification of intermediaries in the community (consejeros or promotoras) who can provide cancer related information, education, and referral.

3. Increasing Breast Cancer Screening Among Older Hispanic Women in Dade County. Dr. Edward Trapido, (Department of Epidemiology and Public Health)

Older Hispanic women appear to underutilize breast cancer screening services. The reasons for this are not known, but may reflect access problems, as well as personal and cultural issues related to knowledge, attitudes, and beliefs about breast cancer and screening. This project surveys the town of Hialeah in Dade County, Florida, which has a large population of older Hispanic women, to determine their breast cancer screening behaviors and the reasons for use/non-use of early detection services. The results of this pilot will be used to design and test new intervention programs.

4. Evaluation of Peer Intervention to Increase Breast Cancer Screening Behavior. Dr. Stephen Richman, (Division of Hematology-Oncology)

Mammography rescreening rates are uniformly poor for all women, regardless of race or ethnicity. This intervention trial tests the hypothesis that community "peer counselors" can improve rescreening rates among women >50 years old compared to approaches that simply use follow-up letters to remind women of their appointments. This study will enroll approximately 2,900 asymptomatic (largely minority) women who have been screened through the Early Detection Program of the University of Miami School of Medicine. The Early Detection Program, operating since 1987, screens women on a mobile mammography van which circulates through county Primary Health Care Centers on a fixed schedule. Women attending one half of the centers will receive "usual" follow-up, i.e., they will be reminded of their follow-up appointment four times after their initial mammogram, as well as receive appropriate educational materials, through the mail. The second group of women will receive a focused intensive educational intervention; that will consist of a one-to-one educational session with a peer counselor who reflects her community, in terms of race, language, and culture. Outcomes will include rescreening rates, as well as changes in attitude and knowledge about cancer rescreening.

B. Cancer Etiology

Interprogramatic Collaborations: Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.

NAME	PROJECT	FUNDING	PROGRAM
Arena, F., M.D.	Search for Families with Breast/Ovarian Cancer in South Florida - Linkage Study	NCI	Cancer Control
Flemming, L., M.D., MPH	Breast Cancer and Organochlorine Pesticides	NIOSH	Cancer Control
Baum, M., Ph.D.	Clinical Trial and Observational Study for the Women's Health Initiative	NIH	Cancer Control

Program's new funded research efforts:

PI NAME	PROJECT	FUNDING
Smith, S., Ph.D.	Multigenerational Breast cancer in African-American Women	DOD

1. Search for Families with Breast/Ovarian Cancer in South Florida - Linkage Study. Dr. Fernando Arena, (Division of Genetics, Pediatrics).

Cloning the BRCA1 gene has been a major undertaking of the scientific community since Dr. Mary Claire King's group mapped this gene to chromosome 17q21 in 1990. Although much has been done to narrow the region to approximately 2 centimorgans, the actual gene responsible for breast cancer has not yet been cloned. This study seeks to increase the number of informative families available for linkage studies and tumor analysis. The immediate goal is to identify patients with three or more first degree relatives with breast and/or ovarian cancer for these studies. The long term goal is to develop the means to provide genetic counseling for families with breast cancer in South Florida's multiethnic population.

2. Breast Cancer and Organochlorine Pesticides. Dr. Lora Fleming, (Department of Epidemiology and Public Health)

Organochlorine chemicals, such as the pesticide DDT and polychlorinated biphenyls (PCBs) are ubiquitously present in the environment due to their extensive use and environmental persistence. These chemicals may have an etiological association with breast cancer because they are lipophilic (found in high concentrations in breast tissue and milk),

have weak estrogenic properties, are inducers of the cytochrome P450 enzyme system and suppressors of immune function, and are known animal carcinogens and suspect human carcinogens. This study analyzes organochlorine levels in breast tissue from breast cancer patients stored in the Tissue Procurement Facility at the Sylvester Cancer Center and from normal control subjects collected through the Dade County Medical Examiner's Office. Dr. Fleming seeks to determine the correlation between exposure to organochlorines and breast cancer risk after adjustment for confounding demographic variables.

3. Multigenerational Breast Cancer Risk in African American Women. Dr. Selina Smith, (Department of Epidemiology and Public Health)

Dr. Smith is studying risk factors for breast cancer in premenopausal African-American women by identifying genetic and environmental influences in the etiology of breast cancer in cases and their families. This population-based, cohort study with a nested case-control investigation is conducted in four phases; a breast cancer risk appraisal completed by 200 breast cancer cases and compared to 200 control subjects; a retrospective examination of the dietary intakes of cases and families; a psychosocial assessment; and a genetic phase including pedigrees and blood collection for DNA extraction. Together, these studies will provide a detailed characterization of specific risk factors for breast cancer in African-American women.

4. Clinical Trial and Observational Study of Women's Health Initiative. Dr. Marianna Baum, (Department of Epidemiology and Public Health)

The overall objectives of the University of Miami's Women's Health Initiative are to recruit South Florida women, more than 60% minority, who meet the inclusion and exclusion criteria of the randomized Women's Health Initiative trial. The University of Miami, with its surrounding diverse communities, provides a unique location to serve as a clinical center for this national study. The specific goal of this study are to identify 1,400 women, aged 50-79 years old, who agree to be randomized in a 3x2x2 partial factorial design involving the following therapies: Hormonal Replacement Therapy; Dietary Modification; and Calcium and Vitamin D. This study will also enroll and engage in the long-term followup of 2,200 participants for the observational component of the study derived from participants either ineligible or unwilling to participate in the interventions.

C. Biopsychosocial Studies

Interprogrammatic Collaborations: Ongoing funded breast cancer research efforts in other programs that contribute to this developing program.

