3rd International Symposium on Molecular Imaging and Nanomedicine

ISMIN 3

April 25-29, 2015

Suzhou, China

3rd International Symposium on

Molecular Imaging and Nanomedicine

April 25-29, 2015, Suzhou, China

Symposium Chair

Prof. Mingyuan Gao

Organizing Committee

Prof. Zhifang Chai

Prof. Mingyuan Gao

Prof. Hans-Joachim Galla

Symposium Secretaries

Dr. Lihong Jing

Ms. Dong Su

Dr. Ruirui Qiao

Dr. Chunyan Liu

Venue

Dushu Lake Hotel, 299 Qiyue Street, Suzhou Industrial Park,
Suzhou 215123, China

26-Apr

8:00-8:30		Opening ceremony Moderator: Prof. Mingyuan Gao
		Section 1. Chairman: Prof. Lily Yang
8:30-9:00	K-1	Prof. Lei Jiang
9:00-9:30	K-2	Prof. Jochen Feldmann
9:30-10:00	K-3	Prof. Zhen Cheng
10:00-10:30		Coffee break & Symposium photo
		Section 2. Chairman: Prof. Ning Zhang
10:30-11:00	K-4	Prof. Jwa-Min Nam
11:00-11:25	I-1	Prof. Haw Yang
11:25-11:50	I-2	Prof. Chunying Chen
12:00		Lunch
Afternoon		
		Section 1. Chairman: Prof. Wolfwang J. Parak
13:30-14:00	K-5	Prof. Xiaodong Chen
14:00-14:30	K-6	Prof. Dongsheng Liu
14:30-14:55	I-3	Prof. Lintao Cai
14:55-15:15	O-1	Prof. Zhen Li
15:15-15:35		Coffee break
		Section 2. Chairman: Prof. Hans-Joachim Galla
15:35-17:00		Flash talk (2 min) and Poster Discussions
17:10-18:00		Lab tour (guided by Prof. Zhen Li)
18:30		Welcome banquet

27-Apr

		Section 1. Chairman: Prof. Jochen Feldmann
8:00-8:30	K-7	Prof. Xiaoyuan Chen
8:30-9:00	K-8	Prof. Ning Zhang
9:00-9:25	I-4	Prof. Nikolai Gaponik
9:25-9:50	I-5	Prof. Xin Zhang
9:50-10:10	O-2	Dr. Ruirui Qiao
10:10-10:30		Coffee break
		Section 2. Chairman: Prof. Takeaki Ozawa
10:30-11:00	K-9	Prof. Lily Yang
11:00-11:30	K-10	Prof. Gaojun Teng
11:30-11:55	I-6	Prof. Marc Schneider
12:00		Lunch
Afternoon		
		Section 1. Chairman: Prof. Thomas Nann
13:30-14:00	K-11	Prof. Wolfgang J. Parak
14:00-14:30	K-12	Prof. Hairong Zheng
14:30-14:55	I-7	Prof. Shirley K. Knauer
14:55-15:20	I-8	Prof. Jian Ji
15:20-15:40		Coffee break
		Section 2. Chairman: Prof. Andrey L. Rogach
15:40-16:20	K-13	Prof. Daxiang Cui
16:20-16:45	I-9	Prof. Hans-Joachim Galla
16:45-17:10	I-10	Prof. Xin Zhou
17:10-17:35	I-11	Prof. Pilhan Kim
17:35-18:00	I-12	Prof. Chuanlai Xu
18:30		Dinner

28-Apr

		Section 1. Chairman: Prof. Jian Ji
8:00-8:30	K-14	Prof. Takeaki Ozawa
8:30-9:00	K-15	Prof. Roland H. Stauber
9:00-9:25	I-13	Prof. Hong Zhang
9:25-9:50	I-14	Prof. Xinjian Chen
9:50-10:10		Coffee break
		Section 2. Chairman: Prof. Roland H. Stauber
10:10-10:40	K-16	Prof. Qiangbin Wang
10:40-11:05	I-15	Prof. Thomas Nann
11:05-11:30	I-16	Dr. Guangchen Xu
11:30-12:00		Closing remarks/Poster awards*
12:00		Lunch
Afternoon		
13:30-18:00		Discussion
18:00		Dinner

29-Apr

Departure

*Award Committee: Chairman: Prof. Hans-Joachim Galla;
Member: Prof. Thomas Nann, Prof. Lily Yang, Dr. Guangchen Xu

April 25, 2015

14:00-21:00 Registration

April 26, 2015

Morning

08:00-08:30 Opening Ceremony
Prof. Mingyuan Gao, Institute of Chemistry, CAS

Section 1 **Chairman: Prof. Lily Yang**

08:30-09:00 Bio-Inspired Interfacial Materials with Super-Wettability
Prof. Lei Jiang, Institute of Chemistry, CAS; Beihang University

09:00-09:30 Plasmonic Heating and Optical Forces for Biophotonic Applications
Prof. Jochen Feldmann, Ludwig-Maximilians-Universität (LMU)

09:30-10:00 Novel Molecular Probes for PET/MRI
Prof. Zhen Cheng, Stanford University

10:00-10:30 Coffee break & symposium photo

Section 2 **Chairman: Prof. Ning Zhang**

10:30-11:00 Plasmonically Coupled Nanostructures for Biomedical Applications
Prof. Jwa-Min Nam, Seoul National University

11:00-11:25 Real-Time Visualization of Nano-Bio Interactions in situ Using 3D Multi-Resolution Imaging
Prof. Haw Yang, Princeton University

11:25-11:50 Multifunctional Nanomateials for in vivo Multimodal Image-guided Photothermal and Chemo-therapy
Prof. Chunying Chen, National Center for Nanoscience and Technology of China and Institute of High Energy Physics, CAS

12:00 Lunch

Afternoon

Section 1 **Chairman: Prof. Wolfwang J. Parak**

13:30-14:00 Nanomechanical mapping of cellular migration
Prof. Xiaodong Chen, Nanyang Technological University

14:00-14:30 DNA Hydrogels and their application in 3D Bioprinting
Prof. Dongsheng Liu, Tsinghua University

14:30-14:55 Imaging-Guided Cancer Theranostics and Combination Phototherapy
Prof. Lintao Cai, Shenzhen Institutes of Advanced Technology

14:55-15:15 Fluorescent Semiconductor Nanostructures: From Quantum Dots to

	Quantum Wires
	Prof. Zhen Li, Soochow University
15:15-15:35	Coffee break
Section 2	**Chairman: Prof. Hans-Joachim Galla**
15:35-17:00	Flash talk and Poster discussions
17:10-18:00	Lab tour (guided by Prof. Zhen Li)
18:30	Welcome banquet

April 27, 2015

Morning

Section 1	**Chairman: Prof. Jochen Feldmann**
08:00-08:30	PET Imaging with Radiolabeled Nanoparticles
	Prof. Xiaoyuan Chen, National Institutes of Health
08:30-09:00	PET Imaging with Radiolabeled Nanoparticles
	Prof. Ning Zhang, Tianjin medical university
09:00-09:25	Quantum dots in aqueous media: synthesis, assembly and bio-applications
	Prof. Nikolai Gaponik, TU Dresden
09:25-09:50	Small Interfering RNA Nanomedicine: Challenges and Our Strategies
	Prof. Xin Zhang, Institute of Process Engineering, CAS
09:50-10:10	Ultrasensitive Detection of Tumor by Using Upconversion Nanoparticles
	Dr. Ruirui Qiao, Institute of Chemistry, CAS
10:10-10:30	Coffee break
Section 2	**Chairman: Prof. Takeaki Ozawa**
10:30-11:00	Tumor Stroma Breaking Theranostic Nanoparticles for Targeted and Image-guided Therapy of Drug Resistant Pancreatic Cancer
	Prof. Lily Yang, Emory University School of Medicine
11:00-11:30	Molecular Imaging in Stroke
	Prof. Gaojun Teng, Zhongda Hospital, Southeast University
11:30-11:55	Multiphoton microscopy for quantitative visualization of size effect on cellular uptake
	Prof. Marc Schneider, Saarland University
12:00	Lunch

