

Principal Investigator: [REDACTED]

**Academic Hematology Career Plans:**

*Goal:* My academic career goal is to become an independent clinician researcher in the field of cancer and aging, with a focus on the relationship between functional status and cancer therapy in older adults. There are multiple aspects of this relationship that I wish to investigate, including: 1) the predictive value of baseline physical function and cognition on treatment response and toxicity in older adults; 2) the impact of cancer therapy on physical function and cognition in older adults; and 3) interventions to minimize disability in older cancer patients.

*Training to Date:* I have completed fellowships in both Geriatric Medicine and Hematology and Oncology at Wake Forest University Medical Center. In addition, to develop my skills in research methodology I am enrolled in the Masters of Health Sciences Research program at Wake Forest University Graduate School. I have completed the course work and will begin writing my masters thesis in the fall of 2006, with graduation anticipated in the spring of 2007. My masters thesis will investigate the association between physical performance measures at the time of cancer diagnosis and development of disability in older cancer patients, through a secondary analysis of the Health Aging and Body Composition Study.

*Additional Training:* During Year 1 of the ASP-ASH award, I plan to complete my Masters of Health Sciences Research (described in the previous paragraph). During Year 2 I plan to attend the AACR/ASCO workshop on Methods in Clinical Cancer Research, which will provide additional exposure to research methodology with a focus on trial design in cancer research. This training will be directly relevant to submission of a proposal for a full-scale study building on the proposed pilot study. During Year 3, the Summer Institute on Design and Conduct of Randomized Clinical Trials through the Office of Behavioral and Social Sciences Research at the NIH would provide additional training on the design of behavioral intervention studies. This training will be directly relevant to designing interventions to improve outcomes in the elderly based on the results of the full-scale study. Funding for these additional training opportunities is available from internal Wake Forest resources.

*Mentorship Team:* I have established a cross-disciplinary mentoring team to provide guidance in research methodologies and the clinical practice of geriatrics and oncology. [REDACTED] is the Section Head of Hematology and Oncology and Director of the Acute Leukemia Service, and is actively involved in my career development as both a clinician and researcher, particularly from the oncology perspective. [REDACTED] is an experienced geriatrician with expertise in cognition and clinical trials research in older adults, and provides key insights from the geriatrics perspective. [REDACTED] is an experienced cancer epidemiologist with a focus on cancer survivorship and the interaction of the cancer and aging process who serves as a mentor in research methodology. [REDACTED] is the chair of my thesis committee, which includes [REDACTED] and [REDACTED] and which will meet regularly throughout the development of my thesis. In addition, I meet on a monthly basis with each mentor individually, and with the team on a quarterly basis. The goal of these meetings is to provide me with broad guidance on my career direction and advice on specific clinical and research issues arising in the course of my work.

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***Involvement with Education:*** I am actively involved in the introduction of geriatric oncology into the didactic curriculum for medical students, geriatric fellows and hematology and oncology fellows. I have provided a yearly lecture to the 1<sup>st</sup> year medical students entitled "Aging Influences: hematopoiesis, anemia and malignancy". I participate in case conferences for the third year medical students as well as morning report for internal medicine residents. I have incorporated lectures on aging and malignancy into the Geriatric fellowship Core Conference Series and have helped develop a case conference for the oncology fellows. In addition, I regularly attend multidisciplinary conferences including Tumor Board, Thoracic Oncology and Hematopathology Conference. I am directly involved with resident and fellow training through the Geriatric Oncology Clinic and am committed to the importance of educating trainees about the unique issues related to the care of older adults.

***Involvement with Patient Care:*** I have helped design and implement the Wake Forest University Health Sciences Geriatric Oncology clinic, which focuses entirely on providing the highest level oncologic care to patients aged 75 and older. In addition this clinic will provide unique opportunities for research and a vehicle with which to teach geriatric oncology principles to students, residents and fellows. I will continue to be the physician responsible for this clinic, and also will attend on the inpatient oncology ward and the inpatient consultation service.

