BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Lily Yang	**Associate Professor of Surgery and Radiology** **Nancy Panoz Chair of Surgery in Cancer Research**
eRA COMMONS USER NAME (credential, e.g., agency login) **LILYYANG**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Department of Medicine, West China University of Medical Sciences, Chengdu, China	MD	July 1983	Medicine
Institute of Epidemiology & Microbiology, Chinese Academy of Preventive Medicine, Beijing, China	Master of Medicine	July 1986	Microbiology and Immunology
Program in Molecular and Cell Biology & Biochemistry, Brown University, Providence, RI	PhD	May 1993	Molecular and Cellular Biology
Postdoctoral Associate and Director of Animal studies, Gene Therapy Laboratories, University of Southern California School of Medicine, Los Angles, CA		Oct 1993 Sept 1995	Cancer Gene Therapy
Postdoctoral Associate, Center of Molecular Medicine, Emory University, Atlanta, GA		Oct 1995 Dec 1996	Mitochondria Gene Therapy

A. Personal Statement

As a translational scientist, I have dedicated my life and career to the search for a cure of breast cancer. My research on breast cancer started with the production of human monoclonal antibodies for targeted therapy of breast cancer in 1986. For over seventeen years, I have been working on gene therapy of breast cancer, transcriptional control of anti-apoptosis genes in breast cancer cells, identification of molecular targets that confer apoptosis resistance and aggressive behavior in breast cancer cells for the development of novel molecular targeted therapy, and the development of multifunctional nanoparticles for targeted imaging and therapy of breast cancer. Since the complex biology of breast cancer makes it extremely challenging to treat effectively using a single approach, I believe that comprehensive approaches for early detection and effective treatment are required to reach our ultimate goal of a cure for breast cancer. Currently, my work is focused on the following areas: ***1) Early detection of breast cancer using receptor-targeted nanoparticles and novel optical and MR imaging methods***. We have developed a novel class of magnetic iron oxide nanoparticles (IONPs) that target EGFR, Her-2/Neu and urokinase plasminogen activator receptor (uPAR), which are receptors highly expressed in breast cancer tissues. We demonstrated that systemic delivery of the targeted IONPs enables specific MRI detection of primary and metastatic breast cancer lesions. We are developing a new MRI method to convert the dark contrast of IONPs to bright signals to enhance the sensitivity and specificity of cancer detection. Preclinical toxicity, biodistribution, and pharmacokinetics studies are underway to bring this targeted breast MRI into a clinical trial in the near future. This research is supported by the Emory University and Georgia Institute of Technology Nanotechnology Center for Personalized Oncology (U54 NIH CCNE) and the Emory Translational Molecular Imaging Center (P50, NIH ICMIC); ***2) Prevention of local and distant tumor recurrence by intraoperative optical imaging of breast tumor margin using targeted imaging probes and novel optical instrumentations***. Clearly defined tumor margins and complete surgical removal of tumors are critical for preventing local and distant recurrence and, therefore, for increasing disease-free survival. Using receptor targeted optical imaging probes that are produced by conjugating our newly synthesized near-infrared dye (NIR-830) labeled, EGFR, uPAR or Her-2 targeting ligands to biodegradable nanoparticles, we have shown that those imaging probes specifically target to primary and metastatic tumor lesions in orthotopic breast cancer animal models and are detectable by optical and MR imaging. In collaboration with Dr. Shuming Nie at Emory University and Dr. Huabei Jiang at the University of Florida, we are developing two new types of optical imaging systems, including a hand-held Pen-like spectral probe (SpectroPen) and a three-dimensional diffuse fluorescence tomography system (DFT), for intraoperative imaging of tumor margin. This research is supported by NIH R01 (PI. Yang) and GO (PI. Nie) grants; ***3) Development of theranostic nanoparticles for targeted therapy and imaging of breast cancer.*** Tumor recurrence and metastasis are the leading causes of mortality from breast cancer. Novel targeted therapy offers a great opportunity to treat recurrent and metastatic breast cancer and improve prognosis for the patients. Based on the receptor-targeted IONPs, we have further developed theranostic nanoparticles that combine receptor-targeted drug delivery and MRI/optical imaging. Those theranostic nanoparticles target orthotopically implanted breast tumors as well as lung metastases, kill tumor cells and tumor endothelial cells, and significantly inhibit the growth of primary and metastatic tumors.