Afternoon

Section 1	**Chairman: Prof. Thomas Nann**

13:30-14:00	Quantitative interaction between nanoparticles and cells Prof. Wolfgang J. Parak, Philipps Universität Marburg
14:00-14:30	Ultrasound molecular imaging probes: from diagnosis to drug delivery Prof. Hairong Zheng, Shenzhen Institutes of Advanced Technology
14:30-14:55	Nanomaterial-based inhibition of the oncological relevant protease Taspase1 Prof. Shirley K. Knauer, University of Duisburg-Essen
14:55-15:20	Bionanointerface: From zwitterionic ligand to mixed charge Prof. Jian Ji, Zhejiang University
15:20-15:40	Coffee break
Section 2	**Chairman: Prof. Andrey L. Rogach**
15:40-16:20	RNA Nanoparticles for Targeting Imaging and Therapy of Gastric Cancer Prof. Daxiang Cui, Shanghai Jiao Tong University
16:20-16:45	The influence of nanoparticles on the blood-brain barriers in vitro Prof. Hans-Joachim Galla, University of Muenster
16:45-17:10	Responsive multimodal MRI agents for tumor microenvironment Prof. Xin Zhou, Wuhan Institute of Physics and Mathematics, CAS
17:10-17:35	In Vivo Cellular Visualization by Intravital Laser-scanning Microscopy Prof. Pilhan Kim, Graduate School of Nanoscience and Technology, Korea Advanced Institute of Science and Technology
17:35-18:00	Pyramidal Sensor Platform for Biomedical Assay Prof. Chuanlai Xu, JiangNan University
18:30	Dinner

April 28, 2015

Morning

Section 1	**Chairman: Prof. Jian Ji**
08:00-08:30	Protein-based luminescent sensors for single cell analysis Prof. Takeaki Ozawa, the University of Tokyo
08:30-09:00	The Dynamic Nanoparticle-Protein Corona - Implications for Nano-Toxicology and -Biomedicine Prof. Roland H. Stauber, University Hospital of Mainz
09:00-09:25	Neuro-Nuclear Molecular Imaging Prof. Hong Zhang, Zhejiang University
09:25-09:50	Retinal Imaging and Image Analysis

	Prof. Xinjian Chen, Soochow University
09:50-10:10	Coffee break
Section 2	**Chairman: Prof. Roland H. Stauber**
10:10-10:40	Ag_2S Quantum Dot: A New Near-Infrared-II Fluorescence Nanoprobe for In Vivo Bioimaging Prof. Qiangbin Wang, Suzhou Institute of Nano-Tech and Nano-Bionics, CAS
10:40-11:05	Nanoparticles for multi-modal bio-imaging Prof. Thomas Nann, Ian Wark Research Institute
11:05-11:30	Advanced Science-Top Science with Maximum Accessibility Dr. Guangchen Xu, Wiley
11:30-12:00	Closing remarks/Poster awards Award Committee: Chairman: Prof. Hans-Joachim Galla; Member: Prof. Thomas Nann, Prof. Lily Yang, Dr. Guangchen Xu
12:00	Lunch
Afternoon	
13:30-18:00	Discussion
18:00	Dinner

Flash Talk and Poster Discussions

15:35-17:00, April 26, 2015

Chairman: Prof. Hans-Joachim Galla

Flash talk

15:35-15:37	Ratiometric Zn^{2+} Fluorescence Imaging in Living Systems Weijiang He, Nanjing University
15:37-15:39	Synthesis and Characterization of Water-Soluble Polythiophene Derivatives for Cell Imaging Libing Liu, Institute of Chemistry, CAS
15:39-15:41	Fabrication of Multi-functional Nanoparticles through Self-assembly Methods and Their Applications as Molecular Imaging Probes Jiaqi Zhuang, Jilin University
15:41-15:43	Innovative magnetic vortex nanoring platform for biomedical application Hai Ming Fan, Northwest University
15:43-15:45	Preparation of biocompatible dual characteristic magnetic and fluorescence carbon coated iron nanoparticles for in vivo imaging and the early cancer detection Tapas K Mandal, Institute of Chemistry, CAS
15:45-15:47	In Situ ^{111}In-doping for Achieving Biocompatible and Non-leachable ^{111}In-labeled Fe_3O_4 Nanoparticles Jianfeng Zeng, Soochow University
15:47-15:49	A Protease-activated Ratiometric Fluorescent Probe for pH-mapping of Malignant Tumor Yi Hou, Institute of Chemistry, CAS
15:49-15:51	Noninvasive Visualization of Ras Proteins Based on Monomolecular Luminescence Complementation Dezhi Li, West China Hospital, Sichuan University
15:51-15:53	The Establishment and Immunohistochemical Analysis of Primary Colorectal Carcinoma Mice Model Yifei Qi, Sun Yat-sen University
15:53-15:55	Size Cnotrolled Synthesis of Highly Water-Dispersible and Stable Fe_3O_4 Nanocrystal Clusters Xiaojun Wei, Institute of Chemistry, CAS
15:55-15:57	Near-Infrared Fluorescent image-guided resection of colorectal cancer in orthotopic colorectal cancer mouse model

Xiaodong Li, the First Hospital of Jilin University

15:57-15:59 The Biological Application of Upconversion Luminescence Core-Shell Nanoparticles
Chunyan Liu, Institute of Chemistry, CAS

16:01-16:03 Study of ICG-DOX Loaded Albumin nanoparticles for Diagnosis and Therapy of Breast Cancer
Siqin Chen, Tianjin Medical University

16:03-16:05 Chemical Spacer Design for Engineering Relaxometric Properties of Rare Earth Nanoparticles
Jiayi Huang, Institute of Chemistry,CAS

16:05-16:07 Star-shaped polycation containing zwitterionic sulfobetaine grafted on β-cyclodextrin core as non-viral gene vector
Qingqing Xiong, Tianjin Medical University Cancer Institute and Hospital

16:07-16:09 A multifunctional nanomicelle system for combining sonodynamic therapy and chemotherapy in the treatment of hepatocellular carcinoma
Yang Liu, Tianjin Medical University

16:09-16:11 Lactosylated PLGA nanoparticles containing ε-polylysine for the sustained release and liver-targeted delivery of the negatively charged proteins
Ping Zhou, Tianjin Medical University

16:11-16:13 Insight into Strain Effects on Band Alignment Shifts, Carrier Localization and Recombination Kinetics in CdTe/CdS Core/Shell Quantum Dots
Lihong Jing, Institute of Chemistry, CAS

16:13-16:15 A novel radiolabeled cyclic arginine-glycine-aspartic (cRGD) conjugated ultrasmall superparamagnetic iron oxide nanoparticles for dual-modality imaging for breast cancer
Shengming Deng, the First Affiliated Hospital of Soochow University

16:15-16:17 Near-Infrared Fluorescent Theranostic Reduction-sensitive Polymeric Prodrug for Pancreatic Cancer
Haijie Han, Zhejiang University

16:17-16:19 Pillar[5]arene based supramolecular prodrug micelles with pH induced aggregate behavior for intracellular drug delivery
Yin Wang, Zhejiang University

16:19-16:21 A multi-modality probe constructed by bio-orthogonal chemistry for imaging of fibroblast activation protein-alpha

	Mi Zhou, Nanjing University
16:21-16:23	Cysteine-Mediated Intracellular Building of Luciferin to Enhance Probe Retention and Fluorescence Turn-On Mengmeng Zheng, Nanjing University
16:23-16:25	Flow Synthesis of Biocompatible Fe_3O_4 Nanoparticles: Insight into the Effects of Residence Time, Fluid Velocity, and Tube Reactor Dimension on Particle Size Distribution Mingxia Jiao, Institute of Chemistry, CAS
16:25-16:27	Near-infrared Light Activated Bioluminescent Probe On the Basis of Photocaged Upconversion Nanoparticles Conjugate Yanmei Yang, Medical College of Soochow University
16:27-16:29	Long-Circulating Iodinated Albumin–Gadolinium Nanoparticles as Enhanced Magnetic Resonance and Computed Tomography Imaging Probes for Osteosarcoma Visualization Yong Wang, Soochow University
16:29-16:31	Rapid 3D-Sodium MRI of Knee Joint In-vivo at 7T Ligong Wang, Medical College of Soochow University
16:31-16:33	Sensitive Detection of Metallo β-lactamases (MBLs)-expressing Bacteria using A Bioluminogenic Probe Haibin Shi, Medical College of Soochow University
16:33-16:35	Phenoxazinium based near-infrared fluorescent probe for the selective detection of potassium ions Chen Fan, Medical College of Soochow University
16:35-16:37	^{99m}Tc labled Zoledronic for colorectal cancer nuclear medicine molecular imaging Ran Zhu, Medical College of Soochow University
16:37-17:00	Poster discussion

***Excellent posters will be nominated by Poster Award Committee headed by Prof. Hans-Joachim Galla and awarded at the end of the symposium.**

Catalog of Abstracts

Invited Lectures

Posters

INVITED LECTURES

Bio-Inspired Interfacial Materials with Super-Wettability

Lei Jiang

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School of Chemistry and Environment, Beihang University, Beijing 100191, China

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Learning from nature and based on lotus leaves and fish scale, we developed super-wettability system: superhydrophobic, superoleophobic, superhydrophilic, superoleophilic surfaces in air and superoleophobic, superareophobic, superoleophilic, superareophilic surfaces under water[1]. Further, we revealed smart switchable super-wettability[2]. The smart super-wettability system has great applications in various fields, such as self-cleaning glasses, water/oil separation, anti-biofouling interfaces, and water collection system[3].