***Progression Toward an Independent Research Career:*** Over the next five years I intend to investigate the relationship between functional status and cancer therapy through analyses of epidemiologic data and design of clinical studies in older adults. This proposed pilot study will provide valuable preliminary information regarding the feasibility and predictive value of functional and cognitive assessment in older adults with acute myelogenous leukemia. Results from this study will be used to incorporate functional assessment measures into the design of a larger multi-center clinical trial to develop a prospectively validated algorithm of risk stratification for older adults. In addition, the experience gained as a principal investigator of a research study in older patients with malignancy will be invaluable for the successful design and implementation of future studies in this population, including studies examining the predictive value of functional and cognitive assessment in other cancers.

In addition to the proposed pilot study and my thesis, both described above, I recently completed a retrospective study investigating the clinical predictors of transplant related mortality in older adults treated with autologous stem cell transplantation. Findings have been presented at two national scientific meetings and a manuscript is under development. I also am participating in a series of discussions with cancer center colleagues about research opportunities in cancer and aging, and plan to collaborate on at least one additional funding proposal and one project per year.

***Summary:*** My unique training background and strong mentoring team puts me in a position to develop a successful career as a clinician researcher in geriatric oncology and become a leader in the field. I hope to impact the approach to older adults with malignancy in the research and clinical setting. This proposal is an important component of my career development and will provide the foundation for future research focused on translating geriatric principles into the care of older adults with hematologic malignancies.

Career Development Plan

Osteoarthritis (OA) is a disease which increases in prevalence with age, and is a leading cause of disability in elders. At present, there are no known treatments that alter the progression or incidence of OA. Given the aging of our population, this represents a huge public health issue that will have a tremendous burden on our society and health care system. Further, from an individual point-of-view, the pain and disability due to OA can lead to loss of independence and diminishment in quality of life for older adults. Thus, from both a patient perspective and a societal perspective, research into the underlying determinants of OA and therapies for OA are of great importance to a geriatric population. Focusing my research efforts in OA will complement the aim of this grant, which is to implement a career focused on the geriatrics aspects of rheumatology. Thus, my long-term career goals are to develop a clinical research program focusing on rheumatologic diseases of older adults, with a specific interest in OA, evaluating risk factors and treatment for the symptoms and structural changes of the musculoskeletal system that increase in prevalence with age.

I have completed my training in internal medicine as well as rheumatology, and am board-certified in both specialties. Most of the rheumatologic conditions that I manage in my clinical practice are diseases of older adults. I am currently an Assistant Professor at Boston University School of Medicine, and am pursuing a doctoral degree in Epidemiology through the School of Public Health at Boston University. Thus my clinical training, as well as the methodologic training I am acquiring through my doctoral degree will set a strong foundation for my future career as a clinical rheumatology researcher, with a focus on the epidemiologic and geriatrics aspects of rheumatic diseases. The goals of this proposal are to study the effects of abnormal bone quality and malalignment on bone abnormalities in OA, and how such bone abnormalities may contribute to the progression of OA. The findings from this study would provide new avenues for evaluating potential therapies in the management of OA, a disease for which there are no effective current therapies.

Mentorship team:

██████████ a Professor of Medicine and Chair of the Clinical Epidemiology Research and Training Unit at Boston University, is a world-renowned expert in epidemiologic studies of osteoarthritis and will serve as my primary research mentor. He is the Director of the Boston University Clinical Research Training Program (CREST), which offers an institution-wide structured clinical research training program for fellows and junior faculty interested in pursuing clinical research careers.

██████████ a geriatrician, is the Director of Medical Research at the Institute for Aging Research, Hebrew SeniorLife, and Associate Professor of Medicine at Harvard Medical School Division on Aging. He currently serves as the Core Leader for the Research Development Core of the Harvard Medical School Claude Pepper Older American Independence Center program project. ██████████ has an expertise in evaluating nutritional risk factors for osteoporosis and osteoarthritis, which are relevant to the current study.

