

## Building Team Science

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### NANOTECHNOLOGY-DERIVED POSITRON-EMITTING PROBES FOR MOLECULAR IMAGING

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Tseng<sup>1</sup>, and Michael E. Phelps<sup>1</sup>*

#### Collaborating Centers:

<sup>1</sup>NanoSystems Biology Cancer Center CCNE  
(NSBCC-CCNE)

<sup>2</sup>Carolina Center of Cancer  
Nanotechnology Excellence  
(C-CCNE)

<sup>3</sup>Center for Cancer Nanotechnology  
Excellence Focused on Therapy Response  
(CCNE-TR)

Positron emission tomography (PET) is a sensitive non-invasive imaging technology for measuring biochemical processes at a whole body level in living subjects. As a result, PET imaging in cancer provides powerful means to (i) identify early

disease, (ii) differentiate benign from malignant lesions, (iii) examine all organs for metastases, (iv) stratify patients based on potential sensitivity to targeted therapies, and (v) provide an early readout of response to therapy. The major roadblock to increasing the applications of PET in preclinical and clinical research, aiding the drug discovery and molecular imaging diagnostics is a convenient and low-cost source of a diverse array of PET probes. New approaches are needed to enable biologists and clinicians to synthesize a wide range of PET probes. Integrated microfluidic technology, with intrinsic advantages of speed, chemical economy, flexibility, user-friendliness, safety, modularity and low cost, is a prime technology platform for producing radiolabeled PET probes. The goal of our project (NSBCC-CCNE Project 3, PI: Dr. Michael Phelps) is to develop new technology platforms that will accelerate the discovery and development processes of new PET probes and facilitate a broader use and value of PET imaging. Our joint team brings together the expertise of eight research

FIGURE 1. Optical micrographs of three generations of microfluidic chips for multi-step radiosynthesis of small-molecule PET imaging probes.

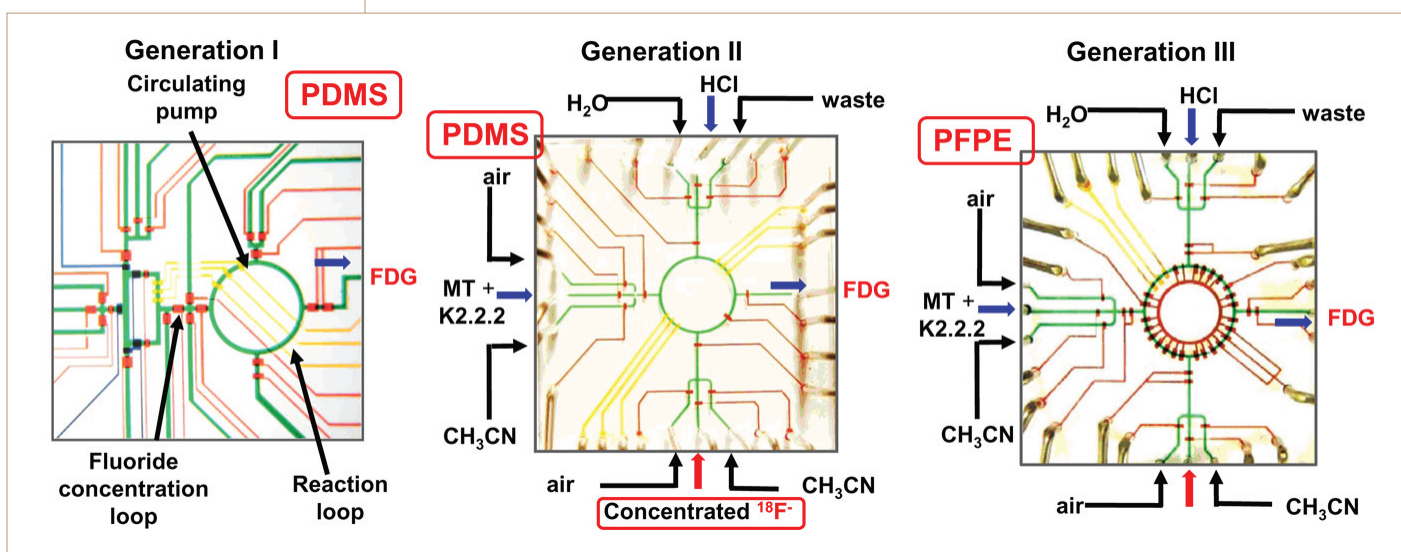
Channels have been loaded with colored food dye to visualize the different components of the chip (green: channels for fluids; red: pressurized control channels for valve actuation; yellow: triplets of pressurized control channels for peristaltic pumping). Each chip is roughly 20mm square.

groups covering the fields of radiochemistry, microfluidics, polymer materials, device prototyping, molecular imaging and antibody engineering.

Over the past three years our team has designed, fabricated and tested three generations of microfluidic devices for automated production of [ $^{18}\text{F}$ ]-labeled PET imaging probes (Figure 1). Compared to the conventional approach, accelerated synthesis of 2- [ $^{18}\text{F}$ ]fluoro-2-deoxy-D-glucose ([ $^{18}\text{F}$ ]FDG), the most commonly used PET tracer for imaging altered glucose metabolic states in cancer, was accomplished with improved radiochemical yield and purity using the Generation-I devices.<sup>[1]</sup> Design modifications in Generation-II devices enhanced reliability and increased the generality of this radiochemical technology platform. The rapid synthesis of a different PET tracer, [ $^{18}\text{F}$ ]-3'-deoxy-3'-fluoro-L-thymidine ([ $^{18}\text{F}$ ]FLT), a PET imaging probe for DNA replication and cell proliferation,

has recently been demonstrated in the Generation-II devices. In collaboration with Dr. Joseph DeSimone at the C-CCNE and Liquidia Technologies, Inc., chemical and solvent resistant polyperfluoropolyether (PFPE) elastomers<sup>[2]</sup> (developed at UNC and commercialized by Liquidia) are utilized to replace the original polydimethylsiloxane (PDMS) materials for the fabrication of the Generation III chips. Using the Generation III chips with improved chemical inertness and device robustness, we will be able to further expand the chip-based radiochemistry for syntheses of a wide range of PET probes.

