CIMIT Center for Integration of Medicine & Innovative Technology

Wellman Center for Photomedicine

Massachusetts Institute of Technology

April 19, 2011
Massachusetts General Hospital
Simches Research Center, Room 3110
4:00 – 6:00PM

Lester Wolfe Workshop in Laser Biomedicine: Photons, Blood Vessels and Angiogenesis

Since the pioneering discoveries of Judah Folkman over twenty years ago, angiogenesis has been a hot topic, both as a possible target for anti-cancer therapy and for its involvement in many other diseases. This Lester-Wolfe Workshop will cover the role of optics and photonics in imaging angiogenesis and blood vessels, and the use of photodynamic therapy to destroy newly formed blood vessels as a cancer therapy.

MODERATOR: CONOR EVANS, PHD, Assistant Professor, Harvard Medical School, Wellman Center for Photomedicine, Massachusetts General Hospital, clevans@partners.org

Antiangiogenic Therapy in Cancer: Current Status and Future Directions
PRESENTER: JEFFREY WILLIAM CLARK, MD, Associate Professor of Medicine, Harvard Medical School, MGH; Director, Clinical Trials Core of Dana-Farber/Partners Cancer Care, MGH; Medical Director, Clinical Trials Infrastructure, Dana Farber Harvard Cancer Center, jclark@partners.org

Several agents targeting angiogenesis have been approved for the treatment of patients with various malignancies. These include: bevacizumab alone for renal cell cancer (RCC) and glioblastioma and in combination with chemotherapy for colorectal and lung cancers; sorafenib for hepatocellular cancer and RCC; sunitinib for RCC and GIST; pazopanib for RCC; and vandetanib for medullary thyroid cancer. These agents all target members of the vascular endothelial growth factor family or their receptor family which have been the best characterized mediators of tumor associated angiogenesis. However, there have also been a large number of studies that have not shown any benefit for anti-angiogenic agents in a number of cancer settings. At present, there are no biomarkers that allow the selection of specific patients who will benefit from anti-angiogenic therapy so that the choice of patients remains empiric based on diagnostic categories. In addition, essential questions remain about how these agents actually mediate their clinical benefit, what appropriate combinations might be, and possible mechanisms of resistance. Research is ongoing attempting to identify biomarkers that would be useful in identifying who might benefit from therapy as well as address these questions. In addition, ongoing clinical trials are evaluating agents targeting other angiogenic factors important for tumor associated angiogenesis such as the fibroblast growth factor family (and the associated receptors) or matrix metalloproteinase's. Improvements in targeting angiogenesis for therapeutic benefit in cancers depends on improved understanding of the critical biological processes involved in cancer associated angiogenesis.

In Vivo Imaging of Angiogenesis Using Optical Coherence Tomography
PRESENTER: BENJAMIN VAKOC, PHD, Assistant Professor, Harvard Medical School and Harvard-MIT Health Sciences and Technology; Wellman Center for Photomedicine, Massachusetts General Hospital, bvakoc@partners.org

Multiphoton microscopies have become commonplace in the biological investigation of angiogenesis. However, the requisite high numerical aperture and exogenous contrast agents that enable multiphoton microscopy result in a limited capacity to investigate substantial tissue volumes or probe

dynamic changes repeatedly over prolonged periods. Dr. Vakoc's team lab has developed new microvascular imaging approaches based on optical coherence tomography and applied this tool to the study of angiogenesis and therapeutic responses in mouse models of cancer. Dr. Vakoc will present the basic principles of optical coherence tomography based microvascular imaging and highlight its application and future potential in the study of the tumor microvascualture.

Nonlinear Optics In Vivo: Using Light to Dissect the Cellular Dynamics Underlying Neurological Disease

CHRIS SCHAFFER, PHD, Assistant Professor, Biomedical Engineering, Cornell University, cs385@cornell.edu

Nonlinear optical techniques provide unique capabilities for the observation and manipulation of in vivo biological systems, enabling the discovery of a microscopic-scale understanding of normal and disease-state physiological processes. Dr. Schaffer's lab uses nonlinear optics as a tool for precise ablation of structures and quantitative observation of dynamical processes in the brain of live rodents. With these methods, they investigate the role of cortical microvascular clots and hemorrhages on the health and function of brain cells and the link between such lesions and neurodegenerative diseases, such as Alzheimer's disease. The team uses tightly-focused femtosecond laser pulses to injure the endothelial cells that line specifically targeted blood vessels and thereby trigger clotting or hemorrhage. This method allows them to selectively lesion any vessel in the top 1 mm of the cortex. The lab also uses optical techniques, such as two-photon excited fluorescence microscopy, to study the physiological consequences of these occlusions in terms of blood flow change, loss of neuronal function and cell death, and exacerbation of other neurodegenerative diseases.

