The University of Texas M.D. Anderson Cancer Center Leukemia SPORE

Principal Investigator: Hagop M. Kantarjian, M.D.
1515 Holcombe Blvd, Box 428
Houston, Texas 77511
(713) 792-7026 – (713) 792-2031 (fax)

Overall Abstract

The University of Texas M.D. Anderson Cancer Center is proposing a Specialized Program of Research Excellence (SPORE) in Leukemia. The primary goal of this Leukemia SPORE is to cultivate and facilitate innovative and significant translational research in the biologic, genetic and clinical aspects of leukemia to improve understanding, therapy, and prognosis. The multidisciplinary group of investigators in the Leukemia SPORE will accomplish this goal through effective integration of laboratory, epidemiologic and clinical investigations. Such activity will further our understanding of genetic susceptibility and leukemogenic molecular processes in leukemia, leading to novel, molecularly targeted strategies in leukemia. The SPORE is designed with 6 research projects and 3 core resources, as well as programs for developmental research and career development. The research projects are designed to target specific areas important in leukemia. Project 1 - Epigenetics of Drug Resistance in Acute Leukemia –targets methylation for therapy in leukemia Project 2 –Adoptive Cellular Therapy of Myeloid Leukemia – targets the use of MPO-Specific Cytotoxic T Lymphocytes (CTL) to treat leukemia Project 3 – Concerted Blockade of Oncoprotein Activity – targets sequential DNA, RNA and oncoprotein blockage in leukemia Project 4 –PPAR-gamma Nuclear Transcription Factor: A Novel Target for Leukemia Therapy – targets PPAR-gamma expression for leukemia therapy Project 5 – Molecular Epidemiology of AML Risk and Progression – evaluates genetic-molecular susceptibilities to development of AML through studies of relevant detoxifying and carcinogenesis-promoting pathways Project 6 – Response of AML Patients to FLT3 Inhibitors – targets FLT3 ligand inhibition in leukemias expressing FLT3 mutations or internal tandem duplication (ITD)Core and other resources are: Core A – Administration, Core B - Pathology and Tissue, Core C - Biostatistics & Data Management, Developmental Research Program, and Career Development Program. Through this leukemia SPORE, our research team will make a significant impact on leukemia prognosis.

Project 1
Epigenetics of Treatment Resistance in Acute Leukemia

Co-Principal Investigator(s): Jean-Pierre Issa, M.D.; Hagop M. Kantarjian, M.D.

Most patients with acute myelogenous leukemia (AML) can achieve complete remissions using chemotherapy; however, relapse with drug-resistant disease is the main cause of failure in AML. While it is assumed that drug resistance results from clonal evolution, the molecular determinants of this process remain incompletely understood. CpG island methylation is a recognized marker of transcriptional silencing in human cells. Such

silencing is clonal and appears to be an alternate mechanism of tumor-suppressor gene inactivation. In AML, hypermethylation-associated silencing is frequent and affects multiple genes. Based on the prominent role DNA methylation appears to play in some AMLs and data suggesting that some genes are differentially methylated in relapsed leukemias, we hypothesize that aberrant CpG island methylation contributes to the drug resistance phenotype in AML by silencing genes whose functions are critical to sensitivity to chemotherapy. In this project, we propose to identify such drug resistance genes. We further hypothesize that methylation of these genes is a marker of poor prognosis and that pharmacologic reversal of aberrant methylation will lead to a higher response and cure rate for leukemias exhibiting this drug resistance phenotype.
To test these hypotheses, we will address the following specific aims:

- Clone CpG islands that are specifically methylated in drug-resistant AML.
- Test the prognostic value of new and candidate methylation markers in primary AML.
- Test the effect of methylation inhibitors alone and in combination with histone deacetylase inhibitors on expression of candidate methylation markers and drug sensitivity in leukemia cell lines.
- Determine, in clinical trials, the effects of DNA methylation inhibitors alone and in combination with histone deacetylase inhibitors on reversal of drug resistance in patients with AML, and if effects on drug resistance are mediated through reactivation of methylated genes.

Through these studies, we will determine the clinical utility of demethylation and histone deacetylation in sensitizing resistant leukemias to standard chemotherapy; these approaches will have significant benefit for patients with poor prognosis AML.