We are also working with Dr. DeSimone's group to study *in vivo* biodistribution of the nanoparticles produced by their particle molding technology known as Particle Replication in Non-wetting Templates (PRINT).<sup>[3]</sup> The PRINT process enables the production and harvesting of monodisperse, shape-specific nanoparticles



made from a variety of polymers. The PRINT nanoparticles decorated with 1,4,7,10-tetraazacyclo-dodecane-1,4,7,10-tetraacetic acid (DOTA) can be labeled with the radioisotope  $^{64}\text{Cu}$  and sequentially imaged in small animals *via* microPET (Figure 2) to obtain their *in vivo* biodistribution properties. These PRINT particles are presently being designed to reach new understandings and therapies in cancer prevention, diagnosis and treatment.

Dr. Anna Wu, from the CCNE-TR, has accumulated extensive experience on exploring the potential of engineering antibody fragments<sup>[4]</sup> as PET probes with improved specificity and well-controlled pharmacokinetics. Our team has been work with Dr. Wu's research group to test the feasibility of performing automated syntheses of [ $^{18}\text{F}$ ]-labeled antibody

fragments in a microfluidic setting. We have been developing a new generation of microfluidic devices, in which two sequential reactions — (i) radiosynthesis of N-succinimidyl-4- [ $^{18}\text{F}$ ]fluorobenzoate ([ $^{18}\text{F}$ ]SFB) and (ii) labeling of small quantities of antibody fragments with the *in situ* prepared [ $^{18}\text{F}$ ]SFB — can be conducted in an automated fashion.

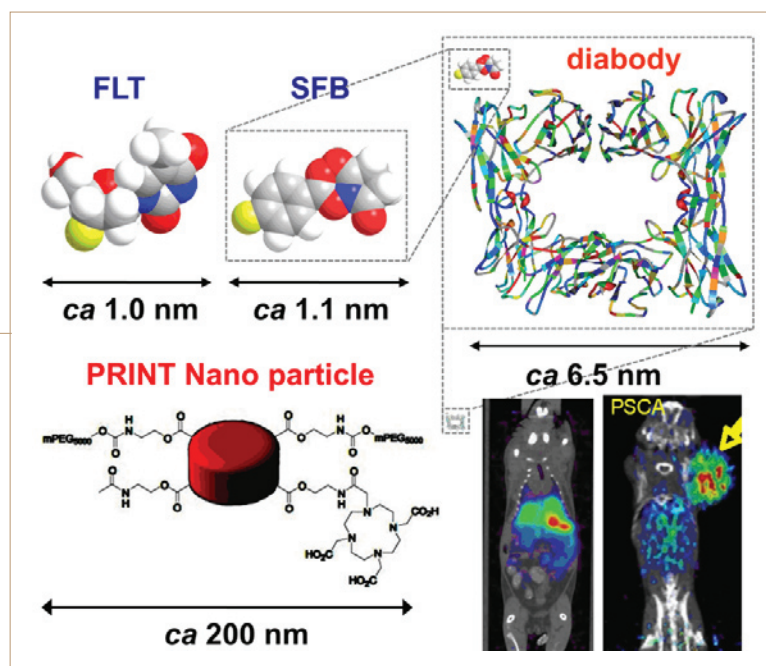
Such collaborative cross-disciplinary efforts significantly advance our goals and provide opportunities for our nanotechnologies and microfluidics platforms to impact molecular imaging and cancer-related research. We envision that a microfluidic-based platform along with the existing widespread commercial supply of [ $^{18}\text{F}$ ]fluoride will provide an enabling technology for routine probe production and for academic and commercial scientists to accelerate their

discovery and development of new tracers for PET in research, drug discovery and development, and molecular imaging diagnostics in patient care.

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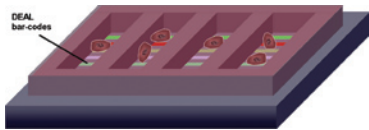
FIGURE 2. Illustration of various categories of small molecules, biomolecules and synthetic nanoparticles which can be labeled with positron-emitting radionuclides (e.g. F-18) using our microfluidics. Micro-PET: PRINT nanoparticles (Cu-64, left) and anti-PSCA (prostate stem cell antigen) minibody (I-124, right).



## Training Across the Alliance



*Postdoc Fellow, Rong Fan, smiles for his happy experience in cancer research at the NanoSystems Biology Cancer Center (NSBCC-CCNE).*



*Single cell chip, developed by Rong Fan and colleagues, can record the secret conversation among individual cells.*

### INTERDISCIPLINARY EXPERIENCE FOR SUCCESS IN CANCER RESEARCH

*By Rong Fan, Ph.D. Postdoctoral Fellow NSBCC-CCNE*

Dr. Leroy Hood, the co-director of NSBCC-CCNE, has a “growth curve” theory that states the path to lead one’s career from one success to another is to find a new growth point. This “theory” has guided Dr. Hood from his success in 1980’s for developing automated gene and peptide sequencing to now being a leading scientist in the area of systems biology. My postdoctoral training at Caltech shows that this theory also provides valuable advice on developing experience for success in clinical cancer research.