NAME	PROJECT	FUNDING	PROGRAM
Antoni, M., Ph.D.	Coping with Breast Cancer Among Low Socioeconomic Status Blacks and Hispanics	ACS (National)	Biopsychosocial Oncology
Antoni, M., Ph.D.	Biopsychosocial Research Training Program in Breast Cancer	DOD	Biopsychosocial Oncology
Carver, C., Ph.D.	Coping with Breast Cancer in Younger Women	NCI	Biopsychosocial Oncology
Carver, C., Ph.D.	Lifestyles and Breast Cancer in Cultural and Sexual Minorities	NCI (Supplement)	Biopsychosocial Oncology
Weiss, S., Ph.D.	Evaluation of an Educational Intervention with Multi-Ethnic/Multi-Cultural Cancer Patients.	NCI	Biopsychosocial Oncology

1. Coping with Breast Cancer Among Low Socioeconomic Status Blacks and Hispanics. Dr. Michael H. Antoni, (Department of Psychology and Psychiatry)

Dr. Antoni's project examines the process of adjustment to early stage breast cancer among economically disadvantaged women of three different groups: African-American, Hispanic-American and Anglo-American. It will establish profiles of distress (in several domains), coping responses, and use of social support and religious resources in the period surrounding surgery and during the year afterward. Several variables will be examined as predictors of differences in the difficulty with which women adjust to breast cancer and its treatment. The focus is on three such variables: dispositional optimism vs. pessimism, the extent to which the woman's self-image is based on her body image, and the woman's perception of her partner's reaction to the diagnosis and surgery.

2. Biopsychosocial Research Training Program in Breast Cancer. Dr. Michael H. Antoni, (Department of Psychology and Psychiatry)

This program provides multidisciplinary research training in Biopsychosocial Research Training in Breast Cancer for psychology graduate students. They participate in weekly psycho-oncology and breast cancer seminars, have assigned rotations in psychosocial assessment, behavioral interventions, statistics, immunology and biochemistry assay core laboratories; and will gain experience working on breast cancer research projects with several training faculty members.

3. Adjustment to Breast Cancer Among Younger Women. Dr. Charles Carver, (Department of Psychology and Psychiatry)

Dr. Carver's project examines the quality of life concerns among premenopausal women diagnosed with and treated for early stage breast cancer. This two-part study proposes first to assess the levels of concerns expressed by younger breast cancer patients, variables of vulnerability/resilience, mediating variables of coping, perceptions of partner reactions and levels of quality of life to determine the extent to which concerns are linked to distress and dysfunction that are the ultimate outcomes of interest. The second part of the study with another sample will implement and test the effectiveness of intervention designed to meet the special needs and concerns of younger breast cancer patients based on findings from other studies, the experience of the research team and the results of the first study. It will target participants sense of confidence, coping responses, utilization of social support, and their self image, in a ten week group therapy format. A control group will receive an educational intervention. Treatment efficacy will be assessed at 3, 6, and 12 months post surgery on quality of life outcome variables. The study will also address the generality of the treatment effects across ethnic/cultural boundaries.

4. Lifestyle and Breast Cancer in Cultural and Sexual Minorities. Dr. Charles Carver, (Department of Psychology and Psychiatry)

As a supplement to the parent grant "Adjustment to Breast Cancer Among Younger Women," Dr. Carver will examine the special needs of lesbian breast cancer survivors, their concerns and their psychosocial adjustment. He intends to create a profile of the types and extent of concerns experienced by multicultural/multiethnic lesbian survivors of breast cancer and assess factors of vulnerability/resilience, coping, perception of partners reactions and levels of quality of life. Based on the results of the first study, he will develop and test the effectiveness of an intervention designed to meet the special needs and concerns of lesbian breast cancer patients.

5. Evaluation of an Educational Intervention with Multi-Ethnic/Multi-Cultural Cancer Patients. Dr. Sharlene Weiss, (Department of Medicine and Psychiatry)

The project examines the use and usefulness of the patient information files of the PDQ/PIF database and identifies new approaches to presenting information in order to assist patients with decision making and impact on their adherence to clinical and treatment regimens. It focuses on ethnic-specific beliefs about health care and cancer, health care delivery, information types and sources, uses of traditional medicines or healers and types of health services utilized. Multi-cultural multiethnic differences in behavioral change and knowledge, attitudes, and beliefs will be assessed at intervals throughout the study.

6. Stress Management Intervention for Women with Breast Cancer. Dr. Gail Ironson, (Department of Psychology and Psychiatry)

Dr. Ironson, a new member of the biopsychosocial effort, has proposed a one year project to test the experimental effects of a ten-week group cognitive behavioral stress management intervention on the quality of life, distress, coping and immunologic status in women with early stage breast cancer. Women will be randomized to either this group or an educational control group. Assessment will occur preintervention, post intervention and at a 9 month followup. This program is based on a successful intervention designed to buffer the initial impact of an HIV diagnosis in gay men. Investigators on that project found that the cognitive behavioral stress management intervention helped to enhance or maintain coping with associated normalizing effect on natural killer cell cytotoxicity and cellular control of immunity. It is unknown however, whether these effects generalize across another illness and whether active efforts to help women maintain their intervention acquired skills predict normalization of psychological and immunologic status at followup.

7. Genetic Counseling for Breast Cancer. Dr. Sharlene Weiss, (Departments of Medicine and Psychiatry)

Little is known about appropriate genetic counseling for women at high genetic risk for breast cancer. In preparation for working with women and their families following cloning of the breast cancer gene, this study proposes to develop a culturally sensitive counseling intervention. Focus groups and psychological measures will provide the empirical data to design a counseling model. In addition, data will be collected on psychosocial adjustment and general indices of well-being to determine whether assumptions about the problems that may affect high risk individuals are accurate, and to examine major ethnic/cultural differences.

