Third Annual

**Fluorescent Proteins in Drug Development**

November 13-14, 2006
Hilton La Jolla Torrey Pines • La Jolla, CA

**Sessions Include:**
- Novel Probes and Techniques
- Assay Development
- Real Time Imaging
- Optical Imaging
- Bioluminescence

**Presenting Companies:**
- AntiCancer, Inc.
- Los Alamos National Laboratory
- Merck & Co., Inc.
- National Institutes of Health
- Novartis Pharmaceuticals Corporation
  ...and more!

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Third Annual

**In Vivo Molecular Imaging**
**Moving from Discovery to Preclinical to Clinical Applications**

November 14-15, 2006
Hilton La Jolla Torrey Pines • La Jolla, CA

**Sessions Include:**
- Bioluminescence
- Preclinical Imaging
- Imaging in - Neurology
  - Cardiology
  - Oncology

**Presenting Companies:**
- Boehringer Ingelheim Pharma GmbH & Co.
- GlaxoSmithKline, UK
- Harvard Medical School
- Kodak Molecular Imaging Systems
- Pfizer, Inc.
  ...and more!

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linkage to HaloLink surfaces. An example will be given showing correlative analysis of p65 biology.

cells by a variety of fluorophores and captured from the cells as protein complexes through covalent
11:00 Solutions Showcase:
assays, including Protein-fragment Complementation Assays (PCA), to perform live cell, pathway-
Biological responses to drugs are determined by the architecture and dynamics of the cellular signal
changes of fluorescence in single bacterial cells. Our approach presents a substantial advance for cellular
and
4:45 Whole-Body Subcellular Imaging in the Live Mouse
Robert M. Hoffman, Ph.D., President, AntiCancer, Inc.
Dual-color cancer cells expressing GFP in the nucleus and RFP in the cytoplasm have been developed. These cells enable nuclear-cytoplasmic dynamics, cell cycle analysis, apoptosis, nuclear and cytoplasmic shape changes, and numerous other processes to be visualized in the living mouse. The Olympus JV100 whole-mouse laser-scanning microscope with ultra-thin diameter objectives enable the dual-color cells to be visualized external to the mouse. Using host mouse models expressing GFP in all cells for the first time the study of tumor-host interaction at the cellular level in real time. This technology will lead to the development of the new field of in vivo cell biology to study both normal and disease processes in the live animal at the subcellular level.

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Fluorescent Proteins in Drug Development &
In Vivo Molecular Imaging

Tuesday, November 14

7:15 Registration and Morning Coffee
(Sponsorship for Breakfast Workshop Available)

8:25 Chairperson's Opening Remarks
Richard Levenson, M.D., Director of Research, Biomedical Systems, CRI, Inc.

Keynote Presentation

8:30 Molecular Imaging: From Research through Drug Discovery to the Clinic-Defining Path Forward
Peter Lassota, Ph.D., Vice President, Oncology, Caliper Life Sciences

Optical Imaging

9:15 In Vivo Optical Imaging Enabled by Soft-Matter Analogues of the Quantum Dots
Michael Thiem, Ph.D., Professor of Chemistry, University of Pennsylvania

9:45 Combining Bioluminescent Reporters and Fluorescent Probes for Studying Tumor Growth and Biology in Mouse Xenograft Studies
Steven Smith, Ph.D., Senior Scientist, Xenogen Corporation, a Caliper Life Sciences Company

Bioluminescence

9:45 Combining Bioluminescent Reporters and Fluorescent Probes for Studying Tumor Growth and Biology in Mouse Xenograft Studies
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Luminescence-based reporters have been widely adopted for studying tumor growth and metastasis in xenograft models. Cells constitutively expressing luciferase (lac) are particularly useful for non-invasively tracking and monitoring the growth of the primary tumor and identifying metastases. Additionally, inducible luc reporters, and specially designed constructs of lac, assay other aspects of tumor biology such as inhibition of the proteasome by drugs, or the induction of angiogenesis. Fluorescent reporters provide another imaging tool that complements bioluminescent imaging. Organic fluorophores can be used to tag protein and peptide ligands, antibodies, and small molecules and these are used to track the presence of extracellular proteins/receptors/enzymes in vivo.

Additional activity-based probes incorporating fluorescence are used to evaluate enzyme activity. Combining bioluminescent and fluorescent imaging modalities in the same xenograft models allows the investigator to probe many aspects of tumor biology simultaneously.

