DANA-FARBER CANCER INSTITUTE | BRIGHAM AND WOMEN'S HOSPITAL

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# *The Brain-Body Interaction in Patients with Cancer: A Pilot Study to Assay Immunologic Activity in Connection with Two Exercise Programs (Modified Exercise and Qigong) in Patients with Cancer.*

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**Question 1:**

There is a large body of experimental data, both in animal and human studies, which suggest that modulation of immune cell function occurs with physical and psychological stress. Preliminary data suggests that the favorable modulation of stress in individuals may enhance protective immune function. Natural killer (NK) cell activity, T-cell and B-cell function are of central importance in tumor immunology. Recently, the elucidation of psychoneuro-immunology in patients with cancer has become an area of intense research interest. Exercise programs and meditation as a method of reducing stress and instilling various health benefits have become increasingly popular. Recent reports have suggested that a particular form of programmed exercise and meditation known as *"Qigong"* can increase levels of neurological activity and physiologic function. Further, the effect of *qigong* training on portions of two lymphocyte subsets has been investigated in healthy volunteers. The results suggest an apparent linkage between *qigong* training and an increase in the ratio and absolute numbers of CD4 positive lymphocytes in the trainee group as compared to controls. This may represent evidence for the behavioral modulation of the immune system and in turn may have a potentially beneficial effect in patients with cancer.

**Question 2:** The proposed research project has the following specific aims:

1) To obtain an initial estimate of changes in NK cell activity and related T-cell/B-cell subsets in patients with the diagnosis of breast cancer, prostate cancer, and chronic lymphocytic leukemia undergoing two exercise programs, one of which will consist of modified exercise and stretching, and the other which will combine exercise and meditation as one hour of *qigong*.

2) To assess changes in natural killer cell activity, other biologic parameters, and quality of life assessments affecting general quality of life and assessments of coping strategies in a larger trial comparing a 12 week program of modified exercise to a 12 week program of exercise plus meditation (*qigong*).

The significance and potential clinical applications of this work will be to better define whether or not the addition of meditation to exercise as compared to exercise alone has an effect on the parameters in the patients detailed above. This preliminary data will also generate a basis for additional hypotheses in studying immunologic parameters, neuroendocrinological parameters, and psychological parameters in cancer patients.

**Question 3:** Study Design.

**a) <u>Pilot Study</u>:**

The goal of this pilot study is to collect serum samples of assays of NK cell activity in connection with two exercise programs from patients with the diagnosis of breast cancer, prostate cancer, and chronic lymphocytic leukemia. Patients will either be chemotherapy or radiation naïve or at least two years from prior treatment with adequate performance status and stratified for stage of disease and non-cytotoxic therapy (eg., hormones). Each program will represent one hour of structured activity, and samples will be obtained at the start of the program (baseline), at the end of the program (1 hour), and two hours after the completion of the program (3 hours). The purpose of the study is to obtain an initial estimate of the mean and standard deviation of changes in NK cell activity, so that a future study can compare the impact of a 12 week

structured program. One exercise program will consist of one hour of light stretching; the second exercise program will combine exercise and meditation as one hour of *qigong*. Ten patients who are not currently involved in an exercise or meditation program will be enrolled in this pilot study, and will be randomized to light stretching in week 1, followed by *qigong* in week 2, or to *qigong* in week 1 followed by light stretching in week 2. By assessing patients in each exercise setting, we will be able to take advantage of with-in patient comparisons. We propose to enroll 20 patients in the pilot program, and structure the program with exercise groups of 10 individuals, which reflects the plan for the 12 week program. We do not currently have estimates of changes in NK cell activity in patients undertaking an exercise program, and so all data used for planning the comparative study will come from this pilot.

**b) Comparative trial:** This trial will compare a 12 week program of exercise to a 12 week program of exercise plus meditation. Each program will offer 3 one-hour sessions per week. Endpoints will be changes in NK cell activity, other biologic parameters, and quality of life assessments reflecting general quality of life and assessments of coping strategies.

Immunologic parameters to be measured will include bioassays of:

1. T cells: CD3, CD4/CD8 ratio, CD45RA/RO, IL-2R, and MHC Class II
2. B cells: CD19, CD5
3. NK cells: CD56, cytotoxicity (against K562)
4. CBC countings for the absolute number of immune cell subsets.

This proposal is a new study and does not constitute a continuation or extension of an existing study. At present, there is no funding for this proposal. A minimum of 20 patients will be enrolled in the pilot program and then based upon the results of this pilot, estimates of appropriate numbers in a comparative trial will be generated. At our institution which is considered one of the premier comprehensive cancer centers in the New England area, there is a more than adequate patient population available to complete the studies envisaged.

**Question 4:** The Principal Investigator (PI) is the Chairman of the Research Committee of the Complimentary Therapy Task Force, and will lead a team of clinical investigators and research scientists expert in study design and the methodology of studying the immune function and other parameters in cancer patients.

The PI is an active member of the Women Cancers Program and has expertise in breast cancer, and high dose chemotherapy.

Collaborators include Arnold Freedman, M.D. (senior clinical investigator and expert in hematologic malignancies and immunology), Philip Febbo, M.D. (clinical investigator and expert in prostate cancer), Donna Neuberg, ScD (expert in biostatistics and study design), Hoon Ryu, Ph.D. (research scientist with expertise in the laboratory study of immune function), Ramel Rones (*qigong* instructor), and Debra Fertig, M.D. (consultant psychiatrist with an expertise in the psychological needs of patients with cancer, quality of life assessment, and coping strategies).