

In this issue:

Note from the Editors

NIH Career Development Grant Awarded

Cancer Systems Biology fellow awarded \$180,000 to study intrinsic tumor dynamics

The John Dystel Nursing Fellowship in Multiple Sclerosis

Natalie V. Zucker Research Grant for Women Scholars

SCA Starter Grant

New Facilities and Administrative Rate Agreement

SEMC Research/Human Subjects Committee (IRB) Updates

OMB Circular A-133: Audits of Non-Profit Organizations

TUSM Academic Appointments

New Clinical Trial protocols approved by the SEMC Research/Human Subjects Committee

AAALAC Accreditation

Invited Lectures

Upcoming Seminars

New Employees & Promotions

Publications

Editors:

Nicolaos E. Madias, M.D., F.A.S.N
Caroline Ward

Note from the Editors

This is the inaugural issue of **DISCOVERY**, the e-newsletter of our research community, encompassing our investigators (in basic, translational, and clinical domains), and all the technical, support, and administrative staff, who collectively pursue the mission of discovery. We are viewing this newsletter as the connective tissue of our research community. It is designed to communicate new ventures and directions, highlight accomplishments, and disseminate noteworthy news. And in the process, we hope that it will transmit the excitement of the pursuit of new knowledge, promote research collaborations, and reaffirm the Caritas vision of broadening our research horizons.

We are delighted to launch this new initiative. We welcome comments and suggestions for improvement.

NIH Career Development Grant Awarded

Mary C. Perianayagam, Ph.D., (*Associate Investigator, Kidney & Dialysis Research Laboratory*) has received a three-year mentored career development award (K01 award) from the NIH, National Institute of Diabetes and Digestive and Kidney Diseases for her project entitled 'Oxidative Stress Related Gene Polymorphisms in Acute Kidney Injury.' The K01 award provides support for

a well-defined research career development program under the guidance of a mentor. The program is expected to prepare the candidate to apply for independent research funding by the fourth year of the award. Dr. Bertrand L. Jaber (*Vice Chairman of Medicine for Clinical Affairs*) will serve as her mentor.

Cancer Systems Biology Researcher awarded \$180,000 to study intrinsic tumor dynamics

The American Association for Cancer Research (AACR) has awarded Dr. Heiko Enderling (*Senior Research Associate, Center of Cancer Systems Biology*), a three-year \$180,000 grant to study intrinsic dynamics in tumor progression.

The programs and services of the AACR, the largest scientific organization in the world, promote the development of new ideas in every aspect of cancer research to prevent and cure cancer through research, education, communication and collaboration (www.aacr.org).

"Being awarded this prestigious grant reflects the recognition of the need for interdisciplinary cancer systems biology initiatives to define future research. "To be named one of the five Centennial Postdoctoral Fellows is a truly outstanding honor, especially for such an unconven-

tional project entitled ‘Paradoxical proliferation-apoptosis-migration dynamics in tumor progression’” said Dr. Enderling.

The supported project combines mathematical and computational modeling techniques to simulate tumor progression in its early stages. The rigorous exploration of how intrinsic cell properties combine to advance or inhibit the disease will inevitably give insights for future treatment planning.

Under the supervision of his mentor, Dr. Philip Hahnfeldt (*Senior Investigator, Center of Cancer Systems Biology*), and with the generous support of this AACR Fellowship, Dr. Enderling will develop a data-driven theoretical model to seek a better understanding of the anomalous long-term tumor growth response often observed in response to treatment. This approach will be a vital augment to existing dynamical models for tumor development and should provide valuable new insights.

Dr. Enderling has recently presented initial ideas and results from this project at the centennial annual meeting of the American Association for Cancer Research in Denver, CO with 17,000 attendees. In addition to listening to lectures by leading scientists in the field, Dr. Enderling had the opportunity to present and discuss his work with colleagues, and establish new contacts with interested researchers from different parts of the world.



Dr. Enderling (second from left) presenting and discussing his work with colleagues at the annual meeting of the AACR, Denver, CO in April 2009.

The John Dystel Nursing Fellowship in Multiple Sclerosis

The John Dystel Nursing Fellowship in Multiple Sclerosis has been awarded to Megan Scully, RN, a research nurse in the neurology department. This 6-month fellowship will provide Megan with the opportunity to practice under the supervision of an MS nurse specialist in a clinical setting. This experience will give Megan the skills and knowledge necessary to provide the highest quality of MS care.