The smart property was further extended into 1D system. Energy conversion systems that based on artificial ion channels have been fabricated[4]. Also, we discovered the spider silk's and cactus's amazing water collection and transportation capability[5], and based on these nature systems, artificial water collection fibers and oil/water separation system have been designed successfully[6].

Learning from nature, the constructed smart multiscale interfacial materials system not only has new applications, but also presents new knowledge: Super wettability based chemistry including basic chemical reactions, crystallization, nanofabrication arrays such as small molecule, polymer, nanoparticles, and so on[7].

Reference:

1. Adv. Mater. 2006, 18 (23), 3063-3078.
2. Adv. Mater. 2008, 20 (15), 2842-2858.
3. Adv. Mater. 2011, 23 (6), 719-734.
4. (a)Chem. Soc. Rev. 2011, 40 (5), 2385-2401; (b) Acc. Chem. Res. 2013, 46 (12), 2834-2846; (c) Adv. Mater. 2010, 22 (9), 1021-1024. (d) ACS Nano 2009, 3 (11), 3339-3342; (e) Angew. Chem. Int. Ed. 2012, 51 (22), 5296-5307;
5. (a) Nature 2010, 463 (7281), 640-643; (b) Nat Commun 2012, 3, 1247.
6. (a) Nat Commun 2013, 4, 2276; (b) Adv. Mater. 2010, 22 (48), 5521-5525.
7. (a) Chem. Soc. Rev. 2012, 41 (23), 7832-7856; (b) Adv. Funct. Mater. 2011, 21 (17), 3297-3307; (c) Adv. Mater. 2012, 24 (4), 559-564; (d) Nano Research 2011, 4 (3), 266-273; (e) Soft Matter 2011, 7 (11), 5144-5149; (f) Soft Matter 2012, 8 (3), 631-635; (g) Adv. Mater. 2012, 24 (20), 2780-2785; (h) Adv. Mater. 2013, 25 (29), 3968-3972; (i) J. Mater. Chem. A 2013, 1 (30), 8581-8586; (j) Adv. Mater. 2013, 25 (45), 6526-6533; (k) Adv. Funct. Mater. 2012, 22 (21), 4569-4576; (l) Acs Nano 2012, 6 (10), 9005-9012.

Memo:

Plasmonic Heating and Optical Forces for Biophotonic Applications

Jochen Feldmann

Chair for Photonics and Optoelectronics
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I will report on our recent efforts to utilize some of the unique plasmonic properties of noble metal nanoparticles for sensing and controlling nano- and microscale processes in aqueous solution. The use of optical forces and local optothermal heating is in the focus of our investigations (1-5). Examples range from controlled laser injection into cells to the direct optical monitoring of microfluidic flow generated by bacterial flagellar rotation.

Reference:

1. A. Ohlinger et al., Phys. Rev. Lett. 108, 018101 (2012)
2. S. Kirchner et al., Appl. Phys. Lett. 104, 9 (2014)
3. R. Schreiber et al, Nature Nanotechnology 9, 74 (2014)
4. M. Li et al., Nano Lett. 15, 770 (2015)
5. S. Nedev et al., ACS Photonics, in press, DOI: 10.1021/ph500371z

Memo:

Novel Molecular Probes for PET/MRI

Zhen Cheng

Molecular Imaging Program at Stanford (MIPS) and Bio-X Program, Canary Center at Stanford for Cancer Early Detection, Department of Radiology, Stanford University, Stanford, CA 94305, USA

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Multimodality imaging techniques provide unprecedented opportunities for scientists and clinicians to better study and management of diseases. Numerous multimodality instruments including positron emission tomography (PET)/computed tomography (CT), PET/magnetic resonance imaging (MRI), and Optical/CT have been developed and some of them have been used in clinic. Recently, PET/MRI became commercially available and their clinical applications have been actively investigated in several medical institutions around the world. Meanwhile molecular probes for multimodality imaging have been pursued in order to keep pace with the rapid development on imaging instrumentations. In this presentation, molecular probes for PET/MRI will be briefly introduced. The design principle and several categories of PET/MRI probes will be discussed in detail.

Memo:

Plasmonically Coupled Nanostructures for Biomedical Applications

Jwa-Min Nam

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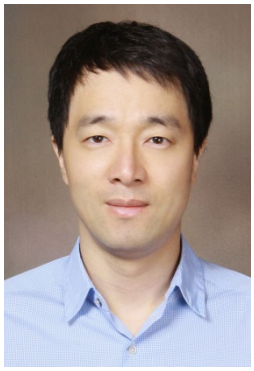


Designing, synthesizing and controlling plasmonic nanostructures such as Au and Ag nanoparticles with high precision and high yield are of paramount importance in optics, nanoscience, materials science, and nanobiotechnology. It is particularly important and challenging to generate and control ultrasmall plasmonic gap between and inside particles because of their potentials as the optical platforms with larger signal amplification and more quantitative signal output. Here, I will describe various functional molecule e.g., DNA, protein, polymer, etc)-based synthetic strategies to build up new types of plasmonic nanostructures with high structural controllability. The use of these plasmonic nanostructures as excellent biosensing, diagnostic and therapeutic probes will be also shown and discussed.

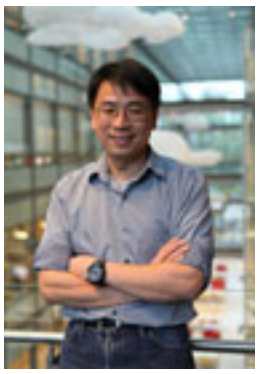
Memo:

Real-Time Visualization of Nano-Bio Interactions in situ Using 3D Multi-Resolution Imaging

Haw Yang

Department of Chemistry, Princeton University, Princeton, NJ 08544, USA

Email: hawyang@princeton.edu



As we look through the microscope and watch the remarkable phenomena a living cell exhibit, we intellectually accept that it is the actions of unseen molecular machineries that give rise to the perceived emergent behavior. Yet, the local nanoscale physical, chemical, and biological conditions inside a living cell remain largely unknown; therefore, the cellular interior represents an exciting new frontier for scientific exploration. This talk will cover some of the new tools we developed to explore and to understand cellular behavior from the molecular and nanoscale perspective, as well the possible new directions that the results enable.

Reference:

1. Welsher, K.; McManus, S. A.; Hsia, C.-H.; Yin, S.; Yang, H., J. Am. Chem. Soc., 2015, 137, 580-583.
2. Welsher, K.; Yang, H., Nat. Nanotechnol. 2014, 9, 198-203.
3. Emerson, N. T.; Hsia, C.-H.; Rafalska-Metcalf, I. U.; Yang, H., Nanoscale, 2014, 6, 6538-6543.
4. Yang, J.-M.; Yang, H.; Lin, L., ACS Nano, 2011, 5, 5067-5071.

Memo:

Multifunctional Nanomateials for in vivo Multimodal Image-guided Photothermal and Chemo-therapy

Chunying Chen, Liming Wang, Jing Liu, Xiaopeng Zheng and Zhanjun Gu

CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, National Center for Nanoscience and Technology of China and Institute of High Energy Physics, Chinese Academy of Sciences, Beijing, China

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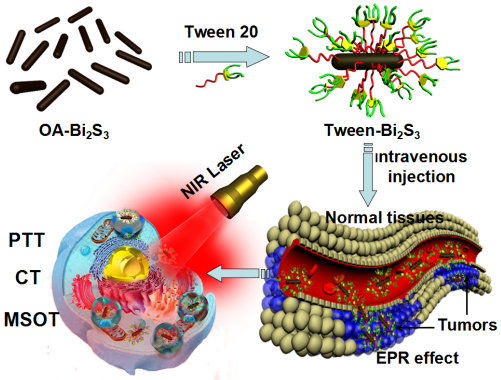
Nanomedicines offer unprecedented opportunities to reach the objectives such as promoting the precision treatment of cancer and mitigating undesired side effects. Over the past decade, precision nanomedicines have been extensively explored to fabricate theranostics that integrate multiple imaging approaches and therapeutic modalities. Among these investigations, imaging-guided photothermal therapy (PTT) has drawn considerable attention. PTT employs an efficient light harvesting agent for the localized conversion of the tissue-transparent near-infrared (NIR, λ= 700-1100 nm) light into heat to ablate cancer cells. Multimodality imaging provides PTT with real-time guidance to diagnose disease, guide procedures, monitor therapeutic response, and treat disease with greater specificity and sensitivity.