VII. BREAST CANCER EVALUATION CENTER

The Breast Cancer Evaluation Center is the central clinical core facility of the Breast Cancer Program. The purpose is to bring together in the Sylvester Comprehensive Cancer Center's clinical facility, all of the disciplines relevant to meet the broad needs of breast cancer patients and their families. Dr. Cassileth has assembled individuals from medical oncology, surgical oncology, diagnostic radiology, radiation oncology, pathology, nursing, social work, psychology, plastic surgery and rehabilitation to constitute a Task Force to develop the facility and oversee its integration and progress. A full range of clinical services will be provided for diagnosis and treatment planning, screening, education and support of family members, rehabilitation (psychological, functional and prosthetic), follow-up, and therapy of patients with advanced disease. Dr. Sharlene Weiss directs this effort and coordinates the integration of services.

This clinical unit serves as the base for clinical research activities in patients with breast cancer and is responsible for the establishment and maintenance of a breast cancer database. This data center will collect epidemiologic, clinical, laboratory (routine and investigative), and outcome data on patients. This is essential to a range of planned studies in the epidemiology of breast cancer and other aspects of cancer control, to the collection of data for clinical research trials; the correlation with laboratory studies of tumor biology; and the identification and classification of specimens stored in the Breast Tissue Repository. The Cancer Center has purchased a DEC Alpha 3000 computer and Oracle relational database software for developing the programs for data entry and retrieval. The Epidemiology and Biostatistics (Epi-Stat) program of the Cancer Center is responsible for this activity under the direction of Dr. Ed Trapido, who leads the project in the Breast Cancer Control Program. The requisite resources for this effort, including biostatisticians, data managers and programmers, are provided by the Cancer Center through its Biostatistics and Clinical Trials Shared Resources.

VII. PROGRAMMATIC DIRECTION AND SUPPORT

A. Program Leader

Dr. Peter Cassileth is the Acting Program Development Director. He is Deputy Director of the Cancer Center and skilled in clinical trials research. He is responsible for the overall direction and integration of the elements of the program. A Breast Cancer Planning Committee meets monthly and functions as an oversight and steering committee to guide research initiatives and the commitment and allocation of resources to this effort.

Dr. Cassileth is responsible for the initial development and scientific direction of the program, including the recruitment of new personnel, providing a framework for scholarly exchange among program scientists, chairing the monthly internal planning Task Force, fostering linkages between clinical and basic science researchers, and encouraging the participation of multidisciplinary teams in research studies. As the program develops, Dr. Cassileth will step down as Program Leader and vest programmatic direction in one of the individuals recruited to the Breast Cancer effort.

B. Resources for the Developing Breast Cancer Program

The Cancer Center has made the development of a breast cancer research program a major priority for the next five years (94-99). In support of this objective, the Cancer Center and the Dean have pledged significant resources to achieve this objective including:

- 1. Recruitment** - The program will recruit six new faculty. These recruitments will include basic scientists with interests in the following areas: hormonal regulation of breast cancer and the interplay between cell surface receptor expression and the regulation of cell proliferation, the immunobiology of breast cancer with the intent of exploiting the established

gene therapy program; and molecular genetics of breast cancer focusing on the interactions of oncogene stimulators and suppressors of tumor growth and the genes controlling DNA repair mechanisms. The clinical component will be strengthened by the recruitment of two additional breast cancer clinicians who are skilled in clinical trials research and adept at integrating their studies with laboratory investigation. These additional recruitments will expand the linkages among our current basic scientists and with cancer clinicians. For example, hormonal regulation of breast cancer and cell surface receptors bear directly on the genetic control of cell proliferation, cell surface proteins involved in invasive and metastatic breast cancer cross-relate to problems in tumor cell recognition by cytotoxic effector lymphocytes, and immunobiologic studies in murine and cellular model systems translate into pre-clinical studies in gene therapy and biologic response modifiers with eventual application in humans.

2. Clinical Trials and DataBase - The Cancer Center provides a Clinical Research Services Shared Resource that includes data managers, biostatisticians, computers, and programmers in support of clinical trials activities and will support the development of the planned comprehensive breast cancer database.

3. Space - The Center has 100,000 square feet of laboratory space in two connected research buildings (Fox and Papanicolaou) on the medical campus. A total of 7,500 ft² of contiguous laboratory space (required renovations will be provided by the Center) in the Papanicolaou building will be made available to accommodate new laboratory efforts and some current and some current investigations with relevant research efforts. The Hematology-Oncology Division also has 2,500 ft² of laboratory space available for this program in the Rosenstiel Medical Sciences Building, near the Department of Immunobiology laboratories. Space for clinical activities will be provided in the Sylvester Outpatient Facility.

4. Equipment - The Center will support the purchase of shared common and specialized equipment for the Program's investigators.

5. Administrative Support - The Cancer Center will provide Dr. Cassileth with the necessary administrative support for the program's development.

6. Financial - The total financial needs of this program are estimated at \$4-5 million over the next five years and will be provided in part by endowment, fund raising, and research grant funding.

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI	Fund Source	Grant Number	Project Period	Grant Title	ABC Program Code	Program %	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
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07 - Breast Cancer:

Research Support

Research: NCI

Cassileth, Peter A	NIH-NCI	1 P20 CA66205-01	09-30-94 08-31-98	Breast Cancer Research Program	B	07	280,586	400,000	280,586	400,000
Morales, Azorides R	NIH-NCI	5 P30 CA14395-20	09-01-92 08-31-95	CCCSG: Developmental Supplement "Searching For The BRCA1 Gene - A Repository Of DNA Information"	A	07	49,987	76,730	49,987	76,730
Sub-Total Research: NCI							310,573	476,730	310,573	476,730

Research: Other NIH

Woessner, J. Frederick	NIH-AMSSD	5 R01 AR16940-21	06-01-83 05-31-98	Human Cartilage Proteases In Arthritis	C	07	132,524	203,822	132,524	203,822
Woessner, J. Frederick	NIH-NICHD	5 R01 HD06773-23	05-01-90 04-30-95	Tissue Collagenase And Its Control By Steroids	B	07	94,560	270,323	94,560	270,323
Sub-Total Research: Other NIH							227,084	474,145	227,084	474,145