██████████ is a nutritional scientist and Director of the Vitamin K Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA), Director of the

Biochemical and Molecular Nutrition Program at the Friedman School of Nutrition Science and Policy at Tufts University, and Associate Professor at the Friedman School of Nutrition Science and Policy at Tufts University. She is a leading expert on vitamin K and other nutritional factors that are important in bone health, and will provide that expertise relevant to the current study.

All three mentors have worked together on the Framingham Osteoarthritis Study, evaluating risk factors for osteoarthritis and osteoporosis, two diseases common to older adults, with direct relevant to the current study.

Mentoring team plan:

I will meet with my primary mentor, [REDACTED] on a weekly basis (each Tuesday, 2-3pm, with additional meetings as necessary) to discuss all aspects of my research projects as well as career development plans. Specifically, we will discuss issues surrounding data collection, data cleaning, data analysis, and interpretation of results. With his expertise in OA and bone-related features of OA as measured on MRI, [REDACTED] will provide guidance regarding appropriate measures to study for this project. In terms of career development, we will discuss future avenues for research in the area of vitamin K and osteoarthritis, as well as developing new research interests. In addition, I will attend the weekly research development meeting called RESCU (Research Evaluation and Statistical Core Unit), which has been elaborated upon in the Career Development section of this application. As mentioned, this weekly meeting is part of the Core Unit of the NIH-funded Boston University Multidisciplinary Clinical Research Center Grant for which [REDACTED] is the principal investigator. These weekly meetings are led by [REDACTED] and my research projects will be presented at these meetings for critical feedback. Project goals will include presentations at RESCU meetings, abstract and manuscript development, presentation at national and international meetings, and subsequent projects. [REDACTED] will also be a member of my thesis committee for my doctoral degree in Epidemiology, and will provide ongoing methodologic mentorship.

I will meet with both [REDACTED] and [REDACTED] on a monthly basis for guidance on my project, with an emphasis on aspects of the project for which they have particular expertise. [REDACTED] will provide an important opportunity to discuss and learn about bone metabolism and remodeling as it is pertinent to osteoarthritis. This will be critical in developing new hypotheses and avenues of research as they related to OA and bone. As well, as a geriatrician, [REDACTED] will ensure that I develop an appropriate geriatrics focus in my research, not only with respect to the questions I pose, but also with respect to how studies are conducted to address the particular needs and difficulties faced by older adults. [REDACTED] expertise in vitamin K and nutrition will be important in not only ensuring high quality vitamin K measures, but also for interpreting results and developing new research questions. Both [REDACTED] and [REDACTED] also have an expertise in vitamin D research. Additionally, [REDACTED] and [REDACTED] are welcome to attend the weekly research meetings ("RESCU") when our collaborative project is being presented. I will also have the opportunity to present aspects of this research project at various stages to both [REDACTED] and [REDACTED] research groups. My meetings with my co-mentors will also afford the opportunity for further career development discussion, and for feedback on any abstracts and manuscripts that arise out of this project.

Structured Geriatrics Activities:

In the course of my regular clinical and teaching duties, I will have an opportunity to be involved in geriatrically-oriented teaching. In my one-half day weekly clinic and annual one-month of Rheumatology consults attending, I will be supervising and teaching medical students, residents, and rheumatology fellows. Given that the majority of patients in my practice and seen on consults are elderly, this will afford the opportunity to teach trainees about the management of rheumatic conditions which occur in the elderly, and the special issues that one must take into account when managing these diseases in the elderly. I will also be involved in teaching monthly journal clubs and giving talks to the medical residents, which often involve issues pertinent to geriatric populations. Finally, I will be involved in teaching second year medical students during the rheumatology portion of their course entitled, "Biology of Disease", which will involve discussion of rheumatic conditions which occur in the elderly.