Project 2
Adoptive Cellular Therapy of Myeloid Leukemia

Co-Principal Investigator(s): Jeffrey Molldrem, M.D.; Richard Champlin, M.D.

The potent graft versus leukemia effect (GVL) associated with allogeneic bone marrow transplant (BMT) can produce lasting remissions in patients with myeloid leukemia, but the potentially lethal complication of graft versus host disease (GVHD) limits the effectiveness of this treatment. Donor T cells mediate both GVL and GVHD, although the target antigens recognized by these T cells are not known. We hypothesize that GVL would be enhanced and GVHD reduced or eliminated if the target antigens that drove those responses were identified and if T cells with GVL antigen specificity could be isolated and adoptively transferred to leukemia patients. We identified the first human leukemia-associated T cell antigen as PR1, an HLA-A2 restricted nonomer peptide derived from proteinase 3, an aberrantly expressed myeloid-restricted protein in leukemia cells. PR1/HLA-A2 tetramers were used to identify PR1-specific cytotoxic T lymphocytes (CTL) in chronic myeloid leukemia (CML) patients in cytogenetic remission after either interferon or BMT treatment. Using the same deductive strategy that identified PR1, we have shown that CTL with specificity for another antigen, MY4, an HLA-A2 restricted nonomer peptide derived from myeloperoxidase, comprise up to 3% of all CTL in acute myeloid leukemia (AML) patients that are in remission after nonmyeloablative stem cell transplant (NST) but are not detectable in patients that relapse. Furthermore, MY4-specific CTL, like PR1-specific CTL, selectively kill AML cells but not healthy bone marrow cells or epithelial cells, a target of GVHD. In this proposal, we will (1) apply this deductive strategy to uncover additional CTL leukemia-associated

antigens (LAA), (2) determine whether LAA-specific CTL are present in patients that receive NST and (3) use LAA peptide/MHC tetramers to select and expand CTL for adoptive transfer into recipients of NST to enhance GVL and reduce GVHD.

Project 3
Concerted Blockade of Oncoprotein Activity

Co-Principal Investigator(s): William Plunkett, Ph.D.; Varsha Gandhi, Ph.D., Jorge Cortes, M.D., Co-Investigator: Rajyalakshmi Luthra, Ph.D.

Survival of tumors such as CML are uniquely dependent on the activity of oncogenes that confer a gain of function. Inhibition of the BCR/ABL function by a variety of means has provided voluminous evidence of the requirement of this oncoprotein for tumorigenesis and maintenance of CML. The impressive clinical success of STI571 (Imatinab mesylate) against chronic myelogenous leukemias and acute lymphocytic leukemias expressing this oncoprotein emphasizes the importance of developing therapeutic strategies aimed at this target. However, evaluation of therapeutic outcome has demonstrated that failure to completely inhibit the activity of BCR/ABL kinase may permit resistance. We hypothesize that therapeutic approaches that decrease expression of target oncoproteins that are essential for tumorigenesis will complement the actions of specific enzyme inhibitors. The goals of this project are to validate and implement a sequential blockade strategy that will diminish expression of BCR/ABL. Specifically, we will develop therapeutic strategies to inhibit transcription of the oncogene and translation of its message that will complement the actions of inhibitors of its enzymatic activity. In such a sequential blockade of molecular target synthesis and activity, the biological context of tumorigenesis will provide the basis for specificity, both in cell lines and in primary leukemia cells during translational clinical trials. To achieve these goals, we will investigate the following Specific Aims:

- Develop rationales and test proof-of-concept for the sequential blockade strategy to inactivating oncoproteins
- Evaluate the sequential blockade strategy in BCR/ABL-expressing primary leukemia cells from patients with CML or ALL
- Validate the sequential blockade concept in pharmacodynamically-designed clinical trials

Project 4
PPAR-gamma Nuclear Transcription Factor: A Novel Target for Leukemia Therapy

Co-Principal Investigator(s): Michael Andreeff, M.D., Ph.D.; Steven Kornblau, M.D.

