



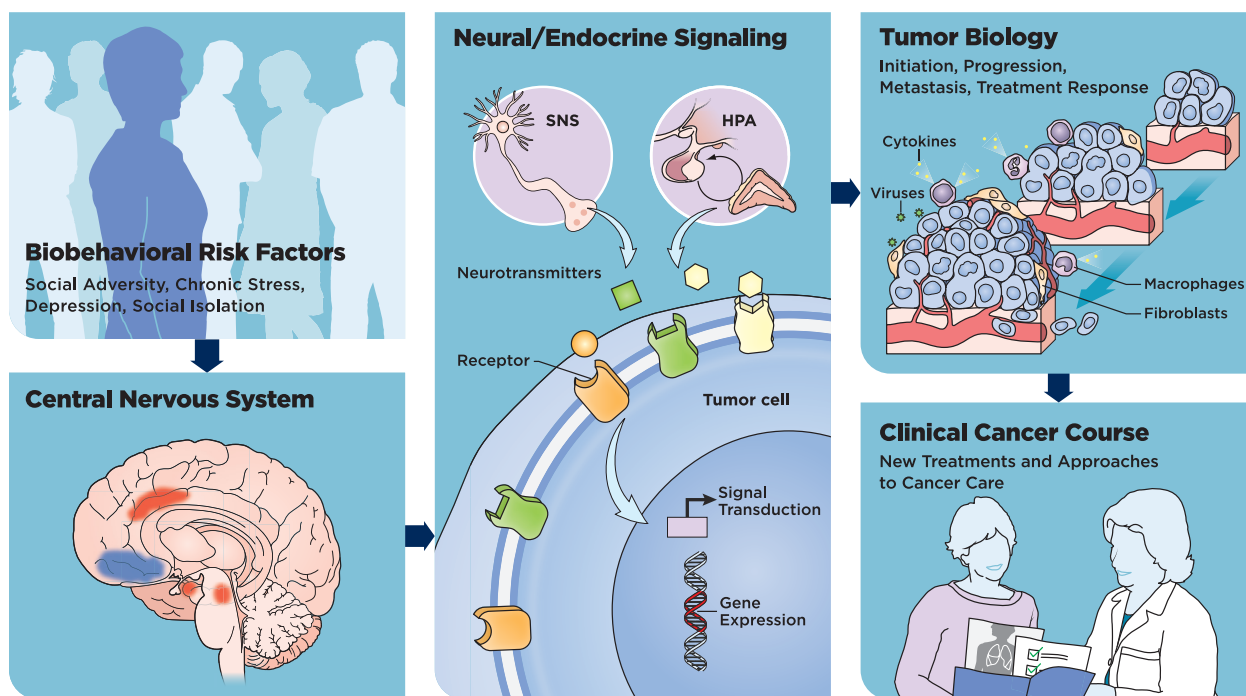
NATIONAL CANCER INSTITUTE  
**NETWORK ON BIOBEHAVIORAL  
PATHWAYS IN CANCER**

The National Cancer Institute Network on Biobehavioral Pathways in Cancer (NBBPC) accelerates the translation and communication of biobehavioral discoveries to advance clinical cancer care.

NBBPC is a consortium designed to support knowledge of the molecular and signaling pathways that link psychological, behavioral, and social factors to cancer biology and apply that knowledge toward the development of efficacious interventions to reduce cancer risk and improve clinical outcomes. NBBPC has specific interest in proof-of-concept basic and translational studies to control disease in cancer patients, prevent recurrence post-treatment, and augment disease-free survival.

Through an ongoing Request for Proposals (RFP) issued by Leidos Biomedical Research, Inc., the Network solicits proposals for small-scale pilot projects to advance the knowledge of molecular pathways that link psychological, behavioral, or social factors to cancer biology. These projects inform further research opportunities to develop effective interventions and improve clinical outcomes.

## Biobehavioral Pathways in Cancer



Heuristic framework for research on the influences of biobehavioral risk factors on clinical cancer course.

Green McDonald, P., O'Connell, M., & Lutgendorf, S.K. (2013).

Psychoneuroimmunology and cancer: A decade of discovery, paradigm shifts, and methodological innovations.

*Brain, Behavior, and Immunity*, 30(0):S1-S9. <https://pubmed.ncbi.nlm.nih.gov/23333846-psychoneuroimmunology-and-cancer-a-decade-of-discovery-paradigm-shifts-and-methodological-innovations>

# Network Pilot Projects

Funded by the National Cancer Institute (NCI)  
Contract No. HHSN261200800001E



# Pilot Project Descriptions

## Effects of Cognitive Behavioral Stress Management Intervention on Clinical Disease Endpoints in Women with Breast Cancer

**Michael H. Antoni, PhD, University of Miami**

This project consists of extensive follow-up of a randomized, controlled trial, which aims to test the effects of group-based cognitive behavioral stress management intervention versus psychoeducational control on clinical disease endpoints over an extended time in women initially treated for non-metastatic breast cancer. It examines whether specific biobehavioral and psychological adaptation processes modified by the intervention in the first year of medical treatment predict differences in clinical endpoints (e.g., survival and recurrence) up to 13 years later.