Natalie V. Zucker Research Grant for Women Scholars

Nava Almog, Ph.D., (*Senior Research Associate, Center of Cancer Systems Biology*) has been awarded a Natalie V. Zucker Research grant to attend the 14th World Congress on

Advances in Oncology and the 12th International Symposium on Molecular Medicine that will be held in Greece in October. Dr. Almog has been invited to give a lecture at the meeting on her recent research work. The annual grant award of the Natalie V. Zucker Research Center for Women Scholars is designed to support and enhance the research careers of women basic and clinical scientists at Tufts University School of Medicine and its affiliates. The award is intended to support items or activities that will advance and benefit the awardee research career and professional stature.

Dr. Almog’s research is focused on the identification of the molecular mechanisms underlying dormancy of human tumors. She has previously developed and characterized in-vivo models of human tumor dormancy. She has used these models together with a genome-wide gene expression

profiling analysis to identify the molecular signature of human dormant tumors. Her team is currently searching for 'master - regulators' of tumor dormancy by analysis of expression of microRNA molecules. This work may advance ongoing efforts to develop dormancy-promoting therapy strategies, the discovery of early tumor biomarkers, and possible therapeutic targets for the blockage of early tumor development.

SCA Starter Grant

A Starter Grant from the Society of Cardiovascular Anesthesiologists has been awarded to Mark A. Lovich, M.D., Ph.D., (*Staff Physician, Department of Anesthesiology*), to continue his work on pericardial inotropic drug applications. The rationale for this work stems from the fact that patients with preexisting myocardial dysfunction are at risk for exacerbated cardiomyopathy following cardiac surgery, especially with cardiopulmonary bypass (CPB). Inotropic drugs are often used to separate heart failure patients from CPB; however, systemic side effects, such as tachycardia, peripheral vasodilation, and hypotension limit their dose and utility. Dr. Lovich's project seeks to examine myocardial contraction and the differential response of hemodynamic measurements, indices of contractility, and intramyocyte signaling molecule levels to systemic intravenous (IV) and local pericardial (PC) delivery of inotropes. Local PC delivery allows the study of the central pharmacologic response in the absence of changes in vascular tone that alters preload and afterload. While preliminary data using beta agonists, such as dobutamine, show promise in small healthy rodent models, this 2 year award will allow

Dr. Lovich to examine the impact of phosphodiesterase inhibitors and models of impaired vascular tone. These studies will delineate efficacious treatments that may improve heart function without interference from effects on the vasculature, and may ultimately improve the care of cardiac surgical patients and patients with acute cardiomyopathy.

New Facilities and Administrative Rate Agreement

CSEMC has concluded negotiations with the Division of Cost Allocation in the Department of Health and Human Services (DHHS) resulting in a new federal rate agreement. This agreement spells out the new Facilities and Administrative (F&A) rates that will be applied to federal grants and contracts through September 30, 2011. The new F&A rate will be charged on new federal research awards. Those awards that predate the new rate structure will continue to charge the rate in effect at the beginning of the award. Also included in the agreement was the new fringe benefit rate of 26.7%.

Indirect Cost Rate: 71.0% (10/01/08-09/30/11, or until amended)
Fringe Benefit Rate: 26.7% (10/01/08-09/30/09, or until amended)

SEMC Research/Human Subjects Committee (IRB) Updates

•The IRB office is using a new stamp on approved informed consent documents. The new stamp displays the date IRB approval expires and the date the approved documents are released from the IRB office.

•Monica Neuman, JD, is a new member of the IRB Committee. Ms. Neuman is an associate in the law firm of McDermott, Will & Emery LLP and is based in the firm's Boston office. She is a member of the Health Department and part of her practice focuses on advising clients on matters relating to research, conflicts of interest, and research misconduct.

OMB Circular A-133: Audits of Non-Profit Organizations

The office of sponsored research (grants) recently completed the OMB Circular A-133 Audit with no findings. OMB Circular A-133 requires annual audits of States, Local Governments, and Non-Profit Organizations who receive federal funding exceeding \$500,000. The audit of selected federal awards was completed by external auditors, Ernest & Young. The A-133 audit includes tests for compliance with the cost principles and for compliance with the grantee's policies.

Tufts University School of Medicine Academic Appointments

Recently, David A. Goukassian, M.D., Ph.D., (*Principal Investigator, Center of Cardiovascular Research, Associate Investigator, Center of Cancer System Biology*) was promoted to an Associate Research Professor of Medicine and Michael V. Orlov, M.D., Ph.D., (*Director of the EP Laboratory, Division of Cardiovascular Medicine*) was promoted to Associate Professor of Medicine at Tufts University School of Medicine.