New approaches are needed to improve cure rates in adult hematological malignancies. PPARg (Peroxisome Proliferator-Activated Receptor Gamma) is a member of the nuclear transcription factor family involved in signaling of differentiation. We have demonstrated that PPARg is expressed in the majority of primary human leukemias but not in normal hematopoietic progenitors, and that ligation of PPARg induces differentiation, growth arrest and apoptosis in leukemias. We propose to extend our initial studies on the mechanisms and efficacy of PPARg signaling in acute myeloid leukemia to acute and chronic (CLL) leukemia, with the goal of developing PPARg as a novel target for the treatment of hematological malignancies. We are encouraged to pursue this goal by the seminal impact on leukemia therapy that was affected by targeting RARa in acute promyelocytic leukemia (APL) with ATRA. First, we will

investigate the expression of PPARg in acute and chronic myeloid and lymphoid human leukemias and leukemic stem cells and study the effects of PPARg ligands on apoptosis and differentiation. We will determine the effects of combined targeting of PPARg and RXR in leukemias, as PPARg and RXR heterodimerization is required to maximize transcriptional activation. In the second aim, we will further elucidate the specific mechanisms of apoptotic cell death and growth arrest that are triggered by PPARg ligation. Preliminary data demonstrate that PPARg ligands induce loss of mitochondrial membrane potential and activation of effector caspases. Finally, we propose to initiate Phase I studies using PPARg ligands, in combination with rexinoids. These studies will utilize FDA approved PPARg and RXR ligands and the new potent triterpenoid CDDO, a novel PPARg ligand that is presently being developed by us with assistance from CTEP/RAID at the National Cancer Institute. The long-term goal of the proposed studies is to determine the molecular, biological and clinical effects of PPARg/RXR ligation in human leukemia and to develop the PPARg/RXR nuclear receptor system as a novel target for leukemia therapy.

Project 5
Molecular Epidemiology of AML
Co-Principal Investigator(s): Sarah Strom, Ph.D.; Elihu Estey, M.D.

Little is known about the epidemiologic risk factors associated with the development of acute myelogenous leukemia (AML), and less is known about the role that genetic susceptibility plays in the development of AML. We propose to conduct a population-based study to investigate genetic susceptibility in adult AML patients, both *de novo* and treatment-related in a well-defined geographical area. Using a case-control design, we will prospectively enroll 400 patients from the greater Houston area (Harris and surrounding counties) and 800 healthy controls. Controls will be recruited using random digit dialing, and will be matched to the cases by age, gender, and ethnicity. Epidemiological and demographic information will be obtained through personal interviews, and will be integrated with clinical information, cytogenetic data, and genotypic markers. Blood specimens will be collected on all participants, who will be genotyped for markers associated with activation and detoxification of chemical carcinogens, including chemotherapy drugs. Polymorphisms in genes such as cytochrome p450 (CYP2E1), glutathione S-transferases (GSTT1, GSTM1, GSTP1), epoxide hydrolase (HYL1), NADPH-quinone oxidoreductase (NQO1), and myeloperoxidase (MPO) will be analyzed.

This study will provide insight into the role that these susceptibility markers, along with clinical epidemiological, and cytogenetic factors, play in the identification of people at risk of developing AML. Understanding how genetic predisposition and exogenous exposures interact to determine AML susceptibility will allow the development of prevention strategies in the future.

Project 6
Response of AML Patients to FLT3 Inhibitors
Co-Principal Investigator(s): Don Small, M.D., Ph.D.; Jorge Cortes, M.D.

AML is the most frequent type of adult leukemia and the second most common pediatric leukemia and remains one of the most difficult to cure, with most studies reporting long-term cure rates of 30-40%. Activating somatic mutations of the FLT3 gene in patients

with AML have been discovered in the past few years. These mutations are the most frequent genetic aberration in AML and portend a worse prognosis for patients expressing them. Though the mutations occur in different parts of the FLT3 gene, they are all characterized by constitutive activation of the tyrosine kinase domain of FLT3. This presents an excellent target for the development of novel therapeutics that might improve the chance of cure for these patients.

We have spent the past several years proving that constitutive activation of FLT3 can transform cell lines and, when expressed in primary cells, results in myeloproliferative disease. We showed that inhibition of FLT3 resulted in cytotoxicity in modeled cell lines, leukemic cell lines and primary human AML samples. Most recently, we developed high-throughput cell-based assays that enabled us to screen thousands of small molecules for their ability to inhibit FLT3 in a highly potent and selective manner.