## Perioperative Use of Beta-blocker and COX2 Inhibitor

**Shamgar Ben-Eliyahu, PhD, Tel Aviv University**

This project uses multicenter randomization to assess the short-term effects of counteracting excess perioperative catecholamine and prostaglandin levels on immune, endocrine, and pro-metastatic serum and histological indices. Results of this project will be used to develop a large-scale clinical trial.

## Behavioral Pathways in Stem Cell Transplantation: CD14+ Gene Expression

**Erin Costanzo, PhD, University of Wisconsin, Madison**

This project examines gene expression patterns of CD14+ cells as a potential pathway by which stress-related psychosocial factors may influence immune recovery and clinical outcomes following hematopoietic stem cell transplantation (HSCT). The study focuses on multiple myeloma patients recovering from autologous HSCT, given evidence in this population for the role of CD14+-derived macrophages in immune recovery, as well as in angiogenesis, apoptosis, and production of disease-promoting cytokines in this population.

## Neural Substrates of Social Support

**Naomi Eisenberger, PhD, University of California, Los Angeles**

This project produced a white paper that served as the basis for the fMRI probe optimization study. The paper provides a literature review of fMRI-based research on behavioral probe paradigms and empirical neural activity correlates of social support, attachment, affiliation, and related psychological constructs.

See Eisenberger, N. (2013). An empirical review of the neural underpinnings of receiving and giving social support: Implications for health. *Psychosomatic Medicine*, 75(6):545-556. [http://journals.lww.com/psychosomaticmedicine/Fulltext/2013/07000/An\\_Empirical\\_Review\\_of\\_the\\_Neural\\_Underpinnings\\_of.6.aspx](http://journals.lww.com/psychosomaticmedicine/Fulltext/2013/07000/An_Empirical_Review_of_the_Neural_Underpinnings_of.6.aspx)

## fMRI Probe Optimization Study of Social Support

**Naomi Eisenberger, PhD, and Julianne Bower, PhD, University of California, Los Angeles**

Based on the white paper referenced above, this project aims to identify and pilot test fMRI probe tasks that can help assess whether individual differences in measures of experienced social support (as measured by the Social Provisions Scale-Attachment and the UCLA Loneliness Scale) relate systematically to individual differences in neural activity to the specialized probe tasks. Phase I of the project will be conducted in healthy volunteer subjects.

## Stress and Tumorigenesis in Normal and p53 Knockout Models

**Wenwei Hu, PhD, Robert Wood Johnson Foundation**

This project is investigating the impact of chronic stress on DNA damage accumulation, which, in keeping with the established chronic stress mouse model system, then promotes tumor initiation. Based on the recent finding that chronic stress attenuates the function of p53, a central player in tumor suppression, this project will test whether chronic stress promotes DNA damage, enhances mutation frequency and copy number variation in a largely p53-dependent manner.

## Beta-Adrenergic Regulation of Acute Lymphocytic Leukemia

**Don Lamkin, PhD, University of California, Los Angeles**

This project examines a potential downstream mechanism by which beta-adrenergic signaling accelerates progression of acute lymphoblastic leukemia (ALL). Specifically, an orthotopic mouse model of human leukemia will be used to understand the role of the CXCR4-CXCL12 chemokine system in stress-enhanced ALL progression.

## Metabolic Fingerprint of Stress Influences in Cancer

**Anil K. Sood, MD, MD Anderson Cancer Center**

This project examines unique metabolic signatures in epithelial ovarian cancer tissues from human subjects with different depression and social support profiles. Global biochemical profiles were studied in tissue samples (n=85) from patients who are categorized according to scores on biobehavioral risk factors. Mechanistic and biological studies to examine the regulation of metabolic pathways in the context of chronic stress effects on the tumor microenvironment were also conducted.

## Interactive Wiki Page

**Tor Wager, PhD, University of Colorado, Boulder**

This project provides a targeted literature review of fMRI-based research on brain stem control of sympathetic nervous system (SNS) activity, and its regulation by higher brain (e.g., cortical) regions. The interactive wiki page (<http://brainstemwiki.colorado.edu>) identifies cortical and sub-cortical brain regions of interest and the relevant fMRI probe paradigm tasks suitable for use in subsequent studies relating social support to SNS activation.