**New Clinical Trial protocols approved by the SEMC Research/Human Subjects Committee
(December 2008 – March 2009)**

TITLE	PRINCIPAL INVESTIGATOR
Device Modification for Uterine Insertion.	Michael Zinaman, MD
Cranial Cup Use for the Prevention of Positional Head Shape Deformity in the NICU.	Debbie Giambanco, MS
An Open-Label, Multicenter Study to Determine Subject Satisfaction in Using the Single-Use Autoinjector with a Pre-Filled Liquid Avonex® Syringe in Multiple Sclerosis Subjects.	Ellen Lathi, MD
A Randomized, Double-Blind, Placebo Controlled, Cross-Over Study of the Effectiveness of Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for the Treatment of Multifocal Motor Neuropathy.	Kenneth Gorson, MD
CONSERV™-1 (Clinical Outcomes and Safety Trial to Investigate Ecallantide's Effect on Reducing Surgical Blood Loss Volume): A Phase 2 Randomized Placebo-Controlled Dose-Ranging Study in Subjects Exposed to Cardio-Pulmonary Bypass During Primary Coronary Artery Bypass Graft Surgery.	Robert Hunsaker, MD
A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II-IV).	Michael Maysky, MD
A Randomized, Double-Blind, Placebo-Controlled Trial Assessing the Efficacy and Safety of Dutasteride at Improving Dysuria, Voiding the Lower Urinary Tract Symptoms in Men with Clinically Localized Prostate Cancer Being Treated with Single-dose Goserelin, Trans-urethral Incision of Prostate, and Interval Brachytherapy.	H. David Mitcheson, MD
Correlation between clinical outcome of coronary artery bypass surgery and presence of vascular disease in the brain.	Michael Henry, MD.
ElectroMap Software Evaluation	Michael Orlov, MD
Comparison of the Supera® Peripheral System to a Performance Goal Derived from Balloon Angioplasty Clinical Trials in the Superficial Femoral Artery (The SUPERB Study).	Peter Soukas, MD
S0720: Phase II ERCC1 and RRM1-Based Adjuvant Therapy Trial in Patients with Stage I Non-Small Cell Lung Cancer (NSCLC).	Paul Hesketh, MD
MARVEL: Marker Validation of Erlotinib in Lung Cancer- A Phase III Biomarker Validation Study of Second-line Therapy in Patients with Advanced Non-small Cell Lung Cancer (NSCLC) Randomized to Pemetrexed Versus Erlotinib N0723.	Paul Hesketh, MD
S0709: A Phase II Selection Design of Pharmacodynamic Separation of Carboplatin/ Paclitaxel/OSI-774 (Erlotinib; NSC-718781) or OSI-774 Alone in Advanced Non-Small Cell Lung Cancer (NSCLC) Patients with Performance Status 2 (PS-2) Selected by Serum Proteomics.	Paul Hesketh, MD
ECOG E5204: Intergroup Randomized Phase III Study of Postoperative Oxaliplatin, 5-Fluorouracil and Leucovorin vs Oxaliplatin, 5-Fluorouracil, Leucovorin and Bevacizumab for Patients with Stage II or III Rectal Cancer Receiving Pre-Operative Chemoradiation.	Leslie Martin, MD
A Randomized, Double Bind, Placebo Controlled Study Evaluating the Efficacy and Safety of Romiplostim Treatment of Thrombocytopenia in Subjects with Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS).	Thein Oo, MD
SWOG S9910: Leukemia Centralized Reference Laboratories and Tissue Repositories, Ancillary.	Rekha Parameswaran, MD
A retrospective analysis of patients with pelvic cancers who received radiation therapy as adjuvant therapy between 2005-2007 and the prevalence of bone disease (osteopenia/osteoporosis).	Rekha Parameswaran, MD
SWOG S0106 : A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg®) During Induction Therapy Versus Standard Induction with Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy with Gemtuzumab Ozogamicin (Mylotarg®) or No Additional Therapy for Patients Under Age 61 with Previously Untreated DeNovo Acute Myeloid Leukemia (AML).	Rekha Parameswaran, MD
SWOG S9007: Cytogenetic Studies in Leukemia Patients.	Rekha Parameswaran, MD



AAALAC Accreditation

The Council on Accreditation of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC International) recently completed their triennial site visit of Caritas St. Elizabeth's Medical Center (CSEMC). On March 16, 2009, CSEMC was notified that it received continuing full accreditation for providing and maintaining a very good program of laboratory and animal care and use. CSEMC has been fully accredited since 1996. The site visitors noted the commitment of administration and the active and engaged Institutional Animal Care and Use Committee (IACUC).

Invited Lectures

Xinhua Yan, M.D. presented her work at the American Association for Cancer Research (AACR) 100th Annual Meeting in Denver, CO this April. Using various transgenic mouse models, Dr. Yan's work demonstrates that inhibition of key survival kinases in the heart worsens chemotherapy drug doxorubicin-induced heart failure. She also demonstrates that the cardiac dysfunction induced by kinase inhibition and chemotherapy could be prevented or circumvented by combination therapies that activate

alternative pathways in the heart. The goal of her work is to increase the therapeutic window in cancer patients treated with novel kinase inhibitors. Some of these new kinase inhibitors are already in clinical use and have been shown to substantially reduce early mortality and recurrence of the disease. There are about 600 new inhibitors in development, and new kinase inhibitors are expected to be widely used in patient care in the next 10 years.