10:15 Coffee Break in the Exhibit Hall

11:00 In Vivo Bioluminescence Imaging Predicts FLT-PET Response to Novel Combination Therapy
Kenna Anderes, Ph.D., Associate Director Cancer Biology, Pfizer, Inc.

The ability to accurately predict which experimental therapies or combination therapies will provide clinical benefit remains a dark art. Bioluminescence imaging (BLI) sheds light on active agents and may predict FLT-PET responses. Correlative studies were conducted using BLI and FLT-PET imaging in xenografts used to evaluate novel combination therapies.

11:30 TBA
Kohkan Shamsi M.D., Ph.D., President, Symbiotic Pharma Research

Panel Discussion:

Moderated by Matthew Silva, Ph.D., Scientist, Imaging Science, Millennium Pharmaceuticals, Inc.

12:00 In Vivo Cellular MRI: Tracking Magnetically Labeled Cells in Disease Models
Joseph Frank, M.D., Chief, Experimental Neuroimaging Section, National Institutes of Health
Mammalian stem cells or other cells are being considered for infusion or transplantation into tissue for purposes of repair, regeneration or other therapeutic approaches. Cellular Imaging is a valuable tool for monitoring cell migration and trafficking in vivo. Magnetic labeling of cells provides the ability to monitor their temporal spatial migration in vivo cellular MRI. The techniques for labeling cells with MRI contrast agents have been well established in experimental systems and are presently being translated to the clinic. In this presentation, I will describe the different approaches used to label cells with contrast agents and show MRI and histological results in various animal disease models. Magnetic Tagging of cells has the potential for guiding future cell-based therapies in humans and for the evaluation of cellular-based treatment effects in disease models.

12:30 Luncheon Technology Workshop: Translational Applications of Optical, MultiModal in Vivo Molecular Imaging
Shahram Haghi, Ph.D., WW General Manager, Molecular Imaging Systems, Kodak Health Group

Multi-modal imaging agents enable highly specific fluorescent, luminescent, and radiolabeled imaging of disease processes within living animals. These in vivo molecular imaging agents provide the potential for rapid detection of specific changes within the target tissues long before morphological changes from disease or from disease treatment are present. Use of these imaging agents in live animals has stimulated the development of multi-modal imaging systems, the application of which will be presented.

1:55 Chairperson's Remarks

2:00 In Vivo Preclinical Imaging in Drug Discovery
Matthew Silva, Ph.D., Scientist, Imaging Science, Millennium Pharmaceuticals, Inc.

The generally accepted role for medical imaging in preclinical pharmaceutical drug discovery and development is to assist in the advancement of animal disease models and to provide additional drug efficacy read-outs. The successful implementation of this strategy requires (1) the full commitment of the institution to support the imaging group and (2) the keen ability of imaging scientists to identify impact projects. This talk focuses on the integration of a multi-modal, small animal, in vivo imaging facility into the drug development process-including project prioritization, "pharmaceuti-cal-grade" throughput, assay robustness, and drug efficacy measurements.

2:30 Imaging Wormtannin: New Sights For An Old Molecule
Lee Josephson, Ph.D., Associate Professor, Center for Molecular Imaging Research, Harvard Medical School

The ability to image the fate of natural products in biological systems can provide valuable information about their behavior, and further development of drug leads based on this important source of materials for pharmaceutical development. Fluorescent forms of wormtannin, a natural product inhibitor of F3 Kinase, provide insights into the mechanism of wormtannin action and development of wormtannin based inhibitors of this enzyme, which plays an important role in controlling tumor cell proliferation. In collaboration with Katie Barnes, Hushan Yuan, and Ralph Weissleder.

3:00 In Vivo Molecular Imaging of Spatio-Temporal Drug Distribution Using the Sub-Millimeter NanoSPECT/CT
Jeffrey P. Norenberg, MS, PharmD, BCNP, FASHP, FAPhA, Executive Director, National Association of Nuclear Pharmacies, Associate Director, New Mexico Center for Isotopes in Medicine, Associate Professor and Director, Radiopharmaceutical Sciences, College of Pharmacy, and Jack Hoppin, Ph.D., Vice President, Imaging Systems, Bioscan, Inc.

We will present descriptions and results of numerous in vivo bio-distribution studies using radio-labeled pharmaceuticals. The talk will describe the imaging capabilities of the four-headed NanoSPECT/CT system including discussions of resolution, sensitivity and uptake quantification capabilities. We will present results of initial pharmacokinetic studies performed with the NanoSPECT demonstrating the new-found strength of temporal imaging with multi-pinhole SPECT.