The first piece of scientific research I conducted dates back to 2000 at the University of Science and Technology of China where I studied the superconductors in the Department of Physics. The next year, I attended the Ph.D program in the Department of Chemistry at UC Berkeley to investigate the synthesis nanomaterials for energy conversion. However, despite my success in studying energy sciences, I was strongly attracted by the beauty of biological systems, and decided to look at biomedical problems after graduation.

In 2006, I was delighted to join the cancer biology research team in Professor Jim Heath’s laboratory. In the beginning, this bold move turned out to be really

a tough cross. Like most postdoc fellows, I was hoping to start my projects as soon as possible and keep myself in a pace of productiveness. I proposed several “quick” ideas in the first month. Professor Heath was always patient in answering my questions and arranged several meetings to discuss technical details of these ideas. However, what is most beneficial to me is his philosophical advice that says we need to let the biology teach us. Thanks to the unique environment of the NSBCC-CCNE, I was able to talk to experts from diverse areas within our center. These scientific communications made me learn a lot and inspired my deep and broad thinking in many cancer biology topics such as oncogenic signaling pathways, cancer heterogeneity, cancer stem cells, etc. Along with learning various hands-on techniques in detection techniques used in Heath lab, I read a lot of research articles in biology. One day after several months, I was excited by an interesting story about the paradoxical role of our immune system with cancer, and then I brought this idea to Professor Heath. The immune system of humans is able to fight many diseases, including cancer. But what a surprising paradox is that the immune response, especially inflammation evoked by tumor-infiltrating immune cells, creates a complicated microenvironment that may facilitate tumor promotion and progression. In this regard, tumors cells hijack the

immune system to assist their “criminal” counterparts that eventually leads to the malignant disease — cancer. The tumor microenvironment is comprised of a large number of different cell types, e.g. normal epithelial, tumor epithelial, macrophages, T-cells, etc. It is so heterogeneous at single cell level. Therefore, it is a grand challenge to perform a comprehensive characterization of tumor microenvironment at both cellular and molecular levels. To tackle this problem, I proposed a microfluidic device that can isolate different cell types from only a small quantity of tumor tissue (e.g. from needle biopsy) and then analyze the molecular network that dictates how these cells function, communicate and coordinate to create favorable tumor microenvironment. Understanding the tumor-immune interaction may help us find ways to prevent tumor progression by suppressing the immune system’s tumor promoting function. Advances in the biology of the tumor microenvironment and in particular, the clinical tool to diagnose the tumor microenvironment, allowing us to imagine a future in which cancer becomes a manageable, chronic, benign ailment one can live with for a whole life.

In the past year, I have made progress that may allow us to assess the impact of heterogeneous tumor micro-environment. First, I devised an integrated bar-code chip

to simultaneously detect multiple cell-cell signaling molecules from a single cell. These molecules include cytokines and chemokines that are the “language” used by immune cells to communicate. For example, the isolated cells or cell colonies of human macrophages, a key player in promoting inflammatory environment in tumor, had very different conversations in the individual chambers even though they are from the identical cell lines. Such single cell heterogeneity might have implications in the heterogenic nature of tumor microenvironment. The second approach is through a comprehensive blood test. As blood is re-circulated throughout body every minute, it brings back information from all organs and tissues. Working with my colleagues, I developed an integrated blood test chip that can measure a panel of plasma proteins (including inflammatory molecules present in tumor microenvironment) from a finger prick of blood. To evaluate its effectiveness in clinical cancer diagnoses, tens of serum samples from prostate or breast cancer patients were assayed. Despite the limit of sample size, an intriguing correlation of cancer and inflammation was observed. We are very excited by this discovery and the future study towards analyzing a large number of clinical samples is under the way.

Although a bold move to cross disciplines provides opportunities for new growth points, a favorable “growth medium” is absolutely a deterministic factor for the success in postdoc research. Our center, the NSBCC-CCNE, joins the forces from Caltech, UCLA medical school and the Institute for Systems Biology (ISB) in Seattle, providing a multidisciplinary stage for new researchers. In the past year, I drove to UCLA medical school every week to attend Professor Hong Wu’s group meetings. Through conversation with our medical school partners, I was able to find where the real challenges are in cancer research faced by biologists and clinicians, and then design solutions to tackle these specific problems. I also participated in the systems biology summer course organized by our NSBCC-CCNE member — ISB at Seattle. I found this training very useful.

The most valuable experience I have had at NSBCC-CCNE is how to find, understand the real problems and design solutions to tackle them in an interdisciplinary field such as clinical cancer research. The unique environment at NSBCC-CCNE provides great opportunities.

## Alliance Young Investigator Spotlight



Hsian-Rong Tseng, Ph.D.  
(Pharmacology/UCLA)

HSIAN-RONG TSENG, PH.D.  
NSBCC-CCNE

Dr. Tseng participates in the NanoSystems Biology Cancer Center (NSBCC-CCNE) led by Drs. Jim Heath (Caltech), Mike Phelps (UCLA) and Lee Hood (ISB). Tseng was trained as an organic and physical chemist and has been an assistant professor at the Crump Institute for Molecular Imaging and Department of Molecular and Medical Pharmacology in the David Geffen School of Medicine at UCLA since 2003.