In this talk, I will highlight our recent studies on using gold nanorod composites for thermo-chemotherapy in cancer treatment and Bi_2S_3 nanorods (NRs) designed specifically for multispectral optoacoustic tomography (MSOT)/X-ray computed tomography guided photothermal therapy.



Schematic illustration of theranostic applications based on the unique properties of Bi_2S_3 NRs.

Reference:

1. J Liu, X Zheng, L Yan, L Zhou, G Tian, W Yin, L Wang, Y Liu, Z Hu, Z Gu, C Chen, Y Zhao. ACS Nano, 2015, 9(1): 696-707.
2. Z Zhang, J Wang, X Nie, T Wen, Y Ji, X Wu, Y Zhao, C Chen. J. Am. Chem. Soc., 2014, 136, 7317-7326.
3. L Wang, X Lin, J Wang, Z Hu, Y Ji, S, Y Zhao, X Wu, C Chen. Adv. Func. Mater., 2014, 24, 4229-4239 (front cover).
4. T Zhou, M Yu, B Zhang, L Wang, X Wu, H Zhou, Y Du, J Hao, Y Tu, C Chen, T Wei. Adv. Func. Mater., 2014, 24, 6922-6932. (back cover).
5. Y Xu, J Wang, X Li, Yg Liu, L Dai, X Wu, C Chen. Biomaterials, 2014, 35, 4667-4677
6. L Wang, J Li, J Pan, X Jiang, Y Ji, Y Li, Y Qu, Y Zhao, X Wu, C Chen. J. Am. Chem. Soc., 2013, 135, 17359-17368.

Memo:

Nanomechanical mapping of cellular migration

Xiaodong Chen

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Due to the importance of cell migration to a diverse range of physiological and pathological processes, including angiogenesis, wound healing, and cancer metastasis, there has been enormous research interest in developing sophisticated platform that can study and control cell migration. It is now widely accepted that the mechanical interaction between cell and the extracellular matrix (ECM) can direct many important cell behaviours especially the cell migration process, but the dynamic and quantitative analysis of cell-ECM interactions are hard to achieve using the conventional microfluidics-based platforms. Hence it is valuable to fabricate a cell migration study platform in which the cell-ECM interactions can be dynamically tracked and quantified. Here, I will present our recent development in using cellular nanomechanical forces to map the cellular migration. By integrally considering the correlation between cell-ECM interactions information obtained and the biochemical signaling, we find an efficient way to regulate cell migration and may get substantial insights into the mechanism investigations of migration-related pathological processes.

Memo:

DNA Hydrogels and their application in 3D Bioprinting

Chuang Li, Yu Shao, Yongzheng Xing, Juan Jin, Enjun Cheng
Dongsheng Liu

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The reversible responsiveness of DNA secondary structures to environmental stimuli has enable to facilitate responsive devices and materials based on pure DNA or hybrid systems. Based on sequence and structure design, we have prepared kinds of pure or hybrid DNA supramolecular hydrogels, which could be formed under physiological condition within a minute at room temperature and without using any organic solvents. By tailoring the length of "sticky ends" of DNA linker, mechanical property of the hydrogel could be varied from hundreds to thousands Pa (G', storage modulus); we also found that the viability of cell in a 4 mm diameter hydrogel is nearly 100% after 24 hours incubation from top in plastic tubes. These hydrogels possess extraordinary healing and fast-responding thixotropic properties, which make them injectable and writable. Because the formations of such hydrogels are based on DNA assembly, by DNA sequence design, they could be easily conferred excellent responsiveness including pH, DNA restriction enzymes, temperature etc., and enable easy removal after cell culture. In addition, we will show their application in 3D cell printing.

Reference:

1. C. Li, W. Shu and D. Liu et al. Angew. Chem. Int. Ed., DOI: 10.1002/anie.201411383
2. C. Li, Z. Li and D. Liu et al. Small 2014, DOI: 10.1002/smll.201401906.
3. J. Jin, S. Wang and D. Liu et al. Advanced Materials, 2013, 25(34), 4714.
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Memo:

Imaging-Guided Cancer Theranostics and Combination Phototherapy

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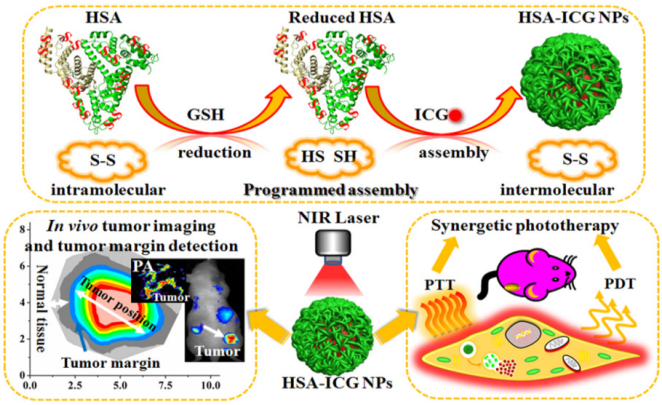
Phototherapy, including photodynamic therapy (PDT) and photothermal therapy (PTT), is a light-activated treatment modality for cancer therapy. To enhance the treatment efficiency of phototherapy and reduce the light-associated side effects, it is highly desirable to improve drug accumulation and precision guided phototherapy for efficient conversion of the absorbed light energy to reactive oxygen species (ROS) and hyperthermia. We reported here several functional theranostic nanomedicines design for cancer imaging and targeted phototherapy in vivo. The polymer-lipid hybrid nanoparticles (DINPs) were used to simultaneously deliver DOX and indocyanine green (ICG) to tumor regions for combined chemo-photothermal therapy, which not only synergistically induced DOX-sensitive MCF-7 or DOX resistant MCF-7/ADR cell death in vitro, but also highly suppressed MCF-7 or MCF-7/ADR tumor growth and effectively prevented tumor recurrence in vivo. We also developed a programmed assembly strategy using the human serum albumin (HSA)-indocyanine green (ICG) nanoprobes for imaging-guided cancer synergistic phototherapy. The tumor and its margin were clearly identified, and the smart HAS-ICG nanoprobe efficiently induced ROS and local hyperthermia simultaneously for synergetic PDT/PTT in a single dose treatment.



Theranostic nanoparticles for cancer imaging and photothermal therapy *in vivo*

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Memo:

Fluorescent Semiconductor Nanostructures: From Quantum Dots to Quantum Wires

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When the size of bulk materials is reduced to nano scale or sub-nanometer scale, they will exhibit novel properties in comparison with their counterparts.[1] One example is II-VI semiconductor nanostructures, which have been extensively studied in the past decades due to their strong quantum confinement effects, tunable properties, and great potential in diverse applications (e.g. bio-labeling and imaging, solar cells, LED).[2] These applications require good control of particle size, morphology, composition, and proper surface modification. Here I will introduce our work (Figure 1) on (i) preparation, modification and bioapplication of fluorescent quantum dots;[3-7] (ii) control-synthesis of colloidal quantum wires through the solution-liquid-solid (SLS) approach;[8-10] and (iii) modulation of optical, electronic, and magnetic properties by chemical doping.

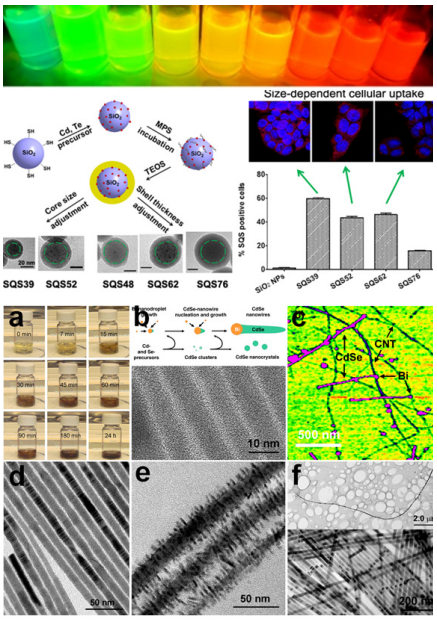

Figure 1. Fluorescent quantum dots and quantum wires.