## Biobehavioral Benefits of Mixed Gender Housing on Survival of Mice with Colon Neoplasia

**Nathan A. Berger, MD, Case Western Reserve University**

To determine mechanisms and provide potential targets for design and implementation of biobehavioral interventions in cancer patients and survivors, this project examines the effect of (1) mixed gender housing, (2) same gender housing, and (3) social isolation on survival and changes in circulating hormones, cytokines, and other mediators and biomarkers in C57BL6J mice bearing the APC<sup>Min</sup> mutation predisposing to gastrointestinal neoplasia.

## Dual Psychosocial Stressor Exposure and Spontaneous Breast Tumor Metastasis in MMTV-PyMT Mice: Does Dual Stressor Exposure Increase Metastasis by Regulating Circulating Exosomes and Tumor Extracellular Matrix?

**Kelley S. Madden, PhD, University of Rochester**

This project will establish how exposure to a dual stressor is linked to metastasis in MMTV-PyMT mice, a spontaneous breast cancer model that mimics metastatic breast cancer in humans. The stressor, a combination of chronic psychological stress (social isolation) and acute restraint stress, may mimic the complex stressors experienced by cancer patients. This project examines distinct and novel biological mechanisms underlying stress exposure: (1) circulating exosomes, a newly defined metastatic mechanism, and (2) alterations in the tumor extracellular matrix.

## Using Propranolol to Decrease Gene Expression of Stress-Mediated Beta-Adrenergic Pathways in Hematopoietic Stem Cell Transplant Recipients

**Jennifer M. Knight, MD, Medical College of Wisconsin**

This project assesses whether gene expression of beta-adrenergic signaling pathways can be altered in individuals undergoing HSCT for multiple myeloma by administering a daily beta-blocker (propranolol). This is the first human trial of a beta-blocker to improve cancer control by pharmacologically intervening in biobehaviorally mediated gene expression. The goal is to leverage these findings for a larger, randomized controlled trial that evaluates clinical outcomes.

## Phase 0 Study to Define the Effect of Perioperative $\beta$ -blockade on Biomarkers of Progression in Newly Diagnosed Breast Cancer

**Erica Sloan, PhD, Monash University**

This project examines the effect of propranolol on primary tumor gene expression, specifically 121 genes related to epithelial mesenchymal transition cancer progression and 52 genes that constitute a conserved transcriptional response to adversity. The findings of this research open a window to using the preoperative period of cancer treatment to better manage the anxiety of a cancer diagnosis, favorably altering tumor biology and potentially impacting patients' long-term cancer outcomes.

Learn more and view upcoming RFP opportunities at:  
<http://cancercontrol.cancer.gov/brp/bbpsb/ncintwk-biopthwys.html>



# Members

## Scientific Steering Committee



**Linda Alexander, PhD**

Associate Professor of  
Health Behavior  
University of Kentucky  
College of Public Health

**Steven W. Cole, PhD**

Professor of Medicine  
and Psychiatry and  
Biobehavioral Sciences  
David Geffen  
School of Medicine  
University of California,  
Los Angeles



**Susan K. Lutgendorf, PhD**

Professor, Departments of  
Psychology, Obstetrics and  
Gynecology and Urology  
University of Iowa



**Paige Green, PhD, MPH**

Chief, Basic Biobehavioral  
and Psychological  
Sciences Branch  
National Cancer  
Institute



**Anil K. Sood, MD**

Professor, Vice Chair  
Translational Research  
in the Departments of  
Gynecologic Oncology  
and Reproductive  
Medicine MD Anderson  
Cancer Center



## NBBPC members:

1. Foster the discovery-to-translation continuum of research related to biobehavioral pathways in cancer;
2. Focus on unmet, understudied, highly exploratory questions that can't yet be addressed through the submission of a research project grant application to NCI; and
3. Develop and conduct proof of concept/principal/feasibility studies in support of the near term submission of research project grant applications to NCI.

Michael H. Antoni, PhD

Wenwei Hu, PhD

Shamgar Ben-Eliyahu, PhD

Jennifer M. Knight, MD

Nathan A. Berger, MD

Don Lamkin, PhD

Julienne Bower, PhD

Kelley S. Madden, PhD

Erin Costanzo, PhD

Tor Wager, PhD

Naomi Eisenberger, PhD

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Alex Konev, Leidos Biomedical Research, Inc.

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## Network Priorities

Stimulate novel scientific  
concepts and paradigms

Foster innovative collaborations  
between diverse disciplines

Disseminate relevant discoveries through  
major scientific conferences and meetings

Accelerate the translation of  
discoveries to patient benefit

Synthesize the state of the science,  
analyze secondary data, and publish

Encourage established scientists  
to apply their expertise to this  
emerging area of research

Cultivate the education, training,  
and professional advancement  
of early career scientists



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