This has now led to a clinical trial of FLT3 inhibitors in AML patients with FLT3 activating mutations at Johns Hopkins that will also be opened soon at the M.D. Anderson Cancer Center. This gives us the opportunity to test hypotheses related to the mechanisms of response, resistance and synergy with chemotherapy for this class of agents, Our specific aims are:

Specific Aim 1: Determine the extent and efficacy of FLT3 inhibition by CEP-701 in clinical trial patients with AML expressing FLT3 activating mutations.

Specific Aim 2: Determine some of the mechanisms involved in resistance to CEP-701-mediated cytotoxicity in FLT3/ITD mutant trial patients.

Specific Aim 3: Utilize primary leukemic blasts from patients with AML expressing FLT3 mutations to establish the optimal combinations of chemotherapy to use with FLT3 inhibitors for future clinical trials.

These studies will improve the outcome of AML patients with FLT3 mutations who currently have a very poor prognosis.

Core A
Administration

Core Leader(s): Hagop M. Kantarjian, Jean-Pierre Issa, Elihu Estey

The specific objectives and responsibilities of the Administrative Core are:

- Oversight and support of SPORE activities, including Projects and Cores
- Compliance with general, governmental, and NCI regulations and requirements
- Communication and consultation with the NCI project officer and other NCI staff to ensure accurate and timely preparation and submissions of required reports and publications
- Coordination of data control quality assurance issues in conjunction with the Internal Scientific Advisory Board and the Biostatistics Core
- Coordination of the clinical trials activities in relation to designs, approval by regulatory bodies, implementation, and eligibility and assignment of patients to different studies
- Oversight and support for the Biostatistics and Data Management Core and the Pathology and Tissue Core
- Responsibility for fiscal and budgetary functions
- Arrangement of meetings of the Executive Committee, the Internal and External Scientific Advisory Committees, monthly investigators' meetings, quarterly research

meetings, lectures, and symposia, including the NCI annual SPORE meetings, and administrative and research retreat meeting

- Administrative support of the Developmental Research Program and the Career Development Program
- Ensuring compliance and improving policies for recruitment of women and minorities
- Coordination with other Leukemia SPORE programs and investigators, and with other organ-site SPORE programs, to promote and maintain communication and integration through sponsoring a yearly conference, and also through the distribution of materials, electronic communications and evaluation of progress reports.
- Establishment of a Leukemia SPORE website focused on leukemia translational research

Drs. Hagop Kantarjian, Jean-Pierre Issa and Elihu Estey will lead the Administrative Core. All three co-leaders have extensive experience and expertise in the successful and productive management of large, multidisciplinary research programs. The Core leaders have already established and work to maintain good working relationships with members of the National Cancer Institute and National Institutes of Health and are familiar and in compliance with policies and procedures required of NCI- and NIH-funded research programs.

Core B
Pathology and Tissue Core
Core Leader(s): Maher Albitar, Steven Kornblau

Effective tissue procurement and utilization is vital for meaningful translational research activities. The Pathology and Tissue Core will work with each SPORE project and the Biostatistics and Data Management Core to ensure efficient and highly coordinated procurement, use and storage of blood and bone marrow samples. The Core will obtain and maintain a repository of blood samples (including peripheral blood, bone marrow biopsies, and bone marrow aspirates) for laboratory use, with an effective coding system for all laboratory specimens to ensure patient confidentiality and prevent experimental bias. Continuous communication between the investigators, research nurses, biostatisticians and hematopathologists, as well as standardized operating procedures for activities will provide for optimal tissue collection and accurate processing, analysis and storage of each sample. Thus, the functions of the Pathology and Tissue Core are to facilitate acquisition, preservation, analysis and dispersal of clinical samples and to provide hematopathologic characterization and specimens for all project investigators.

The Tissue Procurement and Hematopathology Core has the following objectives:

- Develop and maintain a repository of blood and bone marrow specimens, including intact cells, serum, cellular DNA, RNA and protein, from patients with leukemia and MDS (including patients who are newly diagnosed, in remission or in relapse) receiving care or evaluation at M.D. Anderson Cancer Center. Distribute tissue specimens to SPORE investigators for analysis and provide expertise in the interpretation of studies performed on tissue sections within SPORE projects Provide comprehensive histologic characterization of blood and marrow samples used in SPORE projects, including specimens from patients entered onto clinical protocols.
- Maintain a comprehensive, prospective interactive database with detailed clinical and pathologic data for patients with leukemia and MDS receiving care or evaluation at M.D. Anderson Cancer Center

Facilitate inter-SPORE collaborations through sharing of blood and marrow resources.