Tseng's research interests are to develop microfluidic technology platforms and to utilize these technology platforms for applications in the fields of chemistry, molecular imaging and cancer biology. In contrast to conventional bench-top setups, microfluidic devices can be used to manipulate chemical and biological processes on nanoliter (nL) to microliter ( $\mu\text{L}$ ) scales with the profound advantages of sample economy, enhanced heat and mass transfer, and improved control over experimental conditions. During the past four years, the Tseng research group together with several collaborators at UCLA and Caltech initiated the joint efforts to develop a variety of PC-operated, integrated microfluidic devices for (i) sequential syntheses of nanogram-level molecular imaging probes for positron emission

tomography (PET) (*Science* 2005, 310, 1793), (ii) parallel screening of high-affinity inhibitors against proteins involved in malignant transformation (*Angew. Chem. Int. Ed.* 2006, 45, 5276), and (iii) systems-oriented profiling of signaling networks that drive the malignant transformation of cancers. These preliminary data validated the feasibility of performing complicated chemical reactions and biological operations in individual microchips and provide a solid foundation for Tseng's future research plans. Ultimately, Tseng's research team will produce further integrated microfluidic technology platforms for the broader space in chemistry, molecular imaging and cancer biology beyond the existing complexities. Many different existing functional microfluidic modules will be integrated to produce a number of game systems: "Let's Play\_\_\_\_\_", where the blank will hopefully be filled with:

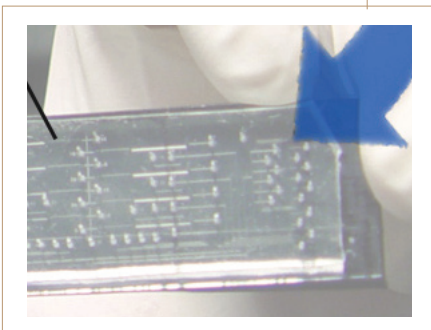
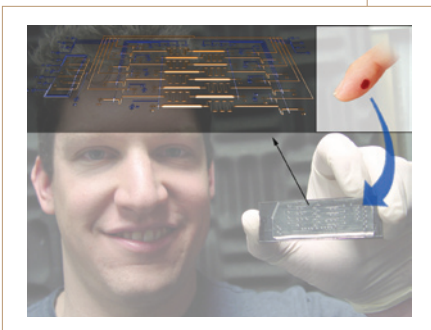
1. Microfluidic reactors for development of in vivo imaging probes and therapeutics.
2. Quantitative systems-biology chips for cancer diagnosis and predictive therapy.

For more information about Hsian-Rong Tseng and his research group please visit the group's website at <http://labs.pharmacology.ucla.edu/tsenglab/>.

## Nanotechnology Highlights



*FIGURE 1. Integrated blood Chip. M.D./Ph.D student, Ophir Vermesh, at NSBCC-CCNE is showing the integrated blood bar-code chip that can measure a panel of proteins plasma of a finger prick of blood within a few minutes.*



### INTEGRATED BLOOD BAR-CODE CHIPS MAKE CLINICAL DIAGNOSES CHEAP AND INFORMATIVE

*By Rong Fan, Ph.D. (rfan@caltech.edu)  
NSBCC-CCNE*

The singular term “cancer” deceptively encompasses multiple diseases that are highly heterogeneous. This heterogeneity is manifested at all levels — from patient to patient and from cell to cell. This is because the molecular origins of cancer are varied. The terms such as Stage 1 or Stage 2, etc., that are utilized to describe the progression of cancer (and often used to guide treatment) are poor predictors of the response to therapy that an individual patient might have. The recent advent of cancer therapeutics targeted at certain specific molecular lesions that are involved in the transformation from health to disease has highlighted this inadequacy of traditional diagnostics. Some of these therapeutics only affect small subpopulations of patients with a given type of cancer (e.g. breast cancer). Patients that don't exhibit positive responses are instead just subject to the negative side effects of these therapies, which can be significant.

Thus, assigning the right drug to the right patient is a challenge. Once the right drug has been assigned, controlling dosage levels to maximize the efficacy while

minimizing the toxicity is important. It is likely that in the near future personalized cancer treatments will involve combination therapies, and this highlights the challenge even more. Clearly meeting this challenge means finding measurement methods that can accurately and comprehensively diagnose the cancer, monitor therapeutic efficacy, and detect recurrence.

State of the art research in cancer biology is beginning to yield clues regarding what needs to be measured to achieve a comprehensive cancer diagnosis. Network models of disease — that is, models of the interacting gene and protein networks that describe tissue function, and how those networks are perturbed by the onset and progression of disease — are beginning to reveal the differentially expressed or otherwise altered genes and proteins that can provide disease fingerprints<sup>1</sup>. Furthermore, those networks can be data mined to identify proteins that are organ-specific (i.e. only expressed in the organ of interest) and secreted into the blood. The key is that each organ has its own unique blood molecular fingerprint, and if the levels of those blood proteins can be measured, then they can be correlated back to the health state of the organ. For example, a toxic response to a cancer therapeutic might be best monitored by measuring the liver-specific blood molecular fingerprint.

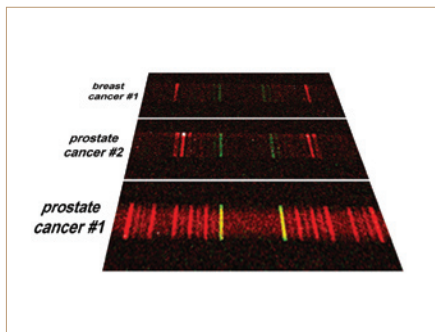
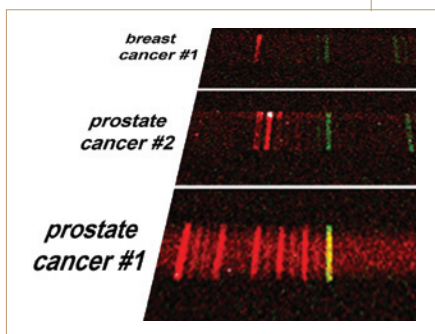


FIGURE 2. Distinct Blood Bar-Codes. Using the integrated microchips, cancer patients can be clearly diagnosed through a rapid blood test. Moreover, by measuring a panel of biomarkers and cell-cell signaling molecules, these chips may be employed to identify the different cancer subtypes based on the unique “blood bar-codes” that aid doctors to give the right patient the right drug.