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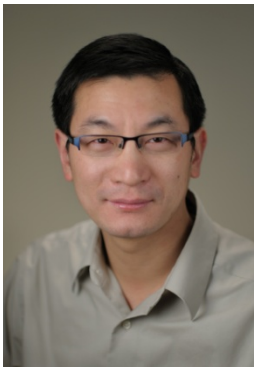
Memo:

PET Imaging with Radiolabeled Nanoparticles



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Despite the ever expanding development of nanoparticle-based imaging agents, most applications are limited to animal models. Concerns about how the body will actually metabolize nanomaterials and whether prolonged exposure to nanomaterials will induce long-term toxicity have greatly slowed their progress toward clinical trials. The complexity of nanoparticles makes it very challenging to understand the biological path and fate in living subjects. With its high sensitivity and the ability to conduct quantitative analysis of noninvasive whole-body images, PET, in turn, is an excellent choice to explore the in vivo fate of nanoparticles. The applications of radiolabeled nanoparticles are based on the premise that the radioisotopes are stably attached to the nanomaterials. Because of the fundamental differences in the various nanoparticles and radioisotopes, most radiolabeling methods are designed case-by-case. This talk will discuss some general rules about selecting appropriate isotopes for given types of nanoparticles, as well as adjusting the labeling reaction according to specific applications. Stability (colloidal and radiochemical) assessment of radiolabeled nanoparticles will be highlighted. Specific examples of PET imaging for evaluating biological fate of the radiolabeled nanoparticles and multimodal molecular imaging will be illustrated, emphasizing the importance of labeling strategies and caution in interpretation of PET data.

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Memo:

An Exploration of Nanotechnology in Hepatoma Diagnosis and Treatment

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Hepatoma is one of the leading causes of mortality among cancer patients in China. The major challenges are the lack of reliable early diagnosis methods and effective drugs. Current AFP-based serum diagnosis shows sensitivity lower than 60%, and is not reliable for hepatoma dection at early stages . In a clinical investigation with 596 serum samples from health individuals, HBV, and Hapatoma patients, we found that a combination of biomarkers were capable of detecting hepatoma at early stage with over 90% sensitivity and specificity. Micro-cantilevel and microfluid chip based assays have been developed by using these biomarkers for the screening of hepatoma patients in a large scale. Hepatoma is notorious resistant to conventional chemotherapies. Using hematoporphyrin based nanoparticle drugs, we were able to harvest the synergistic efficacy of both Photodynamic and chemotherapy. The nanoparticles showed excellent biocompatibility, lowered the toxicity, enhanced tumor targeting, and exerted powerful killing efficacy in animal models. Taken together, we developed novel hepatoma serum diagnosis methods and Photo/chemodynamic therapies by using nanotechnology. These new techniques may provide promising futures for hepatoma patients.

Memo:

Quantum dots in aqueous media: synthesis, assembly and bio-applications

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An overview of colloidal syntheses leading to the quantum dots stabilized in the aqueous media will be provided. The issues of surface ligand design, phase transfer, assembling into desired nanostructures, luminescence quantum efficiency and stability will be discussed from the point of view of their relevance to bio-applications. Potential applications in bio-imaging, enzymatic sensors and energy harvesting will be demonstrated.

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Memo:

Small Interfering RNA Nanomedicine: Challenges and Our Strategies

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Despite small interfering RNA (siRNA) has garnered much interest as a potential drug for various diseases, the clinical application of siRNA still faces considerable obstacles due to its inherent problems. Toward the success in siRNA therapeutics, it is significant to develop efficient and safe vectors to enhance the therapeutic efficiency of siRNA. In my talk, a series of vectors are designed and constructed to overcome the barriers in siRNA delivery.

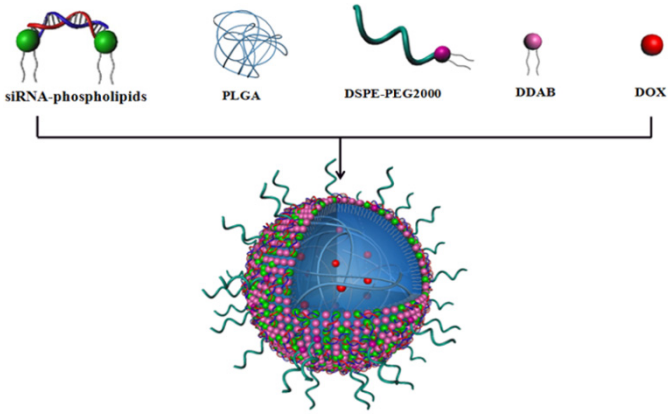

Figure 1. Schematic of siPlk1-PCNPs/DOX as co-delivery platform for siPlk1 and DOX.

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Memo:

Ultrasensitive Detection of Tumor by Using Upconversion Nanoparticles

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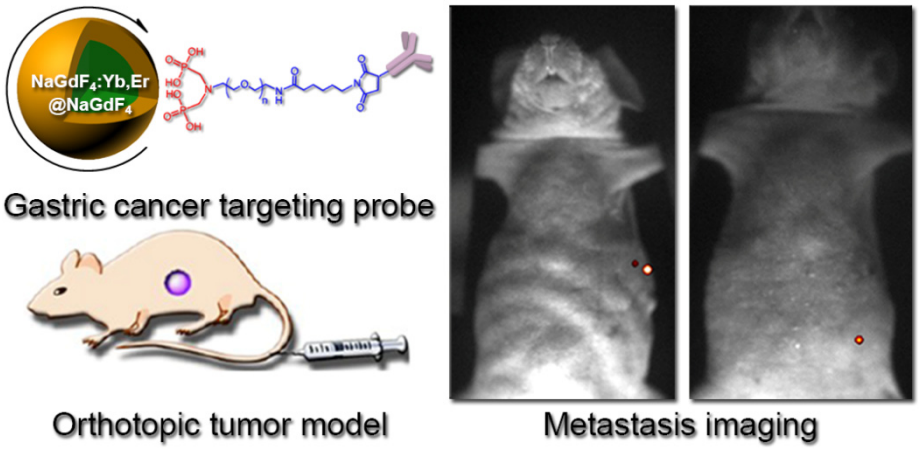
To date, preliminary diagnosis of early tumor and metastasis by using conventional medical imaging tools including CT, MRI, PET or ultrasonography still suffer from low sensitivity or specificity. Owing to the unique magnetic and optical properties, upconversion nanoparticle based molecular probes have provided great hope for early tumor detection. This talk will be focusing on highly sensitive detection of using upconversion nanoparticles. A gastric cancer (GC)-specific probe was constructed through "click" reaction between the maleimide moiety of PEG and the thiol group from partly reduced antigastric cancer antibody MGb_2. The primary tumor and adjacent lymphatic metastasis site were clearly differentiated by upconversion luminescence imaging after the GC-specific probe was delivered through tail vein injection into tumor-bearing mice. Moreover, lymphatic metastases smaller than 1 mm were successfully detected, owing to the ultralow background under 980 nm excitation. It has been demonstrated that both primary and lymphatic metastatic sites in an orthotopic mouse model of human gastric cancer can be optically detected by using GC-specific upconversion luminescence nanoprobes. The current studies may therefore provide a highly effective approach for GC diagnosis.



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Memo:

Tumor Stroma Breaking Theranostic Nanoparticles for Targeted and Image-guided Therapy of Drug Resistant Pancreatic Cancer

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The major challenge in the development of effective therapeutic approaches for pancreatic cancer is the presence of extensive tumor stroma that not only creates barriers for drug delivery but also cultivates aggressive biology and drug resistance in pancreatic cancer cells. To overcome drug delivery barriers, we have developed a multi-functional theranostic nanoparticle platform that combines imaging capability and target specificity of the nanoparticles with novel designs for breaking physical and intrinsic barriers that confer drug resistance in pancreatic cancer[1,2]. Recombinant receptor-binding domain of urokinase plasminogen activator (uPA) and insulin-like growth factor 1 (IGF-1) labeled with a near infrared dye were conjugated to magnetic iron oxide nanoparticles (IONPs) carrying chemotherapy drugs for targeted drug delivery into uPAR and IGF1R overexpressing pancreatic ductal carcinoma and tumor stromal cells. Systemic delivery of the receptor-targeted theranostic IONPs led to improved delivery of the IONPs into orthotopic human pancreatic cancer tissue derived xenografts (PDX) in nude mice. The ability of uPAR and IGF1R targeted theranostic nanoparticles to penetrate tumor stromal barrier and enhance the effect of tumor growth inhibition has been demonstrated in the PDX tumor model. Targeted nanoparticle delivery and response to therapy in orthotopic PDX tumors in mice could be monitored by non-invasive optical and MR imaging. Histological analysis revealed that repeated administrations of the receptor-targeted theranostic IONPs carrying doxorubicin or cisplatin led to the activation of apoptotic cell death in both tumor stromal and pancreatic cancer cells and significant inhibition of tumor cell proliferation. Although a low level of non-targeted theranostic IONPs were delivered into tumor tissues by the enhanced permeability and retention (EPR) effect, it induced cell death in macrophages localized mostly in the peripheral tumor region and had a few tumor cell death. Therefore, uPAR and IGF-1R targeted theranostic IONPs provide promising nanoparticle-drug delivery carriers for the development of novel targeted and image-guided cancer therapeutic approaches for the treatment of stroma-rich human cancers.