Vascular Microenvironment: Instigator or Innocent Bystander in Response to Photodynamic Therapy

THERESA BUSCH, PHD, Research Associate Professor, Department of Radiation Oncology, and Associate Director, Division of Oncology Research, Radiation Oncology Department, University of Pennsylvania, buschtm@mail.med.upenn.edu

Photodynamic therapy (PDT) involves the activation of a tissue-localized photosensitizer by visible light, resulting in cellular and vascular damage within the field of illumination. The contribution of cellular vs. vascular damage is largely determined by the length of the delay between photosensitizer administration and light delivery in relation to how rapidly the drug is cleared from the bloodstream. Dr. Theresa Busch's lab has examined the role of vascular microenvironment as another determinant of PDT-induced vascular damage. Studies were conducted in intradermal tumors propagated from the radiation-induced fibrosarcoma (RIF) murine cell line. An altered vascular microenvironment was created by co-injecting the RIF cells with a small volume (15 ml) of Matrigel basement membrane matrix at the time of tumor initiation. Comprehensive evaluation of tumor microenvironment in RIF vs. Matrigel-supplemented RIF (RIF-Matrigel) tumors found RIF-Matrigel tumors to contain blood vessels that were more regularly distributed throughout the tumor. This did not lead to better oxygenation of the RIF-Matrigel tumors, but photosensitizer (Photofrin) distribution was notably different in RIF-Matrigel compared to RIF tumors. Differences in Photofrin distribution could be attributed to the presence of more collagen in RIF-Matrigel tumors, together with better Photofrin co-localization to vessel areas that contained collagen compared to the vessel as a whole (i.e. areas with and without collagen). Effects on both vascular and tumor responses were found in that RIF-Matrigel tumors experienced greater PDT-induced reductions in tumor blood flow, more vascular congestion and better long-term therapeutic outcome. Confirmatory studies in tumors of squamous cell carcinoma VII (SCCVII) also found better Photofrin localization to vessel areas that contained collagen, as well as PDT-induced reductions in collagen association with blood vessels. As found with the RIF models, SCCVII-Matrigel tumors exhibited better therapeutic outcome than naïve SCCVII tumors. In conclusion, these data support a role for blood vessel structure in determining photosensitizer localization and subsequent PDT response. Pharmacological approaches toward modifying the composition of tumor blood vessels prior to PDT could provide a clinically-relevant means of improving treatment outcomes.

Lester Wolfe Workshops

The Lester Wolfe Workshop in Laser Biomedicine is a series of talks dedicated to a particular aspect in biomedical optics. Speakers are expert researchers in academia, medical/clinical and industry. Named in honor of Lester Wolfe, MIT class of 1919, inventor and benefactor with a special interest in optics, the Wolfe Workshop series is sponsored by the MIT George R. Harrison Spectroscopy Laboratory, MGH Wellman Center for Photomedicine, Harvard-MIT Division of Health Sciences and Technology, and CIMIT. The workshop is hosted alternately at MIT in late fall and at MGH in late spring each year.

Upcoming CIMIT Forums:

4.26.2011

Reorganization of Primary Care as Disruptive Innovation: From Molecules to Practice

PRESENTER: DAVID BATES, Brigham and Women's Hospital

PANELISTS:
JEREMY LIM, Ministry of Health, Singapore
JONATHAN HARDING, Tufts Health Plan, Inc.

LOCATION: Holiday Inn Boston at Beacon Hill, 5 Blossom St., Boston

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5.17.2011

Integrated Clinical Environments (ICE) Delegates: Quality and Excellence Initiatives

LOCATION: Massachusetts General Hospital, Richard B. Simches Research Center, Room 3110, 185 Cambridge St., Boston

To learn more about the CIMIT Forum, visit www.cimit.org. View Forum videos and participate in the Forum blog at www.cimit.typepad.com.

Visit www.CIMIT.org to learn about CIMIT initiatives and ways that you can engage to make a difference.