Core C
Biostatistics and Data Management
Core Leader(s): Donald Berry, Terry L. Smith

The Biostatistics and Data Management Core for the University of Texas M.D. Anderson Cancer Center Leukemia SPORE will be a comprehensive, multilateral resource for data acquisition and management, design of laboratory experiments and clinical trials, development of innovative statistical methodology, statistical analysis, and publishing translational research generated through the Leukemia SPORE program.
The Biostatistics and Data Management Core will incorporate sound experimental design principles within all Projects, will carry out data analyses using appropriate statistical methodology, and will contribute to interpretation of results through written reports and frequent interaction with Project investigators. The Biostatistics and Data Management Core will provide an integrated data management system to facilitate communication among all Projects and Cores, which will be customized to meet the needs of the Department of Leukemia. This process includes prospective data collection, data quality control, data security, and patient confidentiality. Thus, from inception to reporting, translational experiments will benefit from SPORE resources that will be used to augment existing M. D. Anderson biostatistics resources.

To serve all proposed SPORE projects, as well as the Career Development and Developmental Research Programs, the Biostatistics and Data Management Core has the following objectives:

- Provide biostatistical expertise in the design and conduct of laboratory experiments and clinical trials arising from the research proposed in this application
- Provide statistical analysis and interpretation of all data collected under the SPORE Projects, Developmental Projects, and other Cores
- Provide reliable data capture and storage functions, user-oriented retrieval capability, and effective mechanisms for ensuring patient confidentiality

Developmental Research Program
Director(s): Jean-Pierre Issa, Hagop M. Kantarjian

The leukemia SPORE Developmental Research Program will be a source of seed funding to: 1) encourage and explore innovative translational ideas focusing on leukemia, and 2) encourage successful researchers working in other fields to focus their expertise towards the development of innovative translational projects in leukemia. The program will support projects with testable translational hypotheses that have foreseeable clinical relevance for therapy and prognosis of leukemia, and significant impact on changing therapy and prognosis in leukemia. The identification and funding of new ideas will be through a peer-review mechanism. Announcements for developmental funding opportunities will be made twice each year. Up to 4 projects will be funded every year depending on the quality and relevance of the submitted proposals. The program will solicit and advertise for such proposals institutionally and from investigators outside the institution. Initial proposals should be no more than 5 pages and should

clearly focus on leukemia-related translational research. This will then be followed by a 10-page proposal submission patterned after the NIH R01 submissions. Competing proposals will be reviewed by the Developmental Program Committee which includes relevant experts from the Leukemia SPORE Co-PI's, Scientific Internal Advisory Board, and three External Scientific Advisory Board members. Proposals will be ranked and the best 3-4 funded for 1 year, with potential for a renewal for an additional year. Promising projects may be renewed, encouraged to obtain other peer-reviewed support, or expanded and approved as full SPORE projects to replace others that have been completed or judged not successful. As part of our preparation for the Leukemia SPORE, an institution-wide announcement and solicitation resulted in the selection of several projects judged to be potentially meritorious pilot projects with focused relevance on leukemia translational questions. These projects represent diverse areas of research in leukemia and are described briefly later. Each of the projects illustrates direct relevance to leukemia, demonstrates the potential for translation of the research into clinically relevant approaches to leukemia care and prognosis, and could integrate with, or become in the future a full leukemia SPORE project. These projects are described briefly as illustrative examples of the success of the process, but will be later reviewed as part of the total pool of proposals which will follow the formal solicitation process as outlined, and which will consider both institutional and nationwide proposals.

Career Development Program

Director(s): Jean-Pierre Issa, Hagop M. Kantarjian

The Career Development Program aims to encourage and provide training and guidance for academic physicians–scientists, clinician-investigators, and laboratory-based scientists who want to dedicate their endeavors to leukemia translational research. To achieve these aims, the Career Development Program will develop the following objectives:

1. Recruit and train physicians, scientists, and senior postdoctoral fellows to become excellent translational investigators in leukemia research;
2. Educate awardees in the basic principles of cancer biology, at both the molecular and cellular level, with an emphasis on translational science;
3. Provide a firm foundation for awardees in the specific area of leukemia biology, laboratory, clinical and epidemiologic evaluation;
4. Guide awardees to becoming effective leukemia translational researchers.