An inflammatory response might be monitored by assessing proteins from the white blood cells, which can be considered a circulating organ. The cancer itself may be monitored by measuring the blood protein levels that originate from the diseased organ. While this approach represents a huge opportunity for cancer diagnostics and treatment, it also represents a staggering technology challenge. It is meeting that challenge that constitutes the heart of our research within the NanoSystems Biology Cancer Center (NSBCC-CCNE).

The *in vitro* cancer diagnostics team in Heath lab at Caltech devised an integrated blood bar-code chip (IBBC) that can perform blood separation and *in situ* measurement of a panel of plasma proteins from a finger-prick of blood on a 10 minute time scale. The plasma separation was achieved using a simple hydrodynamic principle — the Zweifach-Jung effect. Plasma is skimmed into high-flow-resistance channels, termed plasma channels that are split off from this primary channel. As the resistance ratio between the plasma channels and the primary channel is increased, a critical streamline in the primary channel moves towards the plasma channel split point. Blood cells with a radius larger than the distance separating the critical streamline from the plasma channel are directed away from the primary channel. As a result, 10-15% of the plasma is collected into the downstream of plasma channels where a protein detection array was placed.

This blood separation module enables the rapid separation of a finger prick of blood within a few minutes. It allows the capture of plasma protein profile that closely resembles the patient’s physiology; conventional blood collection methods are impaired by fast blood kinetics that can destroy proteins, coagulate blood, etc.

To meet the challenge in diagnosing cancer heterogeneity and understanding the dynamic evolution of disease networks, a large panel of protein markers is measured simultaneously from a small quantity of blood. The detection mechanism we take is the DNA-encoded antibody library (DEAL) method<sup>2</sup>, a variant of surface-bound immuno-assay array developed in Heath lab. To increase the array density to meet the stringent requirement of assaying tiny amount of clinical samples, the chip is constructed using microscale flow-patterning to spatially encode unique ssDNAs in the likeness of a barcode at a density 10x higher than conventional gene chips. Subsequently, an integrated microfluidic assay device translates the DNA microarray into an antibody microarray through DEAL. Biomarkers can then be detected using surface-bound immuno-sandwich-assays. By taking advantage of high DNA loading and a microfluidic environment, we have shown that the barcode chip has excellent sensitivity (comparable to state-of-the-art ELISA assays), broad dynamic range ( $10^5$ , three orders of magnitude larger than most

bioassays), and high throughput (tens of proteins are simultaneously detected from each of twelve specimens within half an hour).

The integrated blood bar-code chip has shown effectiveness in pre-clinical testing. A dozen cancer markers and inflammatory molecules were measured in a blood bar-code chip from just a few microliters of serum samples taken from twenty-four cancer patients. In this test, analysis of these protein barcodes unambiguously isolated all the prostate cancer patients from the original 24-patient pool and even differentiated several possible subtypes associated with immune/tumor interactions. For example, two categories of inflammatory signatures were observed: one which is TNF- $\alpha$  positive and another which is GM-CSF positive. TNF- $\alpha$  plays an important role in apoptosis, while GM-CSF is responsible for recruiting immune cells to a developing tumor microenvironment and inducing differentiation; this discovery may reflect different mechanisms of immune control in tumorigenesis. The integrated microfluidic bar-code chips can be extended to analyze other biospecimens, i.e. skinny-needle biopsied tissues, etc. We envision this versatile technology can help in searching for disease fingerprints.

An accurate, comprehensive and personalized diagnosis increasingly means

a multiparameter analysis enabled by systems biology. However, it is now extremely costly to perform multi-variant diagnosis using conventional technologies such as ELISA and mass spectrometry. The small amount of sample collected from a patient is often insufficient to complete all necessary assays. Therefore, a major challenge of extending multiparameter diagnostics to the clinic is to reduce the cost to a few pennies or less per measurement. The integrated blood bar-code chip is constructed from only plastic and glass, and we anticipate that it can serve as a very inexpensive and yet informative diagnostic tool. Moreover, its portability and assay speed mean that it can be used for real time diagnosis in the clinic and, eventually, in the home.

NSBCC-CCNE in vitro cancer diagnostics team personnel: the NSBCC-CCNE director Prof. James R. Heath; co-director Dr. Leroy Hood; postdocs Dr. Rong Fan, Dr. Lidong Qin, Dr. Alok Srivastava; graduate students Ophir Vermesh, Gabriel Kwong, and Habib Ahmad.

#### References

1. Heath, J.R. & Davis, M.E. Nanotechnology and cancer. *Annual Review of Medicines* 59, 405 (2008).
2. Bailey, R.C., Kwong, G.A., Radu, C.G., Witte, O.N. & Heath, J.R. DNA-encoded antibody libraries: A unified platform for multiplexed cell sorting and detection of genes and proteins. *Journal of the American Chemical Society* 129, 1959-1967 (2007).

## Alliance Activities



### NCI ALLIANCE FOR NANOTECHNOLOGY IN CANCER 2ND ANNUAL INVESTIGATORS MEETING

On October 16-18, 2007, The Alliance for Nanotechnology in Cancer held its second annual Investigators Meeting in Chapel Hill, NC. Hosted by the Carolina Center of Cancer Nanotechnology Excellence and the University of North Carolina at Chapel Hill, the meeting was attended by over 280 Alliance investigators, students and postdoctoral fellows, a 40% increase in attendance compared to the 2006 Investigators Meeting. All eight Centers

for Cancer Nanotechnology Excellence (CCNEs) and 12 Cancer Nanotechnology Platform Partnerships were represented.