Research: Other Peer Reviewed

Bourguignon, Lilly	DOD	DAMD17-94-J-4121	06-01-94 09-01-98	Role Of CD44 And Variants In Membrane- Cytoskeleton Interactions, Adhesion, Metastasis And Human Breast Cancers	B	07	131,455	196,670	131,455	196,670
Gunja-Smith, Zeenat	DOD	DAMD17-94-J-4295	09-01-94 08-31-98	Role Of Matrix Metalloproteinases And Their Tissue Inhibitors In Human Breast Adenocarcinoma	B	07	132,495	199,501	132,495	199,501
Smith, Selina	DOD	DAMD17-94-J-4245	09-01-94 06-30-98	Multigenerational Breast Cancer Risk Factors In African American Women	B	07	48,764	74,999	24,382	37,499
Sub-Total Research: Other Peer Reviewed							312,714	471,170	288,332	433,670

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI	Fund Source	Grant Number	Project Period	Grant Title	ABC	Program Code	Program %	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
Research: Non Peer-Reviewed											
Fregien, Nevis	SCCC	NGN-506	06-01-94 05-31-95	Pilot: Antisense Gene Therapy for Metastatic Breast Cancer	B	07	100 %	10,000	10,000	10,000	10,000
Gunja-Smith, Zeenat	SCCC	NGN-505	06-01-94 05-31-95	Pilot: Role Of Matrix Metalloproteinases And Their Tissue Inhibitors In Human Breast Adenocarcinoma	B	07	100 %	10,000	10,000	10,000	10,000
Mies, Carolyn	HFSF	NGN-0243	06-01-93 05-31-95	Comparative Analysis Of The Estrogen Receptor Gene In Breast Cancer In Blacks, Hispanic, And Non-Hispanic Whites	A	07	50 %	24,391	24,391	12,195	12,195
Mies, Carolyn	SCCC	NGN-507	06-01-94 05-31-95	Pilot: DNE Sequence Analysis Of The DNA Binding Domain Of The Estrogen Receptor Gene In ER(+), Tamoxifen-resistant Human	B	07	100 %	10,000	10,000	10,000	10,000
Morales, Azorides R	HFSF	NGN-0240	06-01-93 05-31-95	Assessment Of Markers Of Tumor Behavior In Breast Cancer Patients In South Florida	A	07	100 %	78,755	78,755	78,755	78,755
Sub-Total Research: Non Peer-Reviewed								133,146	133,146	120,950	120,950
Sub-Total Research Support								983,516	1,555,190	946,939	1,505,496

Other Support

Other: NCI

Mies, Carolyn	NIH-NCI	1 U01 CA62772-01	09-30-93 09-29-97	Cooperative Breast Cancer Tissue Registry	B	07	50 %	56,902	83,114	28,451	41,557
Sub-Total Other: NCI								56,902	83,114	28,451	41,557
Sub-Total Other Support								56,902	83,114	28,451	41,557
Sub-Total 07 - Breast Cancer								1,040,418	1,638,304	975,390	1,547,052

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI

Fund Source	Grant Number	Project Period	Grant Title	ABC Program Code	%	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
						983,516	1,555,190	946,939	1,505,496
						0	0	0	0
						56,902	83,114	28,451	41,557
						1,040,418	1,638,304	975,390	1,547,052

Report Totals for All Grants

Total All Research Support

Total All Training Support

Total All Other Support

Total for All Grants

September 25, 1995

GRANT OPPORTUNITIES Breast Cancer August 1995							
Announcement	Agency	Title	Deadline	Type of Grant	Award	Proj. Period	Remarks
PAR-95-023	NCI	Small Grants for Therapeutic Clinical Trial of Malignancies	6/1; 10/1; 2/1	R03	50K DC/year	2 years	
PA-93-070	NCI	Cancer Prevention and Control Research Small Grant program	6/1; 10/1; 2/1	R03	50K DC/year	2 years	
PA-94-050	NCI	Exploratory Grants to Stimulate Laboratory Studies and Innovative Clinical Trials	6/1; 10/1; 2/1	R21	100K DC/year	2 years	
ACS Florida	ACS	Research Grant	9/15/95		25 K	1 year	Starter/Pilot/Interim
ACS National	ACS	Research Grant	10/15/95			3 years	
DOD	DOD	Breast Cancer Program	9/13/95	Pilot/New Investig./Research Grant			
South Fl. Health F.			2/1, 5/1, 8/1, 11/1				
The Avon Breast Health Access Funds		Breast Cancer Education & Early Detection SVCS	January /June		5K to 75K	1 year	

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Breast Cancer Grants Funded After 8/1/94