3:15 Solutions Showcase
Get informed on the newest technology and developments.
Contact Carol Dinerstein at 781-972-5471 for sponsorship opportunities.

3:30 Refreshment Break in the Exhibit Hall

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For reservations, please call the hotel directly to make your arrangements. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate.

Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space-and-rate-availability basis. Rooms are limited, so please book early.
Among the many advantages zebrafish offer is their transparency during early development and their small size. These features make it an attractive model for in vivo imaging. We have generated a transgenic line of zebrafish where all T cells are GFP labeled. Using multispectral imaging technology we are able to follow the development, migration, and accumulation of T cells from larval to adult stages. We have also initiated a mutagenesis screen, where we identified immunodeficient and leukemic phenotypes that are now the subject of detailed analysis and positional cloning. In addition, we have started a small molecule screen to identify compounds that can “unmix”, or separate, signals, results in targets appearing displayed against a black, near-zero background. Similarly, microPET in animal models with current PET ligands do not seem to work. An optical approach for non-invasive imaging in animals, and ultimately humans, would be relatively inexpensive and widely available. Our goals are to develop novel small molecule contrast agents that are near infrared fluorescent, cross blood-brain barrier, and target Abeta specifically.

In combination, we are developing novel optical tomographic approaches to detect these agents with high sensitivity and high spatial resolution in living animals. With an orchestrated multidisciplinary approach, we expect to facilitate in vivo drug testing in animal models, and perhaps diagnose early stage Alzheimer's disease in humans.
In Vivo Molecular Imaging (continued)

11:30 A High-Throughput Molecular Imaging Screen to Monitor Therapeutic Response in Vivo
H. Charles Manning, Ph.D., Assistant Professor of Radiology, Vanderbilt University Institute of Imaging Sciences (VUIIS); Assistant Professor of Neurosurgery, Vanderbilt University Medical Center
In this presentation we will demonstrate that molecular imaging will facilitate real-time efficacy monitoring in small animal models of experimental auto-immune encephalomyelitis (EAE) and some forms of cancer. We have prepared a panel of complementary NIR-based imaging probes that give a physiologically relevant readout allowing observation of therapeutic response. These probes measure epidermal growth factor receptor (EGFR) expression (NIR-EGF), glucose metabolism (NIR-GLC), stereospecificity (NIR-confPK11195), DNA replication (NIR-d-thymidine) and angiogenesis (NIR-VEGF) and apoptosis (NIR-Annexin-V). We will show that NIR-confPK11195 and NIR-GLC mimic the translational probes IARPDOG and 11C-PK11195 already in use in the clinic and by utilizing our novel Lanthamide chelate chemistry, we can prepare PET/SPECT versions of the other optical probes for translation of the full efficacy screen to the clinic. It will be shown that the screen is broadly applicable to small animal disease models and can be used to accelerate the preclinical evaluation of biological response modifiers (BRMs) and conventional therapeutics.

12:00 Lunch on your own

1:25 Chairperson’s Remarks

Imaging in Cardiology
Dr. Ulrich Rothbauer, Senior Scientist, Department Biologie II, Ludwig Maximilians University
Fresh from the Press: Brief Communications in Nature Methods, November 2006

2:00 Functional and Molecular Imaging with Micro-Ultrasound
F. Stuart Foster, Ph.D., Department of Biophysics, University of Toronto, Sunnybrook Health Sciences Centre, Canada
This presentation will describe the development, implementation, and application of high frequency contrast enhanced micro-ultrasound to extract quantitative measures of functional and molecular targets in preclinical research. The development of targeted microbuble contrast agents will be described. Applications of this technology to the study of tumor microcirculation and therapeutic response to antiangiogenic agents will also be presented. Untargeted contrast permits the evaluation the morphology and hemodynamics of various tumor models. These methods allow, for the first time, realtime in vivo visualization of the true microcirculation. Molecular studies of targeted molecular targets such as VEGFR-2 will be presented. These results show the ability of micro-ultrasound not only to detect expression of VEGFR-2 in experimental mouse tumors but also to do so with resolution nearly an order of magnitude better than micro PET. The feasibility of clinical translation of these approaches will also be discussed.