Some of the highlights of the meeting included:

- a day-long tutorial aimed at bringing up to speed those new to the multidisciplinary field of cancer nanotechnology
- eight scientific sessions featuring the latest research results from Alliance investigators
- an evening session on the pathway to clinical development, along with two featured talks by Alliance investigators who have experience bringing nanotechnology-enabled drugs through the clinical trials pathway.
- over 100 posters detailing additional work from Alliance-funded laboratories

## EVENTS

### MIT-Harvard CCNE

#### 2008 MIT CCR Symposium

“Nanotechnology and Cancer:  
The Power of Small Science”

June 27th, 2008

Cambridge, MA

Registration will be available at:

<http://web.mit.edu/ccr>

### Northwestern University CCNE

#### All Scout Nano Day

March 8, 2008

Location: Pancoe-Evanston

Northwestern Healthcare

Life Sciences Pavilion,

Abbott Auditorium

2200 Campus Drive

Northwestern University,

Evanston Campus

The very popular annual All Scout Nano Day provides an exciting overview of nanotechnology including hands-activities that demonstrate nanoscale properties, the laser and microscope tour and demonstrations, poster session, careers in science and engineering interactive, juried poster session, and pizza party. Boy Scouts, Girl Scouts and Venturing Crews are welcomed. For more information contact Denise Dooley, Outreach Coordinator ([d-dooley@northwestern.edu](mailto:d-dooley@northwestern.edu)).

## SYMPOSIUMS

### Emory-GT CCNE

2008 Emory-GT Frontiers of Cancer

Nanotechnology Symposium

March 30-April 1, 2008

Callaway Gardens

Pine Mountain, GA

## COURSES

### CCNE-TR

#### Transmission Electron

Microscopy (TEM)

Laboratory Class at Stanford,

Spring Quarter 2008

The laboratory course on Transmission Electron Microscopy will be offered to Stanford students. This practical lab class discusses experimental applications of electron microscopy to typical materials science studies. Topics include microscope operation and alignment, diffraction modes and analysis, bright-field/dark-field analysis of defects, high resolution imaging, and analytical techniques for compositional analysis (EDAX).

### MIT-Harvard CCNE

Access to all MIT undergraduate and graduate courses can be found at:

<http://mit.edu/ocw/>

## SCCNE

Online CME Siteman CCNE Course:

Samuel Wickline, MD,

“Nanotechnology for Molecular  
Imaging and Therapy in Cancer”

Visit: [http://cme-online.wustl.edu/  
user/catalog.asp](http://cme-online.wustl.edu/user/catalog.asp)

Click on Preview Course, Oncology  
and then the course title.

## LECTURES

### CCNE-TR

S. X. Wang, “Molecular diagnostics and  
nanomagnetic biosensors,” Invited Tutorial,  
American Physical Society March Meeting,  
New Orleans, March 9-14, 2008.

*The University of Texas at Austin,*

*Institute for Cellular & Molecular Biology*

A weekly series of so-called “Systems  
Lunches,” emphasize the use of systems  
biology methods and nanotechnology  
for addressing issues in human disease,  
in particular in oncogenesis. As a result  
of these meetings, new collaborations  
with faculty members on the development  
of novel nanotechnologies (multimodal  
nanoparticles, with Dr. Kostia Sokolov)  
for the imaging and treatment of cancer,  
and have begun to define and address  
the gene and interactome networks  
involved in cancer metastasis (with  
Dr. Muhammad Zaman and Dr. Edward  
Marcotte) have occurred.

seminars SEMINARS

*C-CCNE*

The Carolina Center of Cancer Nanotechnology Excellence announces its 2nd Annual Symposium, November 14, 2008 at the Rizzo Conference Center in Chapel Hill, NC. Details will be posted on our website as they are available, contact [ccne@med.unc.edu](mailto:ccne@med.unc.edu) for information.

*CCNE-TR*

Regularly scheduled Nanobiotechnology Seminar Series held 3rd Tuesdays of every month. Please visit [http://mips.stanford.edu/public/nanobiotech\\_seminar.adp](http://mips.stanford.edu/public/nanobiotech_seminar.adp) for all speakers and webcasts.

*Emory-GT Frontiers of Cancer Nanotechnology Seminar Series*

March 24, 2008

Hongjie Dai, Ph.D.

J.G. Jackson-C.J. Wood Professor

Dept. of Chemistry

Stanford University

“Carbon Nanomaterial for Biological Applications”

April 15, 2008

Chad Mirkin, Ph.D.

Professor of Chemistry

Dept. of Chemistry

Northwestern University

“The Polyvalent Oligonucleotide

Nanoparticle Conjugate: A New Frontier in In Vitro Diagnostics and Intracellular Gene Regulation”

May 12, 2008

Vladimir Torchilin, Ph.D.

Distinguished Professor

& Chair Pharmaceutical

Biotechnology & Nanomedicine

Northwestern University

“Multifunctional Pharmaceutical

Nanocarriers for Cancer

Diagnostics and Therapy”

July 7, 2008

Mostafa El-Sayed, Ph.D.