Principal Investigator	Agency	Grant Number	Project Period	Grant Title	Annual Direct Cost
Baum Mariana, Ph.D.	NIH	1 N01 WH 42131-01	9/3/94 - 8/31/98	Clinical Center For the Clinical Trials & Observational Study for the Women's Health Initiative *	\$583,437
Bourguignon, Lilly, Ph.D.	NIH/NCI	1 R01 CA66163-01	4/1/95 - 1/31/2000	CD44/Variant-Cytoskeleton in Adhesion and Breast Cancer	\$120,174
Bourguignon, Lilly, Ph.D.	DOD	DAMD17-94-J-4121	8/1/94 - 9/1/98	Role of CD44 and Variants in Membrane Cytoskeleton Interactions, Adhesion, Metastasis and Human Breast Cancers	\$131,455
Carver, Charles, Ph.D. (Gail Ironson, M.D., Ph.D.)	NIH/NCI	1 R01 CA64710-01S	10/01/94 - 8/30/96	Adjustment to Breast Cancer Among Younger Women (Supplement: Lifestyle and Breast Cancer in Cultural and sexual Minorities)	\$38,461
Cassileth, Peter A., M.D.	NIH/NCI	1P20 CA66205-01	9/30/94 - 8/31/96	Breast Cancer Research Program	\$260,586
Gunja-Smith, Zeenat, Ph.D.	DOD	DAMD17-94-J-4295	9/1/94 - 8/31/98	Role of Matrix Metalloproteinases and their Tissue Inhibitors in Human Breast Adenocarcinoma	\$132,495
Richman, Stephen, M.D.	NIH/NCI	1 R01 CA64056-01	10/1/94 - 9/30/97	Breast Re-Screening in Minority Women	\$180,586
Richman, Stephen, M.D.	DOD	DAMD17-94-J-4233	8/15/94 - 8/14/98	Cancer pain Relief Skills for Minority Outpatients with Breast Cancer (Sub-Contract)	\$42,422
Robinson, David, M.D.	DOD	DAMD17-94-J-4246	10/1/94 - 8/31/96	Development of Microsurgical and Laser Instrumentation for Stereotactically Directed Endoablation of Small Breast Cancers	\$48,765
Smith, Selina, Ph.D.	DOD	DAMD17-94-J-4245	9/1/94 - 8/31/98	Multigenerational Breast Cancer Risk Factors in African American Women	\$97,528
Smith, Selina, Ph.D.	ACS-Institutional	N/A	4/15/95 - 4/14/96	Breast Cancer Counseling in African American Women	\$7,000
Antoni, Michael, Ph.D.	DOD	DAMD17-94-J-4236	9/1/94 - 8/14/98	Biopsychosocial Research Training in Breast Cancer	\$71,996

*Even though the title of the above mentioned grant does not indicate its Breast Cancer relevance, breast, cervical, colon cancer are three outcomes being measured.

September 25, 1995

DOD GRANT APPLICATIONS SUBMITTED FOR 1995 DEADLINE

PI	TYPE	DEPT	TITLE	TOTAL \$
Botazzi/Assoian	Fellowship	Cell Bio & Anatomy	Anchorage-dependent and -independent control of the cyclin A gene: implications for breast cancer	\$125,100
Carraway, K.	Research Project	Cell Bio. & Anatomy	Sialomucin Complex in Human Breast Cancer	\$706,560
Carraway, C.	Research Project	Biochemistry	Epithelial-specific GP55: role in Microfilament, ERB P185 ^{neu} and Cadherin organization in Br. Ca. Cells	\$817,840
Dewanjee, N.	Research Project	Radiology	Radiolabeled Antisense Probes for Noninvasive Diagnosis of Breast Tumor in Mouse Model	\$572,892
Fregien, N.	Research Project	Cell Bio & Anatomy	Control of Breast Tumor Cell Adhesion by C1cNAC-Transferase V.	\$592,523
Gretz, S.	Research Project	Microbiology	Selective Radiosensitization of Human Breast Tumors in Nude Mice with 5-chlorodeoxycytidine and Biomodulators of its Metabolism	\$1,205,928
Ironson, G.	Research Project	Psychology	Biological Changes Following Psychosocial Intervention in Breast Cancer	\$919,142
Krishan/Richman	Research Project	Radiation Oncology	Modulation of Doxorubicin Efflux in Human Breast Cancer	\$798,574
Krishan, A./Lopez	Pilot Project	Radiation Oncology	Chemo-immunomodulation of Breast Cancer	\$149,974
Lee, M.	Research Project	Biochemistry	Role of Human DNA Polymerase S and its Accessory Proteins in Breast Cancer	\$849,283
Lopez, D.*	Research Project	Microbiology	Effects of Taxol on the Immune System During Mammary Tumorigenesis	\$730,772

September 25, 1995

DOD GRANT APPLICATIONS SUBMITTED FOR 1995 DEADLINE

Lopez, D.*	Research Project	Microbiology	Role of Phosphatidylserine in Mammary Tumor Progression	\$714,472
Malek, T.	Pilot Project	Microbiology	Induction of breast tumor-specific CTL by enhancing breast cancer cell immunogenicity	\$152,992
Mian, A.	Pilot Project	Radiation Oncology	Development of Chemoimmunotherapeutic Agents of Human Breast Cancer	\$149,687
Moffat, F.	Subcontract	Surgical Oncology	Buddies to Recruit Minority Women to Clinical Trials	\$11,976
Price, S./ Carraway, K.	Fellowship	Cell Bio & Anatomy	Regulation of Sialomucin Complex Expression	\$86,493
Ramachandran C.	New Investig.	Radiation Oncology	Chemomodulatory Effects of Tamoxifen in Breast Cancer	\$586,967
Richman, S.	Research Project	Medicine	Use of Peer Counselors to Increase Access of Minority Women to NCI Protocols for Adjuvant Therapy of Stage I & II Breast Cancer	\$821,263
Smith, S.	Research Project	Epidemiology/Pub Health	Counseling African American Women at High Risk for Breast Cancer	\$866,449
Spector, N.	Pilot Project	Medicine	Generation of Tumoricidal HER2/neu Specific CTL	\$149,987
Vega-Salas, D.	Research Project	Cell Bio/Anatomy	A Cell Cycle Related Chromosomal-Nuclear Protein Absent in Breast Carcinoma Cells	\$751,136
Markoe, A.*	Research Project	Radiation Oncology	Adaptive Hyperthermia array for breast cancer therapy	\$977,241

September 25, 1995

DOD GRANT APPLICATIONS SUBMITTED FOR 1995 DEADLINE

Pattany/Fishman *	Pilot Project	Radiology	MRI Guidance of Breast Conservation Therapy in Patients with Early Stage Breast Carcinoma	\$141,691
* Advice/Inf. Only				

APPENDIX 3

Description of the Psychosocial Oncology Research Program Sylvester Comprehensive Cancer Center

University of Miami School of Medicine

DEVELOPING PROGRAMS

PROGRAM CODE: #8

BIOPSYCHOSOCIAL ONCOLOGY

PROGRAM LEADER: SHARLENE WEISS, Ph.D.