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Memo:

Molecular Imaging in Stroke

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Stroke remains the second leading cause of death and the leading cause of sever disability in industrialized and developing countries. It is estimated that one sixth of people will suffer a stroke at least once in their life. In clinical practice, the in vivo identification of the pathophysiological markers in stroke remains challenge. Molecular imaging provides the reference standard for the detection of significant pathophysiological changes in stroke, such as the damage of the blood-brain barrier (BBB), neuroinflammation, thrombus and angiogenesis.

As a unique physiological structure of the blood vessels in the brain, BBB precisely regulates the movement of molecules between blood and brain, and maintains a precisely controlled microenvironment for neuronal circuits. Due to the low permeability of BBB, overwhelming majority of small molecular drugs and almost all macromolecular pharmaceutics cannot reach brain tissues. However, the low-density lipoprotein receptor-related protein (LRP) that presents on the brain capillary endothelial cells shows the capacity for intracerebral transport of its corresponding ligand Angiopep-2. We developed a nanoparticle labeled four angiopep-2 peptides targeting the LRP, achieving the highest BBB traverse efficacy. In acute ischemia, local BBB was destructed with enhanced permeability, then the leaky BBB provided the opportunity for delivery of the nanoparticles. Using the supermagnetic iron oxide nanoparticles (SPIONs), it is possible to dynamically image the BBB permeability alterations and ischemic lesions simultaneously with the noninvasive MRI *in vivo*. Additionally, we introduced the nanoprobes (NPs) which uptakes in ischemic region depended on their different diameters to investigate the pore size of ischemic vasculatures by multi-modal imaging *in vivo*.

It has been also well accepted that neuroinflammation is a key component of the pathogenic cascade after stroke. Translocator protein (TSPO) is expressed at low levels in healthy brain but is robustly upregulated in stroke within the first days, which has relationship with neuroinflammation. Using the [^{18}F]DPA-714, a probe specifically targeting the TSPO, reflected the time-course of TSPO overexpression in a real-time and noninvasive longitudinal PET imaging. Fibrin deposition contributes to the “no-reflow” phenomenon after stroke. For the first time, we demonstrated that FXIIIa involved in secondary fibrin deposition in stroke could be specifically and non-invasively revealed by using an infrared FXIIIa–targeted probe. As we known, diabetic patients have an increased risk of stroke and exacerbated ischemic cerebral damage and poorer outcomes after stroke. Moreover, the efficacy of pro-angiogenic therapy is difficult to evaluate with current diagnostic modalities. We developed a novel $\alpha v\beta_3$ integrin-targeted multi-modal nanoprobe to define the temporal characteristics of angiogenesis and to evaluate the response to pro-angiogenic therapy in diabetic stroke mouse models.

In conclusion, we have developed various specific multi-modal molecular probes that selectively highlight certain molecules allow the visualization and characterization of pathological processes in stroke, thus enhancing the detection of early stages of disease, and improving treatment planning and therapy monitoring.

Memo:

Multiphoton microscopy for quantitative visualization of size effect on cellular uptake

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Photodynamic Therapy for cancer treatment is an intriguing and interesting approach for superficial tumors. As many cancer therapies many active pharmaceutical compounds suffer from low bioavailability while being highly active. The approved photosensitizer 5,10,15,20-tetrakis(m-hydroxyphenyl)chlorin (mTHPC) is known to be effective against tumor cells but showing a very low water solubility. Therefore, the administration and treatment are accompanied by severe difficulties including application problems. Furthermore, it is known to cause some adverse effects.

To overcome these kinds of problems, a modular carrier system was designed to deliver mTHPC by nanoparticles. Gold nanoparticles (mAuNP) of 15 nm in diameter were loaded using the layer-by-layer (LbL) technique incorporating the drug[1].

The mAuNP can be monodispersely prepared, successfully loaded with drug, and show good cell culture medium stability. The particles are of biocompatible nature in *in vitro* experiments Furthermore, the cellular accumulation of unloaded and mTHPC-loaded mAuNP could be shown. The uptake was quantitatively analyzed based on multiphoton induced luminescence of colloidal gold and compared to UV/Vis data exploiting the Plasmon peak. The uptake and the size-dependent internalization rates were successfully analyzed[2,3]. Activity of mTHPC delivered by mAuNP is conserved while unwanted dark toxicity can be reduced by the particulate carrier system.

This approach allows a quantitative analysis of drug content and internalized particles and hence drug. It opens a flexible and versatile method for future applications in nanomedicines with respect to controlled release and reduced toxicity.

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Memo:

Quantitative interaction between nanoparticles and cells

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CIC Biomagune, San Sebastian, Spain

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For a detailed and correct understanding of effects of colloidal nanoparticles exposed to organisms, a correlation of such effects to the physicochemical properties of the nanoparticles is a necessity. Such correlation is complex by the fact that many physicochemical parameters such as size, shape, surface charge, and colloidal stability are interlinked, and nontrivial to experimentally determine. This review aims to give an overview regarding such correlations. Particular focus will be given on the role of determining nanoparticle concentrations, which is the basis for most quantitative toxicity evaluations. A comparison of mass versus particle number concentrations is given, and their respective differences are highlighted.

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Memo:

Ultrasound molecular imaging probes: from diagnosis to drug delivery

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Ultrasound molecular imaging is proving to be a powerful and convenient modality for molecular imaging diagnosis. Taking advantage of specific binding between vascular endothelial cell surface receptors and ligands conjugated onto the surface of the targeted microbubbles, the gas-filled microbubbles will attach onto vascular endothelial cell surface and oscillate/vibrate when a sonic energy field is applied. The intense radial oscillation of microbubbles makes them several thousand times more reflective than normal body tissues and emits significantly stronger acoustic signal. The unique acoustic property of microbubbles can be used as sensitive acoustic probes in molecular imaging [1]. In addition to the advantages of real-time imaging, high spatial resolution, and high sensitivity of microbubble detection, ultrasound molecular imaging can visualize molecular and genetic alterations of diseased cells, and to monitor the genesis and development of certain diseases [2].

In addition, microbubbles are also wonderful tool as gene and drug carriers. Ultrasound can not only directly visualize microbubbles bearing chemotherapeutics, but also easily destroy the drug-loaded microbubbles, thus releasing the therapeutic agent at the disease site and increasing penetration into the extravsacualr space through sonoporation. The promise of microbubbles for its potential role in targeted drug and gene delivery has attracted great attentions and stimulated active current research [3-4]. In this talk, we will present our new progress of the research on microbubble-based ultrasound molecular imaging and ultrasound-assisted drug delivery, including the preparation of targeted microbubbles, nonlinear ultrasound molecular imaging methods, its applications in disease diagnosis and ultrasound-mediated drug therapy.

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Memo:

Nanomaterial-based inhibition of the oncological relevant protease Taspase1

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Applications of nanotechnology in life sciences imply the development of materials designed to interact with biomolecules at molecular scales with a high degree of specificity. During protein adsorption to nanoparticles (NP)[1,2], conformational changes may be induced in proteins, depending on both, the structure and chemistry of the protein as well as the physicochemical characteristics of the NP.

Taspase1 mediates cleavage of the mixed lineage leukemia (MLL) protein, leukemia provoking MLL-fusions and promotes solid malignancies. The Taspase1 proenzyme is autoproteolytically cleaved and assembles into an active αβ-monomer, representing the active protease. Notably, no effective and specific Taspase1 inhibitors are currently available, precluding the functional and therapeutic exploitation of the protease.

Here, we report that albeit Taspase1 binds to various NPs, its proteolytic activity is only inhibited by specific NPs. In contrast, other proteins and enzymes, including proteases, are not affected by these NPs. We comment on the structure-function relationships of NP-protein interactions and discuss strategies how the findings may be further exploited for targeted interference strategies.

