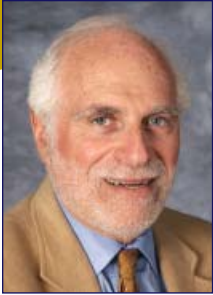


Division of Hematology-Oncology



Lowell E. Schnipper, MD,
Chief

● *Overview*

The mission of the Division of Hematology-Oncology is to provide the highest caliber of technologically expert and humane clinical care for men and women with cancer and benign hematological disorders through the combined efforts of superior clinicians, leading edge scientists, and training programs of unsurpassed excellence. The Division of Hematology-Oncology supports an expanding clinical program along with well-funded laboratory, translational and clinical research programs. These serve as a foundation for clinical and research fellowship training, delivery of unparalleled clinical care, and generation of new knowledge in both specialties. The Division has 44 faculty members with diverse clinical, educational and scientific interests. Eleven are predominantly bench scientists and the others are translational researchers, clinical investigators and clinician-teachers. In addition to the Division Chief, Dr. Lowell E. Schnipper, Dr. Michael Atkins serves as Deputy Director, Dr. Daniel Tenen is Associate Director and head of the Cancer Biology Program, Dr. Steven Come serves as Medical Director of the Hematology-Oncology ambulatory unit, Dr. James Levine serves as the Medical Director of the Heme Malignancy/BMT ambulatory unit as well as the two Hematology-Oncology inpatient floors, and Dr. Reed Drews is Director of the Hematology-Oncology fellowship program. The Administrative Directors are Ellen Volpe and Kerry Brown. The Division's research funding base is steadily growing and is one of the largest within the Department of Medicine.

● *Clinical Activities*

The clinical programs span the breadth of the specialties and emphasize prevention/risk reduction, diagnosis, management, and longitudinal

follow-up of patients with diverse hematological disorders and neoplastic diseases. Many of the clinical programs are multidisciplinary and function as disease site programs within the Beth Israel Deaconess Cancer Center.

Within the past 4 years two new contiguous inpatient hematology-oncology units have opened. The organization of the inpatient service is built around the model of an attending physician-led service and the teaching program directed at the house staff has been strengthened by naming Dr. Stephen Cannistra as the physician-teacher in charge. The ambulatory programs continue to serve as a major resource for clinical education of house staff and fellows.

● *Quality Improvement*

A robust quality assurance program is in place. This effort has resulted in:

- Integration of the electronic chemotherapy ordering system created for the ambulatory setting into the inpatient setting
- Improved monitoring and documenting of pain assessments in routine clinical care for both inpatients and outpatients
- The Bone Marrow Transplant Program, under the direction of Dr. James Levine, conducts internal audits of engraftment data, bone marrow harvest collection data, donor screening and eligibility testing data, donor complication data and treatment related death data.

● *Educational Programs*

Spanning 18 clinical months, the training program comprises inpatient care of hematological and general oncology patients, consultation, and ambulatory experiences that emphasize longitudinal care. Currently there are nineteen fellows in our three year fellowship program.

Since the goal of the program is to produce scholars who will devote their careers, in different proportions, to clinical care, teaching, and research, the second half of training involves investigation. Every effort is made to tailor the program to the specific needs of the trainees.

Research programs in the Division have a wide scope, ranging from basic laboratory science, translational research, investigational imaging and numerous clinical trials involving novel therapies, risk reduction and chemoprevention of cancer.

Color Video

NIR Fluorescence

Color-NIR Merge

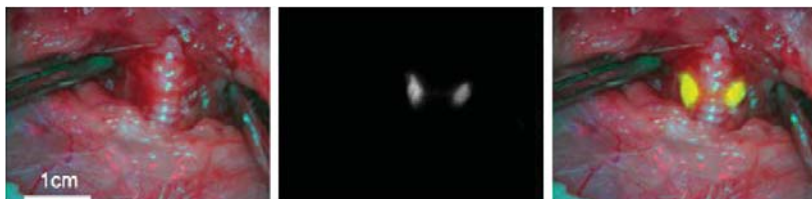


Image-guided cancer surgery using invisible near-infrared light. A novel thyroid-seeking near-infrared fluorophore is injected intravenously, and within 1 hour highlights the cells of the thyroid gland using invisible near-infrared fluorescence. Shown are the color video (left), near-infrared fluorescence (right), and a pseudo-colored merged image of the two. (courtesy of John Frangioni, MD, PhD)

Hence, different programs are available for trainees interested in laboratory research and those interested in more clinical careers.