These objectives will be accomplished through a strong mentorship program. Awardees will be instructed in the principles of leukemia clinical and basic research. The Career Development Program will recruit senior medical or laboratory-based postdoctoral fellows and junior faculty who wish to develop a career in leukemia translational research. In addition, established senior faculty who wish to re-direct or extend their ongoing research programs into leukemia research will be eligible for participation. The unique educational environment that exists at the M.D. Anderson Cancer Center will add much to achieving our goals. Individuals who will make a two-year commitment in their training will be given preference, since this amount of training is ideal to obtain in-depth knowledge to be highly successful in a career of leukemia translational research. Three Career Development awardees will be selected in the first and each subsequent year. Solicitations will be made for qualified candidates from within and outside the M.D. Anderson Cancer Center. Minorities and women will be encouraged to apply.

Leukemia SPORE Investigators

Kantarjian, Hagop M., M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Issa, Jean-Pierre, M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Albitar, Maher, M.D.
UT M.D. Anderson Cancer Center
Pathology, Box 85
1515 Holcombe Boulevard
Houston, Texas 77030

Andreeff, Michael, Ph.D.
UT M.D. Anderson Cancer Center
Blood & Marrow Transplantation
1515 Holcombe Boulevard, Box 448
Houston, Texas 77030

Berry, Donald, Ph.D.
UT M.D. Anderson Cancer Center
Biostatistics
1515 Holcombe Boulevard, Box 447
Houston, Texas 77030

Champlin, Richard E., M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Cortes, Jorge, M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Estey, Elihu, M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Gandhi, Varsha, Ph.D.
UT M.D. Anderson Cancer Center
Experimental Therapeutics
1515 Holcombe Boulevard, Box 0071
Houston, Texas 77030

Garcia-Manero, Guillermo, M.D.
UT M.D. Anderson Cancer Center
Dept. of Leukemia
1515 Holcombe Boulevard, Box 428
Houston, Texas 77030

Hamilton, Stanley, M.D.
UT M.D. Anderson Cancer Center
Pathology, Box 85
1515 Holcombe Boulevard
Houston, Texas 77030

Konopleva, Marina, M.D., Ph.D.
UT M.D. Anderson Cancer Center
BMT- Research, Box 0081
1515 Holcombe Boulevard
Houston, Texas 77030

Kornblau, Steven, M.D.
UT M.D. Anderson Cancer Center
Blood & Marrow Transplantation
1515 Holcombe Boulevard, Box 0048
Houston, Texas 77030

Levis, Mark, M.D., Ph.D.
Johns Hopkins University
24 Sandview Ct.
Baltimore, MD 21209

Luthra, Rajyalakshmi, Ph.D.
UT M.D. Anderson Cancer Center
Pathology - Research
1515 Holcombe Boulevard, Box 0085
Houston, Texas 77030

Molldrem, Jeffrey, M.D.
UT M.D. Anderson Cancer Center
Blood & Marrow Transplantation
1515 Holcombe Boulevard, Box 448
Houston, Texas 77030

Plunkett, William, M.D.
UT M.D. Anderson Cancer Center
Experimental Therapeutics
1515 Holcombe Boulevard, Box 0071
Houston, Texas 77030

Small, Donald, M.D., Ph.D.
Johns Hopkins University
1650 Orleans Street
Baltimore, MD 21231

Smith, Terry L., M.S.
UT M.D. Anderson Cancer Center
Biostatistics
1515 Holcombe Boulevard, Box 447
Houston, Texas 77030

Spitz, Margaret, M.D.
UT M.D. Anderson Cancer Center
Epidemiology
1515 Holcombe Boulevard, Box 0189
Houston, Texas 77030

Strom, Sara, Ph.D.
UT M.D. Anderson Cancer Center
Epidemiology
1515 Holcombe Boulevard, Box 0189
Houston, Texas 77030

Wu, Xiuyuan, M.D.
UT M.D. Anderson Cancer Center
Bone Marrow Transplantation
1515 Holcombe Boulevard, Box 0065
Houston, Texas 77030