Importantly, intratumoral drug delivery and changes in the tumor size can be monitored by MRI. In the current R01 research proposal, we will produce new types of theranostic nanoparticles with single or combined therapeutic agents that are highly relevant for the treatment of TNBC and then conduct preclinical studies in TNBC animal models for the development of a clinical protocol for pre-operative targeted adjuvant therapy and MRI monitoring, followed by intraoperative imaging-guided surgery using these nanoparticles. We believe that such an integrated approach will enable effective treatment of drug resistant TNBC and complete removal of small residual tumors to prevent local and distant recurrence. *This study does not overlap with current funded research projects* that *aim at developing receptor-targeted optical and MRI imaging probes (without therapeutic agents) and novel imaging instrumentations and imaging methods.* ***4) Determination of the role of breast cancer stem cells in developing invasive TNBC and identification of molecular targets and signal pathways that confer aggressive behavior, invasiveness and resistance to apoptosis in TNBCs.*** We have examined key molecular events in the progression of ductal carcinoma in situ (DCIS) to invasive breast cancer for the identification of prognostic biomarkers and therapeutic targets for TNBC. We are developing therapeutic approaches to modulate those key signal molecules. This project was supported by a NIH R01 grant for which I served as the PI.

As a woman scientist, finding a cure for breast cancer and improving the quality of life of breast cancer survivors and patients not only have special meaning, but also are the very reason why I chose my career in the beginning. Over the years, I have been searching for novel technologies and applying them to breast cancer research. Our invention and research led to three patent applications and twelve NIH and DOD grants on nanoimaging of breast cancer (NCI CCNE), targeted breast MRI (NIH ICMIC), optical imaging guided breast surgery (NIH R01 and NIH GO), quantum dots for multiplexed biomarker detection for breast cancer, magnetic separation and detection of circulating breast cancer cells (four NIH SBIR grants). Our work has been published in nanotechnology as well as clinical journals, such as Nature Biotechnology, Nature Nanotechnology, Small, Biomaterials, Cancer Research, Gastroenterology, and Clinical Cancer Research. Our finding was featured on the cover of the July 2009 issue of Clinical Cancer Research and highlighted in the January, June, and July issues of the NIH/NCI Nanotech News Release, Nanotech Wire News, and BreastCancer.Net News in 2009.

B. Positions and Honors.

Positions

Sep1986 – Aug 1988	Research Associate, Department of Tumor Immunology, Beijing Institute for Cancer Research, Beijing, China
Jan 1997 - Jul 1998	Assistant Professor, Department of Surgery, Emory University School of Medicine, Atlanta, GA
Aug 1998 - Jul 1999	Research Fellow, Group leader for the preclinical study group on antiangiogenesis, Aventis Pharma, Gencell, Hayward, CA
Aug 1999 - Aug 2007	Assistant Professor, Department of Surgery, Emory University School of Medicine
2007 - Present	Associate Professor with tenure, Nancy Panoz Chair of Surgery in Cancer Research Departments of Surgery and Radiology, Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA

Awards and Honors

2000 - 2002	Avon Scholar for Breast Cancer Research
2000 - 2009	Scientific Peer Review Panel Member, Breast Cancer Research Program, Department of Defense (DOD)
2005 - Present	Editorial Board Member for *Apoptosis* journal
2006 –present	NIH Study Sections, Adhoc, Drug Development and Molecular Pharmacology (DMP), ZRG1ONC-U92, Challenge grant review panels, SBIR review panel Development of Therapeutics (DT, Charter Member), ZCA1 SRLB-9 (ICMIC)
2007-present	Scientist Reviewer, California Breast Cancer Research Program
2008	Scientist Reviewer, Susan Komen Foundation
2008-present	Editorial Board of Breast Cancer-Targets and Therapy
2008	Best Post Award of 2008 NCI Nanotechnology Alliance Investigators Meeting

C. Peer-reviewed publications or manuscripts in press (selected most relevant publications).

1. **Yang L**, Cao ZH, Yan H and Wood WC. Co-existence of high levels of apoptotic signaling and inhibitor of apoptosis proteins in human tumor cells: Implication for cancer specific therapy. Cancer Research 63: 6815-6824, 2003. (PMID: 14583479)

2. Peng XH, Cao ZH, Xia JT , Carlson W. G, Lewis MM, Wood, WC and **Yang L**. Real-time detection of Gene expression in cancer cells using molecular beacon imaging: New strategies for cancer research.