My structured geriatrics activities will be four-fold. First, the Geriatrics Section at Boston Medical Center became a Center of Excellence in 1998, funded by the John a. Hartford Foundation. The mandate of this Center is to "attract additional outstanding physicians to careers as geriatrically-oriented faculty". One of its foci is to produce future leaders in geriatrics research, and to have such professionals "meet the health needs of increasing numbers of elderly". Scholars participating in this program have included those in the following disciplines: general internal medicine, family medicine, psychiatry, physical medicine and rehabilitation, emergency medicine, gynecology, cardiology, hematology/oncology, urology, and geriatrics. I plan to attend the Geriatrics Content Module, which is offered each summer and occurs on a weekly basis. [REDACTED] the Chief of the Geriatrics Section, has agreed to have me attend these sessions. For the summer of 2006, the topics include dementia and delirium, biology of aging, polypharmacy, rehabilitation, falls, osteoporosis, etc. Throughout the year there is a weekly Geriatrics Conference series which is a combination of clinical topics, journal club, interdisciplinary EBM clinical conferences, and research. Additionally, the Geriatrics Section sponsors the Dean Faulkner Visiting Professorship in Geriatrics, during which the Professor gives conferences for the Section as well as Medical Grand Rounds. This past year's Professor was [REDACTED] the Director of Longitudinal Studies at the NIA. I would attend these events on a yearly basis.

Second, the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) at Tufts University, is the institution at which one of my mentors and collaborators, [REDACTED] is located. The HNRCA's investigators conduct studies on nutrition and aging. Given that one of the main areas of investigation that I am pursuing is vitamin K's relation to osteoarthritis, furthering my understanding of nutrition and aging would be beneficial to my research and enable another venue for achieving further geriatrics-related training. According to the HNRCA website, their "research focuses on determining nutrient requirements necessary to promote well-being for older adults. HNRCA scientists examine how nutrition plays a major role in the prevention of the major chronic degenerative conditions associated with aging." The HNRCA holds weekly seminars which I will attend. Past topics have included talks about specific nutrition factors and skeletal muscle, obesity (a major risk factor for OA), immunity, exercise, bone remodeling, as well as nutritional interventions in community-living frail elderly.

Third, I will continue to participate in a weekly research development meeting called RESCU (Research Evaluation and Statistical Core Unit), attended by rheumatology clinical research physicians, physical therapy researchers, work disability researchers, epidemiologists, biostatisticians, and researchers in-training. This weekly meeting is part of the Core Unit of the NIH-funded Boston University Multidisciplinary Clinical Research Center Grant. At this meeting, researchers present their works-in-progress to receive feedback from peers with diverse expertise for the purpose of improving the final product prior to formal presentation or submission. I will periodically present my work to this group for feedback. Among the participants in this group, we have researchers who are primarily interested in the functional limitations and disability experienced by elders with OA, including community barriers and facilitators and work disability, those who are evaluating the risk for falls in institutionalized elderly, as well as those who are investigating various etiologic and therapeutic aspects of OA. My weekly participation in this meeting will allow me to be exposed to these various research areas that encompass geriatrics-related research issues in rheumatology. As well, I will have an opportunity to present my work at seminars that I will attend as part of my doctoral degree in Epidemiology program, which will allow further methodologic feedback on my current work.

Fourth, my meetings with my co-mentors will also serve to provide a focus on the geriatrics aspects of rheumatology as it pertains to my research, as outlined in their letters and the mentoring plan. Specifically relevant to geriatrics, I will be meeting with [REDACTED] on a monthly basis to discuss my projects. As a geriatrician, he will be an important member of my team to help me think about the geriatric aspects of my projects, not only from a scientific point-of-view, but also with respect to study design. He will also provide guidance as to the implications of my study findings for a geriatrics population.

#### Research Activities:

With the protected time afforded by this award, in addition to my structured geriatrics activities and meeting with mentors, I will spend at least 75% of my time on my proposed research activities, which will focus on evaluating risk factors for bone pathology in OA. This data will be used to support an independent investigator grant application (R01) to the NIH that will enable me to establish an independent line of research inquiry for myself. Specifically, should this study demonstrate that mechanical and/or systemic factors contribute to abnormal bone pathology in OA, this would support future studies of therapies directed at altering the mechanical and/or systemic abnormalities as potential treatments for OA.