A talented faculty that reflects the major areas of contemporary interest in hematology and oncology provides research training. A Cancer Biology training grant (Steven Balk, MD, PhD, PI), the Harvard Hematology Research Training Grant (Daniel Tenen, MD, co-director) and a Vascular Biology Training Grant (Bruce Furie, MD, PI) are available to support young scientists as they launch their careers.

● Research Activities

The research activities of the division continue to prosper, with multiple faculty members having received new investigator grants from the National Institutes of Health. In July 2000, BIDMC became a founding member of the Dana Farber/Harvard Cancer Center (DF/HCC) and numerous investigators from the BIDMC Hematology-Oncology program have major leadership roles in this multi-institutional collaborative research endeavor. BIDMC faculty members hold leadership roles in five of the seven funded SPORES of the Dana Farber/Harvard Cancer Center (including those in cutaneous oncology, kidney cancer, lung cancer, breast cancer, ovarian cancer, and prostate cancer). Dr. Schnipper serves as an Associate Director (Membership) of the DF/HCC, Deputy Associate Director for Clinical Science and is a member of the Executive Committee of the DF/HCC.

Research Funding • AY'07

Federal Direct	10,974,327
Federal Indirect	4,992,042
Other Direct	8,296,904
Other Indirect	1,023,668

- Dr. John Frangioni, in Hematology-Oncology and Dr. Robert Lenkinski, the Director of Radiology Research, have spawned a large and productive program in investigational imaging.
- Drs. Daniel Tenen and Bing Lim lead an effort that is focused on the cellular and molecular biology of hematopoiesis.
- An extensive effort is focused on understanding signal transduction as the key to the regulatory processes for cell growth in normal and malignant cells. This group is internationally known, and its lead investigators are Drs. Sheila Thomas and Ping Lu in Hematology-Oncology and Dr. Lewis Cantley in the Division of Signal Transduction.
- Investigators are using hormone-refractory prostate cancer cells as a means of investigating androgen-independent disease (Drs. Steven Balk, Xin Yuan and Glenn Bubley).
- Studies are exploring the use of a monoclonal antibody developed by one of our faculty members (Dr. Mark Exley) to enable concentration of "NKT" cells, as a means of harvesting sufficient numbers of these cells to employ therapeutically (Drs. Steven Balk and Mark Exley).
- Other efforts are directed at developing a mechanistic understanding of the basis for sensitivity and resistance to hormone therapy in breast cancer (Dr. Steven Come).
- Dr. Ralph Scully's laboratory studies DNA damage and repair in cancer susceptibility syndromes such as the Familial Breast-Ovarian

Cancer Syndrome and Dr. Nadine Tung leads a research effort on the Clinical Genetics of the Breast-Ovarian Cancer Syndrome.

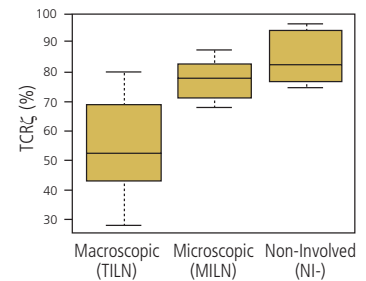
- The Breast Cancer program is exploring multi-modality therapies for early breast cancer and the development of new targets for therapy in both early and advanced disease (Drs. Come, Wulf, Schnipper, Tung, Zarwan, Lange).
- The Biologic Therapy program is using cytokines and vaccines to treat established cancer or prevent recurrence, particularly for melanoma and renal cell cancer. BIDMC investigators have pioneered the use of high dose interleukin-2 for the treatment of melanoma and renal cancer and targeted therapies in renal cancer and melanoma. Current efforts focus on overcoming acquired resistance to VEGFR inhibitors in kidney cancer, exploring the role of mTOR and PI3Kinase inhibitors in kidney cancer, and identifying selection criteria for particular treatment approaches in both kidney cancer and melanoma (Drs. Atkins, McDermott, Mier, Panka, Cho, Bhatt).
- The Gyn Oncology program has pioneered research in translational genomics which has employed expression array analyses to define prognostic and predictive signatures in ovarian cancer (Drs. Cannistra and Spentzos).
- The tumor vaccine program (Drs. Avigan, Rosenblatt and Zarwan) is based upon a novel technique in which malignant cells are fused with dendritic cells and then used

as an antigenic stimulus. Clinical trials are showing promise in multiple myeloma and kidney cancer and will soon be opening in leukemia, ovarian cancer and breast cancer.