Cancer Research 65 (5), 1909-1917, 2005. (PMID: 15753390)
3. Peng XH. Karna P. Cao Z. Jiang BH. Zhou M. **Yang L**. Cross-talk between epidermal growth factor receptor and hypoxia-inducible factor-1 alpha signal pathways increases resistance to apoptosis by up-regulating survivin gene expression. Journal of Biological Chemistry 281(36):25903-14, 2006.
4. Peng X, Karna P, Regan RM, Xiuju Liu, Wood WC, Lee HY and **Yang L**. Downregulation of the inhibitor of apoptosis proteins by deguelin selectively induces apoptosis in breast cancer cells. Molecular Pharmacology 71: 101-111, 2007. (PMID: 17035597)
5. Li Z, Niu G, Wang H, He L, **Yang L**, Ploug M and Chen X. MicroPET Imaging of Urokinase-type Plasminogen Activator Receptor Expression Using a 64Cu-Labeled Linear Peptide Antagonist. Clinical Cancer Research 14(15); 4758-66, 2008. (PMID: 18676745)
6. Wang X, **Yang L**, Chen G, Shin DM. Application of Nanotechnology in Cancer Therapy and Imaging. CA- A Cancer Journal for Clinicians Vol 58(2), 2008. (PMID: 18227410)
7. Qian XM, Peng XH, Ansari D. Yin-Goen Q, Shin DM, **Yang L**, Young AN and Nie S. In-Vivo Tumor Targeting and Spectroscopic Detection with Surface- Enhanced Raman Nanoparticle Tags. Nature Biotechnology 26(1):83-90, 2008. (PMID: 18157119)
8. **Yang L**, Mao H, Wang YA, Cao Z, Peng X, Wang X, Duan H, Ni C, Wood WC, Gao X, and Nie S Single Chain Epidermal Growth Factor Receptor Antibody Conjugated Nanoparticles for in vivo Tumor Targeting and Imaging. Small 5(2):235-43, 2009. (PMID: 19089838)
9. **Yang L**, Cao Z, Sajja HK, Mao H, Wang L, Gene H, Xu H, Jiang T, Wood WC, Nie S and Wang YA. Development of Receptor Targeted Magnetic Iron Oxide Nanoparticles for Efficient Drug Delivery and Tumor Imaging. Special issue on Cancer nanotechnology, J Biomed Nanotechnology 4(4): 439-449, 2008.
10. Sajja,HK, East MP, Mao H, Wang, AY, Nie S, and **Yang L**. Development of Multifunctional Nanoparticles for Targeted Drug Delivery and Noninvasive Imaging of Therapeutic Effect, Current Drug Development and Therapy 6(1): 43-51, 2009. (PMID: 19275541)
11. **Yang L**, Mao H, Cao Z, Wang YA, Peng X, Wang X, Sajja H, Duan H, Ni C, Staley CA, Wood WC, Gao X, and Nie S. Molecular Imaging of Pancreatic Cancer in an Animal Tumor Model Using Targeted Multifunctional Nanoparticles. Gastroenterology 136(5): 1514-1525.e2, 2009. (PMID: 19208341)
12. Smith MQ, Staley CA, Kooby DA, Styblo T, Wood WC, and **Yang L**. Multiplexed Fluorescence Imaging of Tumor Biomarkers in Gene Expression and Protein Levels for Personalized and Predictive Medicine. Current Molecular Medicine 9:1017-1023, 2009. (PMID: 19747113)
13. **Yang L**, Peng XH, Wang YA, Wang X, Cao Z,Ni C, Karna P, Zhang X, Wood WC , Gao X, Nie S and Mao H. Receptor-Targeted Nanoparticles for In Vivo Imaging of Breast Cancer, Clinical cancer Research, 15(14): 4722-4732, 2009, featured on the cover of the journal. (PMID: 19584158)
14. Galanzha E, Shashkov EV, Kelly T, Kim JW, **Yang L** and Zharov VP. In vivo duplex targeting and enrichment of circulating tumor cells with magnetic nanoparticles guided by two-color photoacoustic flow cytometry. Nature Nanotechnology, Dec;4(12):855-60, 2009. (PMID: 19915570)
15. Chen H, Wang L, Yeh J, Wu X, Cao Z, Wang YA, Zhang M, **Yang L**, Mao H: Reducing Non-Specific Binding and Uptake of Nanoparticles and Improving Cell Targeting with an Antifouling PEO-b-P<gamma>MPS Copolymer Coating, Biomaterials, 2010, 31(20): 5397-5407.

Patent Applications

5/02/2006	U.S. patent in prosecution: 11/919,681. Co-inventors: Yang, Nie, and Gao "Multifunctional Nanostructures, methods of synthesizing thereof, and methods of use"
5/04/2007	U. S. patent in prosecution: (12/299,079). Co-inventors: Yang, Nie, Mao and Gao "Nanostructures, methods of synthesizing thereof, and methods of use thereof"

D. **Research Support**

Targeted Nanoparticles for Intraoperative Optical Imaging of Breast Cancer Margins

NIH, NCI, **R01#CA133722-01** (**PI: Yang**) 2008 – 2013

The objective of this research project is to develop uPAR targeted NIR **optical imaging nanoparticle probes** and three-dimensional diffuse optical fluorescence tomography (**3D-DFT**) for intra-operative imaging of **breast cancer margins**. This funded research project doesn't overlap with the new R01 proposal since the current proposed study is to combine preoperative adjuvant therapy using **NIR-830-dye-labeled IONPs-drug nanoparticles** with intraoperative imaging guided removal of **drug resistant tumor lesions** using a **2-D SpectroPen video-imaging system**.