On May 5th, Heiko Enderling, Ph.D., (*Senior Research Associate, Center of Cancer Systems Biology*) gave an invited lecture entitled "Agent-based Model of Tumor Growth, Morphological Evolution and Treatment" at the Dana-Farber Cancer Institute.

Upcoming Seminars

Interdepartmental Seminar Series

Friday, June 12th at 10:00am in the Center for Biomedical Research (CBR) building 1st floor conference room. The speaker will be David A. Goukassian, M.D., Ph.D., Principal Investigator, Center of Cardiovascular Research, Associate Investigator, Center of Cancer System Biology and Associate Professor of Medicine, Tufts University School of Medicine. The title of Dr. Goukassian's presentation is "Two Faces of the Same Coin - Signaling via TNFR1/p55 and TNFR2/p75 for Regulation of Therapeutic Neovascularization and Pathological Angiogenesis."

New Employees

The research community welcomes the following individuals to CSEMC:

Richard Gilbert, MD, Director
Bioenergy Research Laboratory

Ezra Levy, Research Technician,
Department of Neurology

Andrew Perrin, PhD,
Postdoctoral Fellow, Bioenergy
Research Laboratory

Fabrizio Pizzolante, MD obtained his medical degree from the Catholic University School of Medicine of Rome, Italy in 2001. He completed a Residency Program in Internal Medicine at the A. Gemelli University Hospital in Rome, Italy, in 2006. He is currently enrolled in a PhD program in "Molecular and Morphological Sciences in Anatomy and Cell Biology" at the Catholic University School of Medicine. In April 2009, Dr. Pizzolante joined the research group of Dr. Roberto Pola (*Associate Investigator, Center of Cardiovascular Research*). Dr. Pizzolante's scientific interests include degenerative diseases of the central nervous system and alterations of the blood-brain barrier. At CSEMC, he is working on a scientific project entitled "Sonic hedgehog signalling in the adult hypoxic cerebellum".

Mariangela Palladino, MD obtained her medical degree from the Catholic University School of Medicine of Rome, Italy in 2003. She completed a Residency Program in Hematology at the A. Gemelli University Hospital of Rome, Italy, in 2007. She is currently enrolled in a PhD program in "Molecular Oncology

and Hematology” at the Catholic University School of Medicine of Rome, Italy. Dr. Palladino’s scientific interests include bone marrow transplantation, bone marrow-derived stem cells, and regenerative medicine. In March 2009, Dr. Palladino joined the research group of Dr. Roberto Pola. At CSEMC, she is working on a scientific project entitled “Angiogenic and vasculogenic effects of combined intramuscular bone marrow-derived endothelial progenitor cells and Sonic hedgehog gene therapy in peripheral ischemia”.

Andrea Piccioni, MD, obtained his medical degree from the Catholic University School of Medicine of Rome, Italy in 2007. Dr. Piccioni’s scientific interests include angiogenesis, stem cells, tissue regeneration, and diseases of the cardiovascular system. In March 2009, Dr. Piccioni joined the research group of Dr. Roberto Pola. At CSEMC, he is working on a scientific project entitled “Sonic hedgehog and skeletal muscle regeneration”.

Valentina Neri is a senior student at the School of Biomedical Sciences of the Catholic University of Rome, Italy, class of 2009. In March 2009, Ms. Neri joined the research group of Dr. Roberto Pola. Ms. Neri works on several different scientific projects and provides a fundamental contribution for the generation of an animal model of peripheral ischemia, the isolation and culture of bone marrow-derived endothelial progenitor cells, the production of plasmids for gene therapy, and the execution of various molecular, histological, and functional analyses.

CSEMC Promotions

The research community congratulates the following individuals, on their promotions:

Heiko Enderling, Ph.D.
Senior Research Associate

Han-Kyu Lee, Ph.D.
Senior Research Associate

Mary C. Perianayagam, Ph.D.
Associate Investigator

Publications

Almog N, Ma L, Raychowdhury R, Schwager C, Erber R, Short S, Hlatky L, Vaikoczv P, Huber PE, Folkman J, Abdollahi A. Transcriptional switch of dormant tumors to fast-growing angiogenic phenotype. *Cancer Res* 2009;1:69(3):836-44.

All suggestions, comments, or submissions for publication are appreciated.

Please direct to Caroline Ward,
Research Administration,
caroline.ward@caritaschristi.org