- The Thoracic Oncology program (Drs. Tenen, Costa, Huberman) has made a seminal observation on the basis of resistance to epidermal growth factor receptor inhibitors by identifying a common site for a second mutation that causes resistance to agents such as erlotinib (an EGFR inhibitor). Drs. Costa and Tenen are co-leaders of the Lung SPORE program at DF/HCC and direct a project entitled "Foxa2 and C/EBP transcription factors in the pathogenesis and treatment of lung cancer."
- The AIDS oncology program is studying novel forms of therapy for Kaposi's sarcoma and AIDS-related lymphoma (Drs. Dezube and Doweiko). This group is part of the AIDS Malignancy Consortium of the National Cancer Institute, and is among the most active participants in this national clinical trials program.
- Dr. Paula Fraenkel has launched a productive research program that is investigating the genetics of iron transport and their relevance to human diseases.

● *Awards and Honors*

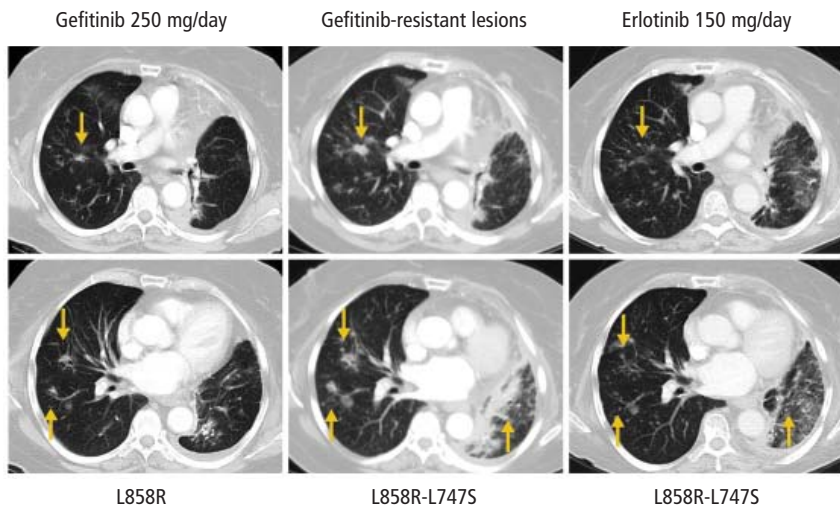
Drs. John Frangioni and Ping Lu were elected to the American Society of Clinical Investigation. Dr. Ping Lu received the Senior



- TCRζ expression relates inversely to melanoma involvement in draining lymph node.

● *Faculty*

Michael Atkins, MD	Steven Come, MD	Michael Goldstein, MD	David McDermott, MD	Arthur Sytkowski, MD
David Avigan, MD	Daniel Costa, MD	Mark Huberman, MD	James Mier, MD	Daniel Tenen, MD
Steven Balk, MD, PhD	Bruce Dezube, MD	Sanjay Jain, MD, PhD	Rebecca Miksad, MD	Sheila Thomas, PhD
Rupal Bhatt, MD, PhD	Reed Drews, MD	Robin Joyce, MD	Jacalyn Rosenblatt, MD	Nadine Tung, MD
Stuart Bless, MD	Mark Exley, PhD	Stephen Landaw, MD	Diane Savarese, MD	Gerburg Wulf, MD
Vicki Boussiotis, MD, PhD	Laurie Feldman, PhD	Roger Lange, MD	Lowell Schnipper, MD	Corrine Zarwan, MD
Glenn Bublely, MD	Paula Fraenkel, MD	James Levine, MD	Susan Schumer, MD	Xiao Zhou, MD
Stephen Cannistra, MD	John V. Frangioni, MD, PhD	Bing Lim, MD, PhD	Ralph Scully, MBBS, PhD	Jeffery Zwicker, MD
Daniel Cho, MD	Marc Garnick, MD	Kun Ping Lu, MD, PhD	Dimitrios Spentzos, MD	



• The Thoracic Oncology program identified a rare EGFR secondary mutation, L858R-L747S, that explains why some patients become resistant to the EGFR inhibitor gefitinib but remain sensitive to an alternative inhibitor erlotinib. The more common T790M mutation is resistant to both inhibitors. (*J Clin Oncol* 2008; 26:1182-84.)