1. PROGRAM PARTICIPANTS

Name	Department	Title
Michael Antoni, Ph.D.	Psychology, Psychiatry	Assoc. Professor
Fernando Arena, M.D., Ph.D.	Pediatrics	Asst. Professor
Charles Carver, Ph.D.	Psychology	Professor
Robert Duncan, Ph.D.	Epidemiology & Public Health	Professor
Mary Ann Fletcher, Ph.D.	Medicine & Microbiology/Immunology	Professor
Karl Goodkin, M.D., Ph.D.	Psychiatry, Neurology, Psychology	Asst. Professor
Gail Ironson, M.D., Ph.D.	Psychology, Psychiatry	Professor
Mahendra Kumar, Ph.D.	Psychiatry, Psychology	Assoc. Professor
Arthur LaPerriere, Ph.D.	Psychiatry, Psychology	Asst. Professor
Silvina Levis, M.D.	Medicine	Asst. Professor
Neil Love, M.D.	Medicine	Assoc. Professor
Peggy O'Hara, Ph.D.	Epidemiology & Public Health	Assoc. Professor
Patrick Reynolds, M.D.	Psychiatry	Asst. Professor
Neil Schneiderman, Ph.D.	Psychology, Bioengineering, Medicine, Psychiatry	Professor
JoBeth Speyer, M.S.W. Director	Cancer Center	Program
Sharlene Weiss, Ph.D.	Medicine, Psychiatry	Assoc. Professor

No CCSG support is requested for this developing program.

2. PROGRAM DESCRIPTION

2a. Rationale and Need for Developing Program

The overall aim of this program is to expand multidisciplinary studies on the interactions between the biological, psychological and behavior aspects of cancer with a special focus on multiethnic populations.

Although death rates from heart diseases, stroke and other conditions have been decreasing, deaths due to several important cancers, such as lung and prostate, have risen substantially in the past 30 years despite several important therapeutic discoveries. For breast cancer, mortality among White women increased by 14% since 1973, and by 30% in Blacks.

Currently there is a 5-year relative survival rate of 53% for White Americans and 38% for Black Americans. One of the intriguing questions in cancer research is the differential response of patients to treatment; why two patients with the same tumor status and prognostic indicators will have vastly different outcomes. Increasing evidence indicates that other factors may be implicated in addition to the biological effects of the disease and its treatment, and investigations must be expanded.

Early research on the psychological aspects of cancer focused on the "cancer prone" personality; results were equivocal and unsubstantiated. Behavioral and psychological research with cancer patients began in the 1970's with a focus on issues of rehabilitation. Many of these studies were aimed toward preventing or reducing the psychological and behavioral burdens of the disease. During the last 10 years, many studies have documented the deterioration in "quality of life" associated with the disease process. Research has increased our understanding of this multidimensional construct which includes functional ability, psychological functioning, social adjustment and disease and treatment-related symptoms. Quality of life is now widely perceived to have substantial potential as an endpoint in therapeutic assessments. Health related quality of life endpoints are being used increasingly for the evaluation of pharmacologic agents in clinical trials.

"Quality of life" research has identified many of the stressors that patients encounter during treatment, including emotional distress, interrupted life tasks, interpersonal disruptions, dealing with the side effects of treatments, and financial hardship. This line of research has led to an interest in studying the effects of long term stressors on cancer patients, the relationship of psychological distress and stressors (both acute and chronic), and the mechanisms by which psychological and behavioral responses may influence biological processes, behaviors, and even health outcomes.

Research also suggests that there are health behavior sequelae for individuals who experience psychological stress from cancer. Distressed individuals often have appetite disturbances that are manifested by eating less often or meals of lowered nutritional value. Individual who are depressed, anxious or both are more likely to self-medicate with alcohol and other drugs. Distressed individuals often report sleep disturbances with either early morning waking, or insomnia. Cancer stressors may influence the initiation or frequency of positive health behaviors, such as exercise. Reliable associations have been found between mental health and physical activity; exercise is an important primary or adjunctive therapy for mood disorder, including anxiety and depression. Positive mood effects and increased functional capacity have been found for breast cancer patients receiving chemotherapy and participating in a program of aerobic training.

The contribution of stress to the alteration of health behaviors is made more complex by the direct effect that cancer treatment may have on some behaviors. Sensory changes may occur with radiation therapy, changes in eating patterns occur with learned taste aversions and changes in taste or smell acuity. The pathophysiology of weight loss in cancer is not entirely

understood but may be explained in part by the direct and interactive effects of energy balance, altered carbohydrate or protein metabolism, the disease process itself, and from learned behavior as the result of a conditioned response.

A variety of data suggest that stress can also influence the autonomic, endocrine and immune systems. Stress may be routed to the immune system via the central nervous system, by activation of the sympathetic nervous system, or through neuroendocrine immune pathways. A variety of hormones released under stress have been implicated in immune modulation including the immune catecholamines, cortisol, growth hormones, and endogenous opioid peptides. In fact, the immune system may be one of the more important biological determinants in the control of certain malignant disease. There is some evidence for both the classical and natural immune responses in host resistance against progression and metastatic spread of tumors.

A recently published meta analysis reviewing studies of the association between immunity and depression showed strong and reliable effects for several large alterations in cellular immunity. Immune alteration included lowered proliferative response of lymphocytes to mitogens, lowered natural killer cell activity, and alterations in number of several white blood cell populations. The implications of these findings need further study as little is known about normal variations in immunity and how it relates to disease. Studies are needed that link variation in affective states to indicators of immunity and then to disease outcomes.