Julius Brown Chair

& Regents Professor

Dept. of Chemistry

Georgia Institute of Technology

“Metallic Gold is More Precious

on the Nanometer Size Scale: Some

Properties & Applications of Gold

Nanoparticles of Different Shapes

in Nanophotonics, Nanomotors,

Nanomedicine, & Nanobiology”

\*Many seminars also webcast from

[www.wcigtccne.org](http://www.wcigtccne.org)

May 8, 2008

Guest Speaker: Paul Weiss,

Pennsylvania State University

Title: TBD

Location: Pancoe-Evanston Northwestern

Healthcare Life Sciences Pavilion,

Abbott Auditorium

2200 Campus Drive

Northwestern University,

Evanston Campus

SCCNE partnership with Program of Excellence Nanotechnology (PEN) at Washington University

A list of past and upcoming SCCNE-PEN Seminars is available on the following website: <http://www.nhlbi-pen.net/default.php?pag=seminars>

Topics include:

- Special Topics in Organic Chemistry-Nanomedicine
- Current Topics in Nanomedicine
- Principles and Applications of Biological Imaging
- Contrast Agents for Biological Imaging

For an update on the upcoming seminars, and for an access to the videos of the above lectures along with the lecture slides, please contact Monica Shokeen at [shokeenm@mir.wustl.edu](mailto:shokeenm@mir.wustl.edu).

## Alliance Classifieds

### Internships

#### CCNE-TR

Summer Internship Opportunities:  
The National Nanofabrication Infrastructure Network (NNIN) invites applications from undergraduates to participate in the REU (“Research Experience for Undergraduates”) summer internship program. Participating students will be hosted at one of the twelve NNIN labs (which include the Stanford Nanofabrication Facility) and mentored in nanoscience and technology research project over the course of 10 weeks. Housing and stipend are provided. Application are due Feb. 19, 2008. For more information, visit the website at: [http://www.nnin.org/nnin\\_reu.html](http://www.nnin.org/nnin_reu.html)

#### NU-CCNE *Frontiers in Nanotechnology Seminar Series*

April 3, 2008

Guest Speaker: Sandra Rosenthal,  
Vanderbilt University

Title: “Structure-Property Relationships in Functional Quantum Dots: From Biological Imaging to White Light Solid State Lighting”

Location: Pancoe-Evanston Northwestern Healthcare Life Sciences Pavilion,  
Abbott Auditorium  
2200 Campus Drive  
Northwestern University,  
Evanston Campus

### Job Postings

#### C-CCNE

#### Liquidia Technologies Internship Position:

Cell/Molecular

Biology Technician

Research Area: Cellular Biology

Description: Liquidia Technologies

([www.liquidia.com](http://www.liquidia.com)) is a privately-held nanotechnology company that designs, develops, and manufactures precisely engineered particles and films for a wide variety of life and materials science applications. We are currently looking for a Cell/Molecular Biology Intern to play a critical role in execution of key experiments and analysis of nanoparticle engineered drug therapies. The intern will assist the biological team with in vitro and in vivo studies to analyze nanoparticle binding, uptake, internalization, and toxicity. Additional information and job opportunities are available at: [www.liquidia.com/careers.html](http://www.liquidia.com/careers.html).

Requirements: Masters or B.S. in cellular biology, molecular biology, biochemistry, pharmacology or related field. Several years of academic or industry laboratory experience is required. Internship or full-time experience in the biotechnology or pharmaceutical industry is highly preferred. Please send resumes to: [careers@liquidia.com](mailto:careers@liquidia.com); Refer to job code Cell Bio Intern in the subject line when corresponding about this position.

#### CCNE-TR

#### Scientific Program Manager

The Molecular Imaging Program at Stanford (CCNE-TR) is searching for a Scientific Program Manager to help manage its NIH funded Center for Cancer Nanotechnology Excellence (CCNE) U54 Grant. The candidate will assist faculty and postdocs with the preparation of manuscripts and writing some portions of grants. Will work with Lab Project, Core Leaders and Investigators to establish a working relationship with a diverse group of scientists and NIH officials from various companies to further enhance the CCNE program. The candidate will supervise the nanobiotechnology lab experiments; coordinate projects between various labs, and assist with scientific issues that come across the various labs within the center (CCNE-TR). Occasionally, some wet-lab research in nanotechnology will be required.

Qualifications: The ideal candidate will have a Ph.D. in materials science, chemistry, or in a relevant field. Must have 1-2 to years experience with nanotechnology and ideally the use of nanotechnology in biological applications such as cancer. Preferably, the candidate will have a background in engineering or biology in a bionanotechnology environment. Excellent verbal and written communication skills are critical. Ability to interact with a diverse group of scientists and a proven track record in scientific management is highly desirable.

Interested applicants may submit their CV to: [http://jobs.stanford.edu/find\\_a\\_job.html](http://jobs.stanford.edu/find_a_job.html)

### Research Post Doctoral Position

The Louis Warschaw Prostate Cancer Preclinical Research Laboratory at the Cedars-Sinai Medical Center is focused on translational therapeutics development. The laboratory is part of NCI Center for Cancer Nanotechnology Excellence Program focused on Therapeutic Response. There is currently an opening for a highly motivated and talented protein biochemist to work on a project related to EGFR-TKI resistance mechanisms in solid tumors. The overall goal of the project is to identify and isolate protein biomarkers that can be subsequently utilized in nanodelivery studies to target resistant cancer cells. Project will involve lipid raft purifications and mass spectrometric analysis. A basic biology background is required. Experience with mass spectrometry, proteomics studies, and associated data analysis required. The ideal candidate will have excellent writing and communication skills. Recent Ph.D's are welcome. A publications record is necessary. Education/Experience: Ph.D in a related field; 5+ years of related research experience. Interested and qualified individuals may send their CV with three references to: [jaina@cshs.org](mailto:jaina@cshs.org)