Investigator Award from the Sandler Program for Asthma Research. Dr. Michael Atkins is the 2007 recipient of the Eugene Schonfeld Award of the Kidney Cancer Association. Rebecca Miksad received a Young Investigator Award from the American Society of Clinical Oncology. Dr. Daniel Costa received the AACR Fellowship in Translational Lung Cancer.

Dr. Steven Come co-chaired the 6th Annual International Conference on Endocrine Manipulation of Breast Cancer. Drs. Lowell Schnipper and Michael Goldstein received the Statesman Award from the American Society of Clinical Oncology. Dr. Marc Garnick is Editor-in-Chief of *Perspectives on Prostate Disease*, a new health publication which won the second place award in the 2008 Editorial Excellence Awards from the Specialized Information Publishers Foundation. Dr. Rupal Bhatt received the VHL Family Alliance Award. Dr. Reed Drews was a 2007 Nominee, Harvard Medical School Prize for Excellence in Teaching (Years 3 & 4).

● Selected Publications

Bhatt RS, Landis DM, Zimmer M, Torregrossa J, Chen S, Sukhatme VP, Iliopoulos O, Balk S, Bublej GJ. Hypoxia-inducible factor-2-alpha: effect on radiation sensitivity and differential regulation by an mTOR inhibitor. *BJU Int* 2008; 102:358-63.

Costa DB, Schumer ST, Tenen DG, Kobayashi S. Differential responses to erlotinib in EGFR mutated lung cancers with

acquired resistance to gefitinib carrying the L747S or T790M secondary mutations. *J Clin Oncol* 2008; 26:1182-1184.

Dooley KA, Fraenkel PG, Langer NB, Schmid B, Davidson AJ, Weber G, Chiang K, Foott H, Dwyer C, Wingert RA, Zhou Y, Paw BH, Zon LI, and Tübingen 2000 Screen Consortium. Montalcino, a zebrafish model for variegate prophyria. *Exp Hematol* 2008; 36:1132-1142.

Flaumenhaft R, Tanaka E, Graham GJ, De Grand AM, Laurence RG, Hoshino K, Hajjar RJ, Frangioni JV. Localization and quantification of platelet-rich thrombi in large blood vessels with near-infrared fluorescence imaging. *Circulation* 2007; 115:84-93.

Lee TH, Tun-Kyi A, Shi R, Lim J, Soohoo C, Finn G, Balastik M, Pastorino L, Wulf G, Zhou XZ, Lu KP. Essential role of Pin1 in the regulation of TRF1 stability and telomere maintenance. *Nat Cell Biol* 2009; 11:97-105.

Masiello D, Mohi MG, McKnight NC, Smith B, Neel BG, Balk SP, Bublej GJ. Combining an mTOR antagonist and receptor tyrosine kinase inhibitors for the treatment of prostate cancer. *Cancer Biol Ther* 2007; 6:195-201.

Negin B, Panka D, Wang W, Siddiqui M, Tawa N, Mullen J, Tahan S, Mandato L, Polivy A, Mier J, Atkins M. Effect of melanoma on immune function in the regional lymph node basin. *Clin Canc Res* 2008; 14:654-659.

Panka DJ, Cho DC, Atkins MB, Mier JW. GSK-3beta inhibition enhances sorafenib-induced apoptosis in melanoma cell lines. *J Biol Chem* 2008; 283:726-32.

Stadler Z, Come SE. Review of gene-expression profiling and its clinical use in breast cancer. *Crit Rev Oncol Hematol* 2009; 69:1-11.

Tzachanis D, Li L, Lafuente EM, Berezovskaya A, Freeman GF, Boussiotis VA. Twisted Gastrulation (Tsg) is regulated by Tob and enhances TGF-beta signaling in T lymphocytes. *Blood* 2007; 109:2944-2952.