Imaging in Oncology

2:30 Molecular Diapextics—New Approaches to Cancer Detection and Treatment
Jamey Weichert, Ph.D., Associate Professor, Department of Radiology, Medical Physics and Pharmacometrics, University of Wisconsin
We have developed a radioiodinated phospholipid ether analog that has displayed striking tumor uptake and prolonged retention in 30/30 animal and human tumor models to date. We have now successfully labeled this agent with iodine-124 (I-124) and Iodine-131 (I-131). Injection of a microdose (<100 µg) of I-124-labeled HER2 Scan (110-130 MBq) resulted in high quality SPECT and PET/CT images enabling the detection of small lesions (12-14 mm) after 2-3 hour post injection. Patients were carefully monitored and no adverse effects were observed.

3:00 Networking Refreshment Break

3:30 Clinical and Preclinical Application of HER2-Specific Affibody Molecules for Diagnosis of Recurrent HER2 Positive Breast Cancer by SPECT or PET/CT
Dr. Anders Wennborg, Head, Pharmacology, Affibody AB
The HER2-specific Affibody molecule ZHER2:342 belongs to a novel class of small non-immunoglobulin affinity ligands with high target-binding affinity and specificity. Preclinical characterization of radiolabeled HER2-Scan in mice bearing HER2-expressing xenografts showed high specific tumor targeting with 23 % ID/g at 1 hour post injection, rapid biodistribution kinetics and blood clearance and allowed high contrast gamma camera imaging as early as 1 hour post injection. For the first time in human study, we evaluate the use of labeled HER2-Scan to specifically detect and stage HER2-expressing metastatic lesions in patients with recurrent breast cancer. Injection of a microdose (~100 µg) of 111In or 68Ga-labeled HER2-Scan (110-130 MBq) resulted in high quality SPECT and PET/CT images enabling the detection of small lesions (12-14 mm) after 2-3 hours post injection. Patients were carefully monitored and no adverse effects were observed.

4:00 An Early MRI Biomarker of Cancer Treatment Response
Brian Ross, Ph.D., Professor, Department of Radiology, University of Michigan
This presentation will detail how the functional diffusion map (fDM) can be used as an imaging biomarker for quantification of early treatment response in solid tumors. In brief, changes in tumor MRI diffusion values were found to be highly correlatie with drug dose and biological outcome measures revealing fDM is an effective early biomarker for prediction of efficacy in rodents and in human brain tumor patients. Thus, early fDM measurements can be used to provide an early biomarker of response in patients thus allowing for an opportunity to individualize treatment.

4:30 Engineered Antibodies for Imaging Cell Surface Phenotype
Tove Olafsen, Ph.D., Associate Researcher, Department of Pharmacology, UCLA
Engineered antibodies have been developed for imaging carcinoembryonic antigen (CEA) in colon cancer, HER2 in breast cancer, CD20 in B-cell lymphoma and prostate stem cell antigen (PSCA) in prostate cancer. Recombinant antibody fragments such as diabodies (a dimer of single-chain Fv; 55 kDa), minibodies (dimer of scFv-CH3; 80 kDa), and scFv-Fc (dimer of scFv-CH2-CH3; 105 kDa) exhibit favorable characteristics for in vivo imaging, including rapid, specific localization to xenografts in mouse models and fast blood clearance. MicroPET imaging using fragments labeled with Iodine-124 (I-124) and Copper-64 (Cu-64) results in high contrast images. Factors influencing selection of the optimal fragment (including size, radiolabel, antigen internalization, etc.) will be discussed. Engineered antibodies recognizing cell surface targets represent a broad platform for developing novel imaging agents.

5:00 End of Imaging Week
YES! Register me for Fluorescent Proteins in Drug Development □ In Vivo Molecular Imaging

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*Email is not a mandatory field. However, by excluding your email you will not receive notification about online access to pre-conference presenter materials, conference updates, and networking opportunities.

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Please send information on exhibiting and opportunities to present workshops.

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I am interested in presenting a poster at:

□ Fluorescent Proteins in Drug Development □ In Vivo Molecular Imaging

and will submit a completed one-page abstract by October 24, 2006. (Please Note: Registration must be paid in full to present poster.)

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• Credit your registration to another Cambridge Healthtech Institute program
• Request a refund minus a $100 processing fee per conference
• Request a refund minus the cost ($500) of ordering a copy of the CD

NOTE: Cancellations will only be accepted up to two weeks prior to the conference.

Program and speakers are subject to change

Video and audio recording of any kind is prohibited onsite at all CHI events.

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