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Memo:

Bionanointerface: From zwitterionic ligand to mixed charge

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A great promise for nanotechnology in medical applications has focused on the development of different forms of nanoparticles for cancer therapy. However, for further biomedical applications, these nanoparticles should not only be high colloidal stable and biocompatible in the physiological environment, but also present targeting to tumor cells.

We explore to solve this problem by take advantage of the phosphorylcholine (PC), which is the natural molecules present the out most of cell membranes. For the first time, to our knowledge, we demonstrate that the covalent conjugation of PC onto GNs not only brings better dispersion stability than the neutral EG4, but also leads to targeting cell uptake within cancer cells. Considering that most cancer cells have over expressed choline acceptors and present more aspiration of choline than normal cells, phsphorylcholine was explored here as a versatile ligand for selective uptake of GNs by different originated cancer cells.

We further demonstrated that the surface tailoring of nanoparticles via mixed-charge SAM can provide a facile method to present better ‘‘stealth’’ properties and higher accumulation in tumor than PEG-2000 modified nanoparticles. Combing with the pH-responsive properties of weak electrolytes, the mixed charge bionanointerface can be explored as a robust method to control the aggregation of NPs sensitive to enhance the retention and cellular uptake of inorganic NPs in tumors, which has perfect stealth properties and pH-sensitivity for tumor targeting and photothermal treatment.

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Memo:

RNA Nanoparticles for Targeting Imaging and Therapy of Gastric Cancer

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Gastric cancer ranks no.3 in commonest cancer in China, and is the second leading cause of cancer-related death worldwide. Here we reported the use of bacteriophage phi29 DNA packaging motor pRNA three-way junction (3WJ) to escort folic acid, NIR image marker and BRCAA1 siRNA for targeting, imaging, delivery, gene silencing and regression of gastric cancer in animal models. *In vitro* assay revealed that the RNA nanoparticles specifically bind to gastric cancer cells MGC803, and the BRCAA1 gene was significantly silenced by the siRNA incorporated in the RNA nanoparticles. The apoptosis of gastric cancer cells was confirmed by the finding of silencing of anti-apoptosis factor BCl-2 and up-regulation expression of the proapoptosis factor Rb and Bax. Animal trials using gastric tumor-bearing nude mice model confirmed that these RNA nanoparticles could be used to image gastric cancer *in vivo*, while showing little accumulation in crucial organs and tissues several hour post systemic injection. The volume of gastric tumor noticeably decreased during the course of treatment. No damage of important organs by RNA nanoparticles was detectible. All the results indicated that this novel RNA nanotechnology can overcome conventional cancer therapeutic limitations and opens new opportunities for specific delivery of therapeutics such as siRNA, microRNA and/or chemotherapeutic drugs to stomach cancer without damaging normal cells and tissues, reduce the toxicity and side effect, improve the therapeutic effect, and exhibit great potential in clinical tumor therapy in near future.

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Memo:

The influence of nanoparticles on the blood-brain barriers *in vitro*

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Silver nanoparticles (Ag-NPs) have gained an increasing attention due to their antimicrobial and antiviral activities, but also due to their presence in paint, clothing, food and medical devices. But besides their widespread use and favorable characteristics, there has been some concern about their safety. *In vivo* studies in rats have shown that Ag-NPs accumulate in various organs including the brain after both oral exposure and inhalation. Since the mechanism of brain transfer is not known it is important to study the effects of Ag-NPs on the barriers of the central nervous system, namely the blood-brain barrier (BBB) and the blood-cerebrospinal fluid (CSF) barrier.

The aim of the present *in vitro* study was to analyze the effects of two differently modified Ag-NPs (Ethylene oxide [EO] and Citrate) on primary porcine brain capillary endothelial cells (PBCEC) and, for the first time, on primary capillary choroid plexus epithelial cells (PCPEC). Impedance spectroscopy as well as permeability measurements have been used to quantify the barrier properties. We also evaluated the cellular responses after addition of Ag-NPs including cytotoxicity, oxidative stress, inflammation. Electron microscopic studies show the incorporation and localization of the nanoparticles within the cells. In addition we applied secondary ion mass spectrometry (ToF-SIMS) as new technique for imaging cells and tissue to analyze the 3-D distribution of the nanoparticles within the cells. This new and promising technique will be introduced.

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Memo:

Responsive multimodal MRI agents for tumor microenvironment

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Magnetic resonance imaging (MRI) is widely used for *in vivo* applications, due to its safety, spatial resolution, soft tissue contrast, and hence, clinical relevance. Notably, MRI responsive contrast agents (CAs) add important physiological information, complementing routine anatomical images. Responsive agents capable of reporting physicochemical properties of diagnostic interest of the microenvironment in which the contrast agent distributes (such as pH, temperature, metabolites, ions, proteins, or enzymes) have gained tremendous attention.

A pH-triggered nanoprobe was fabricated for ^{19}F MRI and fluorescence imaging (MRI-FI) of cancer cells[1]. Fluorescent imaging reveals the highly selective uptake of these nanoprobes by lung cancer cells, and that the Au lids were efficiently uncapped in the acidic intracellular compartments of cancer cells. It induced the release of the ^{19}F MRI contrast agent from the pores of the FMSNs into the cytosol, appreciably enhancing the intracellular ^{19}F MRI signal. The biocompatibility, durability, high internalizing efficiency and pore architecture justify the Au-fluorescent mesoporous silica nanoparticles as ideal, highly sensitive and highly specific vectors for ^{19}F MRI and FI of cancer cells.

A novel thermo-sensitive micelle contrast agent was developed to detect body temperature by using the CEST enhancement of the PARACEST micelle. [2]. The morphology changes sharply near 37^{o}C, resulting in a significant amplification of the CEST MRI signal. As the micelle's LCST was nearby the human body temperature, the CEST enhanced NMR and MRI methods may open a new way for hypersensitive detection of temperature change in different tissues. Due to its smart features, this thermo-sensitive micelle system may be useful for detection of temperature changes under abnormal conditions or during hyperthermia treatment. A reconstituted high-density lipoprotein nanocomposite was prepared for high-sensitive MRI-FI[3], it's able to enhance the MR sensitivity up to 129 folds in comparison to the traditional small molecule MRI agent based on PARACEST.

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Memo:

In Vivo Cellular Visualization by Intravital Laser-scanning Microscopy

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Recent advances in genomic technology have allowed a creation of animal model for human disease with genetically encoded biomarkers such as green fluorescent protein (GFP), which has opened up a new avenue to investigate complex pathophysiology of human disease in much greater details at cellular and molecular level. Over the recent years, intravital laser-scanning microscopy has demonstrated dynamic 3D visualization of various biological processes in the living subject, which provides unprecedented insights those were impossible to obtain by traditional static 2D snapshots (e.g. histopathology and cytometry). It has been utilized to monitor gene expression, protein activity, drug delivery, cell trafficking, cell interaction, physiological response under external stimuli in live animal *in vivo*, which provides new insights unobtainable by conventional *ex vivo* and *in vitro* observation.

In this talk, recent *in vivo* cellular imaging studies utilizing custom-design ultrafast laser-scanning intravital microscopy system will be introduced. First, *in vivo* visualization of T and B lymphocyte trafficking at the high endothelial venule (HEV) of lymph node will be demonstrated. Individual endothelial cell of HEV can be clearly identified with its distinctive cuboidal morphology. Dynamic flowing behaviors of T and B lymphocytes and their dynamic migrations across endothelial cells and fibroblastic reticular cells were analyzed *in vivo*. Second, *in vivo* monitoring of small lipid and drug molecules in intestinal villi will be described. By utilizing lacteal-reporter (Prox-1-GFP) mouse, we successfully visualized transepithelial absorption of molecules across villus enterocyte, diffusion through lamina propria and subsequent transport via lacteal. Interestingly, we observed active contractile movement of lacteal in concert with villi motion, which suggests lacteal may act as an active pump during lipid absorption, not merely as a passive conduit. Moreover, we identified highly diverse pattern in absorption dynamics of various exogenous molecules as well as intrinsically fluorescent drugs through enterocytes and lacteal *in vivo*. Third, *in vivo* quantitation of blood circulating tumor cell (CTC) will be introduced. Direct *in vivo* visualization of circulating cells in great saphenous vein (GSV) was achieved. By extracting a calibration factor through hemocytometric analysis of intravenously injected red blood cells, we could quantitate any circulating cells including CTC in whole body blood *in vivo*. We repeatedly monitor the number of CTC at the GSV of various type of tumor mice model over 6 weeks, allowing us longitudinal observation of CTC number disseminated from the implanted primary tumor along with its growth and distant organ metastasis.