Role: PI

Theranostic Nanoparticles for targeted treatment of pancreatic cancer

NIH U01CA151810-01 (CO-PIs: Yang and Mao) 09/01/2010-08/31/2015
This pending proposal aims at the development of a magnetic iron oxide nanoparticle platform for carrying different types of therapeutic agents, including hydrophilic and hydrophobic drugs or small molecules, and siRNA expressing DNA cassette for targeted therapy of pancreatic cancer.

Emory-GA Tech Nanotechnology Center for Personalized and Predictive Oncology

NCI Center of Cancer Nanotechnology Excellence (CCNE)

U54 CA119338-01 (**PI: Nie S**) 2006-2011

Project 1. Quantum Dots and Targeted Nanoparticles Probes for Tumor Imaging The objective of this research is to develop novel tumor targeted quantum dots and other nanoparticles for non-invasive tumor imaging. Research activities in this project involve in the development of targeted optical and MR imaging probes, which have built a strong foundation for the proposed study on theranostic nanoparticles but there is no research overlap with the current proposal.

Role: Project Co-PI.

Emory SPORE in Head and Neck Cancer

NIH, NCI P50CA128613 (**PI: D. Shin**) 2007-2012

Project 4: Biodegradable Nanoparticle-Formulated Taxol for Targeted Therapy of Head and Neck Cancer

The objective of this study is to develop folate receptor targeted biodegradable polymer-based taxol delivery nanoparticles for the treatment of head and neck cancer.

Role: (Co-Project Leader)

Emory Molecular and Translational Imaging Center grant (EMTIC, P50 ICMIC)

NIH, NCI 1P50CA128613-01 (**PI: C. Meltzer**) 2008-2013

Project 3: uPAR Targeted in vivo Molecular Magnetic Resonance Imaging of Breast Cancer

The goal of this research project is to develop a novel uPAR-targeted MRI nanoprobe that contains the ATF of uPA conjugated to a magnetic iron oxide nanoparticle and novel MR imaging methods for early detection of breast cancer by MRI. The ICMIC funded research focuses on the development of targeted IONP based MRI probes and novel MR imaging methods. The results from this research project should benefit greatly the current proposed studies. However, there are no research and budget overlaps with the new R01 proposal.

Role: (Multi-PI, Co-PI)

Nanotechnology for Multiplexed and Intraoperative Cancer Detection

NIH/NCI (Go Grant) 1RC2CA148265-01 (**PI: Nie**) 09/30/2009-08/31/2011

This study is to develop a multiplexed SpectroPen-based optical imaging system for intraoperative detection of lung, breast and pancreatic cancer lesions using targeted surface-enhanced Raman scattering (SERS) nanoparticles. The objective of this grant is to develop the SpectroPen optical imaging system and Raman nanoparticle probes that are based on gold-nanoparticles, which doesn't overlap with the research proposed in the current proposal.

Role: Co-investigator

Multifunctional Nanotubes for in vivo detecting/purging Circulating Cancer Cells

NIH/NIBIB (R01) 5R01EB009230-02 (**PI: ZHAROV, VP**, University of Arkansas) 07/15/2009-04/30/2013

The objective of this study is to detect and destroy circulating breast cancer cells in blood vessels non-invasively using targeted nanotubes and photothermal therapy.

Role: Consultant

Completed research projects during last three years

Target Specific and Drug Loaded Iron Oxide Nanoparticles for Cancer Imaging and Therapy

NIH SBIR Contact No. HHSN261200900078C (PI. AY Wang, Ocean nanotech, LLC) 2009-2010

Nanoparticle Based Magnetic Microfluidic Enrichment System (MMES)

NIH, STTR, CO-PI (PI, YA Wang**,** Ocean Nanotech) 2008-2009

Magnetic nanoparticles for imaging enhancer

NIH SBIR R41CA130986-01(Co-PI) (PI. Wang, YA, Ocean Nanotech, LLC) 2008-2009

IAPS As Novel Targets for Cancer Therapy

NIH/NCI R01 # CA95643-01 (PI: Yang) 4/1/2003 - 3/31/2009

Early detection of breast cancer using molecular beacons. (Principal Investigator)

Department of Defense Idea Award BC021952 (Yang) 4/1/2003 - 12/31/2007

Death signaling in HSV-TK Gene modified tumor cells (Principal Investigator)

NIH/NCI R29 CA80017-01 (Yang) 8/1/1999 - 7/31/2005