### Research Post Doctoral Position

The Louis Warschaw Prostate Cancer Preclinical Research Laboratory at the Cedars-Sinai Medical Center is focused on translational therapeutics development. The laboratory is part of NCI Center

for Cancer Nanotechnology Excellence Program focused on Therapeutic Response. There are currently several openings for highly motivated individuals interested in kinase signaling pathway interactions and novel targeted therapeutic mechanisms of response and resistance in solid tumor mouse models. Most projects translate directly into a clinical setting. The ideal candidate will be skilled in molecular and cellular biology techniques with some experience in small animal handling. Candidates should also have excellent writing and communication skills. Recent Ph.Ds are welcome. Publications in premier journals is required. Education/ Experience: Ph.D in a related field; 5+ years of related research experience. Interested and qualified candidates may send their CV with three references to: [jaina@cshs.org](mailto:jaina@cshs.org) For more information on employment at CCNE-TR, please visit <http://mips.stanford.edu/public/grants/ccne/employment.tcl>

### Emory-GT CCNE

#### Post-Doc Fellow (Biomedical Engineering)

The Emory-Georgia Tech Center of Cancer Nanotechnology Excellence (CCNE) and the Bioengineering Research Partnership (BRP) invite applications for postdoctoral research associates in biomedical engineering, nanotechnology, medicinal chemistry and bioinformatics. Specific research topics include: (1) nanoparticles for gene and siRNA delivery; (2) nanotechnology for molecular

analysis and detection of atherosclerosis plaques; (3) nanoparticle reagents for sensitive imaging of Alzheimer's and other neurodegenerative diseases; (4) nanoparticle organ uptake, distribution, and toxicology; (5) biomedical applications of Raman and surface-enhanced Raman spectroscopy; (6) cellular image processing and 3-D reconstruction; (7) synthesis of biocompatible and biodegradable polymers for targeted delivery of imaging and therapeutic agents; and (8) molecular histopathology and correlation of biomarkers with clinical outcome. The minimum requirements include a PhD or MD degree in engineering, chemistry, biology or medicine, at least two first-author papers in high-quality journals (impact factor>5.0), and an interest in collaborative work at the interface of science, engineering, and medicine. Exceptional candidates will be considered for the prestigious CCNE fellowship at Emory University and the Georgia Institute of Technology. We offer competitive salaries plus fringe benefits. To apply, send a cover letter, an updated CV, and names of 3-5 references to Mr. Ryan Jowers, Cancer Nanotechnology Center Manager, Department of Biomedical Engineering, Emory University, 101 Woodruff Circle Suite 2007, Atlanta, GA 30322. Electronic applications are encouraged and should be addressed to Mr. Ryan Jowers at [ryan.jowers@bme.emory.edu](mailto:ryan.jowers@bme.emory.edu). For further information, see [www.nielab.org](http://www.nielab.org) and [www.wcigtccne.org](http://www.wcigtccne.org). All positions are open until filled.

### *MIT-Harvard CCNE*

MIT is an equal opportunity/affirmative action employer. Applications from women, minorities, veterans, older workers, and individuals with disabilities are strongly encouraged. For current employment opportunities, please visit: <http://hrweb.mit.edu/staffing/>

### *NU-CCNE*

#### **NU-CCNE Research Experience for Undergraduates**

June 23-August 22, 2008  
\$4,000 stipend (plus funding for dormitory housing and travel)  
Northwestern University  
9-week Summer Program, includes an intensive immersion in laboratory-based scientific research, which is augmented by research seminars, a field trip to Argonne National Laboratory (ANL), professional communication workshops, technical writing workshops, and access to and training on state-of-the-art instrumentation, social activities, a final symposium, and experience as a submitter and peer reviewer in *Nanoscope: The Journal of Undergraduate Research in Nanotechnology*. For more information contact Denise Dooley, Outreach Coordinator ([d-dooley@northwestern.edu](mailto:d-dooley@northwestern.edu)).

## Funding Opportunities

### *CCNE-TR*

#### New User Grants:

The Stanford Nanofabrication Facility invites applications from researchers in medicine and biology for New User Grants. Applicants should be a faculty member at a US university, other than Stanford University, and must be new to the Facility. There is no application deadline as awards are made on an ongoing basis. SNF is a shared-equipment, open-use facility serving researchers from a wide variety of disciplines. As part of the National Nanofabrication Infrastructure Network (NNIN), SNF is especially committed to encouraging use of micro- and nano-fabrication technologies in non-traditional research areas of biology and medicine. For more information about SNF, please visit our website (<http://snf.stanford.edu>) and contact one of our technical liaisons to learn about micro- and nano- fabrication technologies in biomedicine.

## Technology Opportunities

### *CCNE-TR*

#### In the Lab:

Multiple high-throughput methodologies are maintained in the Center for Systems and Synthetic Biology at the University of Texas at Austin that have proven useful in the development of reagents and systems methods for nanotechnological innovations in cancer diagnostics and therapeutics. These include high-throughput fluorescence microscopy, high-throughput siRNA knockout methods, computational assistance in network analysis, and an automated facility for the selection of aptamers and antibodies. This latter facility will be on display at a NCI co-sponsored (along with the Human Proteome Resource and Structural Genome Consortium) conference in Stockholm where the target problem (how to generate multiple protein targets for the development of useful affinity reagents) will be explored.

*The NCI Alliance Nanotechnology in Cancer Bulletin is a collaborative effort developed and facilitated by the Communications and Integration Working Group (CIWG) of the Alliance program. The group is currently led by Alliance co-chairs, Ryan Jowers (Emory-GT CCNE) and Kathleen Cook (NU-CCNE), with coordination from NCI co-chairs, Travis Earles and Jerry Lee, Ph.D.*

*The CIWG's mission is to catalyze effective Alliance-wide and external communications, facilitate Alliance team science integration, create education outreach opportunities, and leverage best practices.*

*For comments or article ideas, please contact your Alliance CIWG Primary Contact(s):*

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