Another important behavioral pathway is non adherence. Data suggest that psychological or behavioral effects of cancer treatment can be so disruptive that patients become discouraged and refuse or fail to complete treatment. Non-compliance has received little research attention in cancer studies despite the potential for negative consequences, including lowered chances for survival, and more broadly, the invalidation of clinical trials of new therapeutic agents.

2b. How Long Has This Activity Been Under Development?

Discussion of this subject has taken place over the last five years and some projects were underway. Plans at the 1994 retreat called for the establishment of this program. Dr. Weiss' arrival in March of 1994 enabled us to combine the projects under one program. Now that the Multidisciplinary Breast Cancer Center, and the Psycho Oncology program are underway, the Biopsychosocial Research activity will encompass these clinical programs.

2c. How Does it Fit in with the Overall Plan for the Cancer Center?

The development of this program provides an opportunity for further collaboration and integration of SCCC investigators from a number of different disciplines. It spans the basic science through clinical research continuum and has particular relevance to the programs in breast cancer, prostate cancer, cancer control and experimental therapeutics. It focuses on a number of key populations with an increasing incidence of disease. It spans the health to

disease continuum through the immunology studies and extends studies on individuals or small groups (i.e. Adherence Studies) that can have a major impact on large numbers of people.

2d. Plans for Building the Program Include:

The overall aim of the Biopsychosocial Oncology Program is to expand multidisciplinary studies on the interactions between the biological, psychological and behavioral aspects of cancer by providing a coordinated framework for a variety of related research activities. This will be accomplished by:

- Providing core resources for pilot studies to develop and/or integrate common data elements for cross-study comparisons of different populations
- Establishing collaborative relationships with ongoing programs in other departments and laboratories in order to foster multidisciplinary research
- Convening regular seminars and research meetings with principal investigators of relevant research projects, potential new investigators, and extramural scientists to share information, stimulate cross-project collaboration, and facilitate communication between laboratory and clinical investigators.
- Establishing a comprehensive psycho oncology database for all clinical oncology patients
- Recruiting new clinical and basic science investigators to the program

2e. Projected Time

The projected time for the development of the program is 5 years (94-99), during which the new clinical and basic scientist faculty will be recruited, integrated with other center members and research activities, and compete for peer-reviewed funding.

Timeline	Year 1	Year 2	Year 3	Year 4	Year 5
Hold Planning Retreat	x	x	x	x	x
Establish Meeting Schedule	x				
Refine Goals	x				
Establish Clinical Entities	x	x			
Seek Available Preliminary Data	x	x			
Establish Database		x			
Develop Pilot Studies/Applications	x	x			
Recruitment	x	x	x		
Develop Full Applications		x	x	x	x
Develop/Refine Collaborations with Laboratories	x	x			
Integrate with Other Campus Departments	x	x	x	x	x
Evaluate Program's Effectiveness in Light of SCCC and Program Goals		x		x	

2f. Focus and Breadth of the Program

The Biopsychosocial Oncology program will provide a coordinated, integrated structure for interdisciplinary studies on the interactions within the biological, psychological and behavioral aspects of the etiology and progression of cancer.

Research areas will include:

1. **Examination of the interactive effects of stress, behavior, and psychosocial components on neuroendocrine, hormonal, and immune function in cancer patients; how it differs across sites, gender, age, race/ethnicity, prognostic variables;**

For example:

For the past eight years, Drs. Antoni (psychologist) and Ironson (physician, psychologist) have completed and published a series of studies on the effects of stress and changes in immune function in HIV positive men. Both Dr. Antoni and Dr. Ironson are interested in following this line of research with cancer patients. Dr. Antoni is currently examining changes in immune function of cancer patients in a small study with the Dutch Cancer Foundation and Drs. Ironson and Weiss have proposed a developmental grant (pending) to test a behavioral stress management intervention on immunologic status in women with early stage breast cancer.

Investigators working in this area include: Antoni, Duncan, Fletcher, Kumar, Schneiderman, Goodkin, Ironson and Weiss.

2. **Developing and evaluating of psychosocial interventions directed toward reducing stress, enhancing quality of life and improving compliance as well as other health-related behaviors (smoking, diet, etc.).**

As an example, Dr. Charles Carver (psychologist) is the PI of a newly funded NIH grant "Adjustment to Breast Cancer Among Younger Women" which is a two part study that proposes to assess the levels of distress and dysfunction in younger breast cancer patients. The second part will implement and test the effectiveness of an intervention designed to meet the special needs and concerns of these younger breast cancer patients based on the results of the first study.

Dr. Sharlene Weiss (psychologist, nurse) is PI of a newly funded NCI project to evaluate the use of educational information (patient information files) with multiethnic cancer patients. In addition to the main study, a pilot will be conducted on a subset of patients to examine differences in adherence to treatment regimens among different ethnic groups after the educational intervention.

Dr. Weiss, in collaboration with Dr. Fernando Arena (geneticist), has a pending developmental grant application to explore different counseling approaches for multi/ethnic women at familial risk for breast cancer.

Investigators working in this area include: Carver, Arena, Love, LaPierre, Levis, O'Hara, Weiss, Speyer and Reynolds.

3. The investigation of the concurrent influence of psychological variables on the suppression or enhancement of immune function and cancer outcomes.

Recent studies suggests that psychological factors may play a significant role in immune suppression following cytotoxic chemotherapy in a similar fashion as occurs with "conditioned" chemotherapy side effects such as anticipatory nausea and vomiting. Such findings have significant implications for the development of innovative interventions to enhance immunosuppression with lowered doses of drugs. We would seek to recruit investigators who are familiar with psychoneuroimmunology research, (neuroimmunologist or neuropsychologist) to develop this important area of inquiry.

2g. Program Leader

Dr. Sharlene Weiss was recruited to the University of Miami to become the director of the Multidisciplinary Breast Cancer Center and the Director of Biopsychosocial Research during its first phase. She is a nurse and a psychologist who brings extensive experience in research administration of multidisciplinary studies from her previous position as a program director at NIH, and as a PI on grants and contracts. Dr. Weiss' research and clinical activities over the past two decades have focused on the application of behavioral strategies to assist patients in behavioral change related to the management of acute and chronic illness. She has extensive clinical experience in working with individuals and groups and has developed innovative biobehavioral approaches for medical patients. From 1987-1990, she was an investigator in one of the first research studies that examined immunological responses of breast cancer patients to behavioral interventions.

Dr. Weiss's initial contributions to this program have been in establishing the Breast Cancer Clinic and reorganizing the Psycho Oncology clinical program in collaboration with the Department of Psychiatry and Social Work. The Breast Cancer Clinic planning group meets weekly; all clinicians involved with the program meet monthly. The Psycho Oncology planning group meets twice monthly to make program decisions; there is a monthly meeting for all Psycho Oncology staff with a consultant to discuss patient issues and problems. Research groups meet on an "as needed" basis to discuss specific projects.

2h. Resources for the Developing Biopsychosocial Oncology Program

Development of the Biopsychosocial Oncology program is considered to be a priority by the Cancer center for the next five years (94-99). In support of this objective, the Cancer center has pledged the resources to achieve this objective including:

Recruitment - the program intends to recruit four new faculty for the program. These recruitments will include two basic scientists in the area of psychoneuroimmunology (human and animal immunology), and two clinical investigators, skilled at integrating their studies with laboratory investigations.

Clinical Trials and Data Base - the Cancer Center provides a Clinical Research Service shared resource that includes data managers, biostatisticians, computers and programmers in support of clinical trials activities and will support the development of the planned psycho oncology database.

Space - A total of 2,000 square feet of continuous laboratory space will be made available to investigators recruited to the Biopsychosocial Oncology Program. Required renovations including a Psychoneuroimmunology laboratory will be provided by the Center.

Space for clinical activities will be provided in the Sylvester Clinical Facility. Plans for renovation of clinical space are in process and include 10 offices and 2 group rooms. Renovation will be provided by the Sylvester Clinical Facility through Dr. Goodwin.

Financial - The total financial needs of this program are estimated at \$2.5 million over the next five years and will be provided in part by fund raising, research grant funding, and the clinical practice.

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI	Fund Source	Grant Number	Project Period	Grant Title	ABC	Program Code	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
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08 - Biopsychosocial Oncology:

Research Support

Research: NCI

Carver, Charles	NIH-NCI	1 R01 CA64710-01	10-01-94 08-30-96	Adjustment To Breast Cancer Among Younger Women (supplement: Lifestyle and Breast Cancer in Cultural and Sexual Minorities)	B	08	38,461	49,999	38,461	49,999
Carver, Charles	NIH-NCI	1 R01 CA64710-01	07-01-94 08-30-98	Adjustment to Breast Cancer Among Younger Women	B	08	107,717	164,926	107,717	164,926
Weiss, Sharlene	NIH-NCI	NOT AVAILABLE	08-30-94 08-30-95	PDOQ/PIF Evaluation In Multiethnic Populations	A	08	23,148	25,000	23,148	25,000
Sub-Total Research: NCI								239,925	169,326	239,925

Research: Other NIH

Schneiderman, Neil	NIH-NIMH	1 P01 MH495480-2	02-01-93 01-31-98	Behavioral Management and Stress Responses In HIV-1	C	08	838,240	1,005,888	838,240	1,005,888
Sub-Total Research: Other NIH								1,005,888	838,240	1,005,888

Research: Other Peer Reviewed

Antoni, Michael H	ACS-National	PBR-82	07-01-93 08-30-95	Coping With Breast Cancer Among Low SES Blacks And Hispanic	B	08	99,725	124,656	99,725	124,656
Sub-Total Research: Other Peer Reviewed								124,656	99,725	124,656

Research: Non Peer-Reviewed

Antoni, Michael H	Dutch Cancer F	INGN-0030	01-01-92 12-31-96	Behavior Intervention In Psycho-Oncology	B	08	60,000	60,000	60,000	60,000
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Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI	Fund Source	Grant Number	Project Period	Grant Title	ABC	Program Code	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
Sub-Total Research: Non Peer-Reviewed										
							60,000	60,000	60,000	60,000
Sub-Total Research Support										
							1,167,291	1,430,469	1,167,291	1,430,469

Training Support

Training: Other NIH

Schneiderman, Neil	NIH-NIMH	1 T32 MH18917-01	01-01-94 12-31-98	Biopsychosocial Research Training in Immunology and AIDS	C	T	171,427	205,712	171,427	205,712
Sub-Total Training: Other NIH										
							171,427	205,712	171,427	205,712

Training: Other Peer Reviewed

Antoni, Michael H	DOD	DAMD17-94-J-4236	09-01-94 08-14-98	Biopsychosocial Research Training in Breast Cancer	B	T	71,996	80,409	71,996	80,409
Sub-Total Training: Other Peer Reviewed										
							71,996	80,409	71,996	80,409
Sub-Total Training Support										
							243,423	286,121	243,423	286,121
Sub-Total 08 - Biopsychosocial Oncology										
							1,410,714	1,716,590	1,410,714	1,716,590

Summary 2 - Existing Funded Projects

by Program Area / Fund Source

PI	Fund Source	Grant Number	Project Period	Grant Title	ABC Program Code	%	Direct Cost Annual	Total (Direct + Indirect)	Program Amount (Direct)	Program Amount (Total)
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Report Totals for All Grants

Total All Research Support	1,167,291	1,430,469	1,167,291	1,430,469
Total All Training Support	243,423	286,121	243,423	286,121
Total All Other Support	0	0	0	0
Total for All Grants	1,410,714	1,716,590	1,410,714	1,716,590