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Memo:

Pyramidal Sensor Platform for Biomedical Assay

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Three-dimensional pyramids with significant plasmonic circular dichroism (CD) signals in the visible region (400-800 nm) were assembled using gold nanoparticles, silver nanoparticles, fluorescent quantum dots and single-stranded DNAs. The origin of chirality of nanoparticle pyramids can be interpreted from the following aspects: 1) the addition of different nanoparticles breaks the symmetric frame of pyramids; 2) the interactions between plasmonic nanoparticles with different shape and size; 3) the chirality of DNA molecules was transferred to the nanoparticles in pyramids. The pyramids were well dispersed and highly stable in water. A rapid and ultrasensitive chiral sensor based on gold pyramids for DNA detection was established. With the addition of target DNA, the conformation of pyramids was changed, which altered the CD signals. The limit of detection (LOD) for DNA was as low as 3.4 aM.

Taking advantage of the multi-element of pyramids, a multiplexed Raman sensor for bio-marker proteins was constructed based on three Raman reporter molecules and three protein aptamers. Three targets used in this work were prostate-specific protein, thrombin, and mucin-1, the corresponding LOD were 1.2 aM, 158 aM and 26 aM, respectively. For the first time, we fabricated the silver nanoparticle ornamented–gold nanoparticle pyramids using an aptamer-based self-assembly process and investigated their surface-enhanced Raman scattering (SERS) properties in the detection of vascular endothelial growth factor (VEGF). Under optimized conditions, the SERS signal was negatively related to VEGF concentration over the range 0.01–1.0 fM and LOD was as low as 22.6 aM.

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Memo:

Protein-based luminescent sensors for single cell analysis

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A current focus of biological research is to quantify and image cellular processes in living subjects. To analyze such cellular processes, genetically-encoded reporters have been extensively used. The most common reporters are firefly luciferase, renilla luciferase, green fluorescent protein (GFP) and its variants with various spectral properties. Herein, novel design of split GFP and split luciferase will be described; the principle is based on reconstitution of the split-reporter fragments; The basic strategy of the reconstitution is to split a reporter protein into two non-active fragments that are fused to a pair of interacting proteins. The interaction between the two proteins brings the two fragments into close proximity, allowing reconstitution of an intact reporter protein. To demonstrate the usefulness of the reconstitution technology, we have applied the reporters for developing a genetic method to identify mitochondrial proteins and their localization, and imaging dynamics of endogenous mRNA in single living cells. We have recently used split-luciferase reporters with different spectral characteristics for GPCR-β-arrestin interactions in living subjects. We have developed another design of reporter proteins; a cyclic luciferase by protein splicing to monitor protease activities in living cells and mice. Herein, we will focus on recent advances in the imaging technologies with fluorescent and bioluminescent proteins.

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Memo:

The Dynamic Nanoparticle-Protein Corona - Implications for Nano-Toxicology and -Biomedicine

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Nanomaterials adsorb biomolecules upon contact with all biological environments. Therefore, the biomolecules-coated nanomaterials may need to be considered as ‚new materials' compared to the pristine nanomaterials during their manufacturing. Particularly, the so called "nanoparticle-protein corona" is expected not only to critically impact nanotoxicology and nanoecology but also influences the success and safety of nanobiomedical applications. As most biological systems are (highly) dynamic, also a time-resolved knowledge of particle-specific protein fingerprints is required to understand the coronas' evolution, enabling predictions, prevention or rational enforcement of nanoparticle-induced (patho)physiological effects, affecting nanosafety.

Employing label-free liquid chromatography mass spectrometry, we present not only a qualitative but also a quantitative systematic analysis of the human blood protein corona on nanoparticles varying in distinct physico-chemical features. Our results provide novel insights into the complexity and kinetic evolution of particle-specific protein signatures. Collectively, we demonstrate that already the rapid corona formation is (patho)biologically relevant and provide bioinformatic potential risk predictors. Combined with comprehensive cell-based (high-throughput) assays, the impact of corona evolution as well as its rational exploitation for advanced nanomaterial with improved safety will be discussed.

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Memo:

Neuro-Nuclear Molecular Imaging

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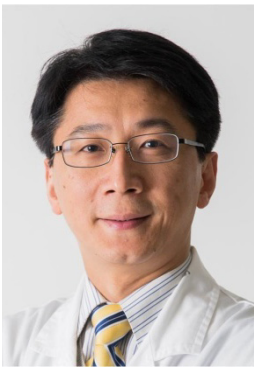

Neuroscience is the scientific study of how the nervous system develops, its structure, and what it does. With the development of different sciences and technologies, neuroscience has become an interdisciplinary science that collaborates with other fields, and the research approach of neuroscience has also changed greatly. Molecular imaging is a powerful tool for neuroscience that can be used for understanding disease, identifying biomarkers, and developing novel therapeutics. Nuclear molecular imaging is one of the most effective approach which plays an important role in neuroimaging, especially for investigations of the living brain. While CT and MRI provide important structural and anatomical information on the brain, neuro-nuclear molecular imaging allows the in vivo visualization and measurement of cellular/molecular processes in the living brain. This talk will introduce the principle of neuro-nuclear molecular imaging and the recent research achieved by our group. In summary, neuro- nuclear molecular imaging can integrate metabolomics and neurobiology and provides novel insights into pathophysiology in the brain. This approach provides a platform on neuroscience research from molecular imaging technology which may have a high impact on brain science from basic to translational medicine.

Memo:

Retinal Imaging and Image Analysis

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Abstract: Many important eye diseases as well as systemic diseases will be manifested in the retina. This talk focuses on retinal imaging and image analysis. Following a brief overview of the most prevalent causes of blindness in the realistic world that includes age-related macular degeneration, diabetic retinopathy, and glaucoma, this talk is devoted to retinal imaging and image analysis methods and their related clinical applications. Specific focus is devoted to 3-D OCT images analysis, describing methods for segmentation and analysis of retinal layers, 3-D detection of symptomatic exudate-associated derangements, detection of disruption area in external limiting membrane, retinal layer intensities analysis, as well as detection of disruption area in is/os layer.

Biography: Xinjian Chen received the PhD degree in 2006 from the Center for Biometrics and Security Research (with honor), Institute of Automation, Chinese Academy of Sciences, Beijing, China. After graduation, he entered Microsoft Research Asia and researched on Handwriting Recognition. From Jan. 2008 to May 2012, he has conducted the Postdoctoral Research at several prestigious groups: Medical Image Processing Group, Department of Radiology, University of Pennsylvania (Jan.2008 - Oct. 2009); Department of Radiology and Image Sciences, Clinical Center, National Institutes of Health (Oct. 2009 - Aug. 2011); Prof. Milan Sonka's Group, Department of Electrical and Computer Engineering, University of Iowa (Sep. 2011 - May 2012). Untill now, he has published more than 60 top international journal/conference papers, which includes IEEE Transactions on Medical Imaging, IEEE Transactions on Image Processing, IEEE Transactions on Biomedical Engineering, Radiology, Medical Physics, etc. He has also been granted with 3 patents. In 2012, He was the recipient for "One Thousand Young Talents" Award in China.

Currently, he is a Distinguished Professor and Director of Medical image processing, analysis and visualization lab at Soochow University. The lab has 6 faculties now, and 20 Ph.D and master students. Xinjian leads the group working on medical image analysis field, and have made substantial achievements within two years. The lab currently has more than ten National and Provincial level grants, including China National Basic Research Program of China (973) Young Scientist grant, and has published numerous top journal papers, such as IEEE Transaction on Medical Imaging, IEEE Transactions on Biomedical Engineering et al.

Memo:

Ag_2S Quantum Dot: A New Near-Infrared-II Fluorescence Nanoprobe for In Vivo Bioimaging

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Fluorescent imaging in the second near-infrared window (NIR-II, 1.0~1.4 μm) is appealing due to minimal autofluorescence and negligible tissue scattering in this region, affording maximal penetration depth for deep tissue imaging with high feature fidelity. Herein, for the first time, we reported a new type of NIR-II QDs-Ag_2S QDs and executed a series of bioapplication studies by using Ag_2S QDs. The results show that, by using Ag_2S QDs, the tissue penetration length can reach 1.2 cm, and the spatial and temproal resolution of the in vivo imaging can down to 25 μm and 50 ms, respectively, which are improved several to dozens of times in comparison with those using conventional fluorescence nanoprobes.

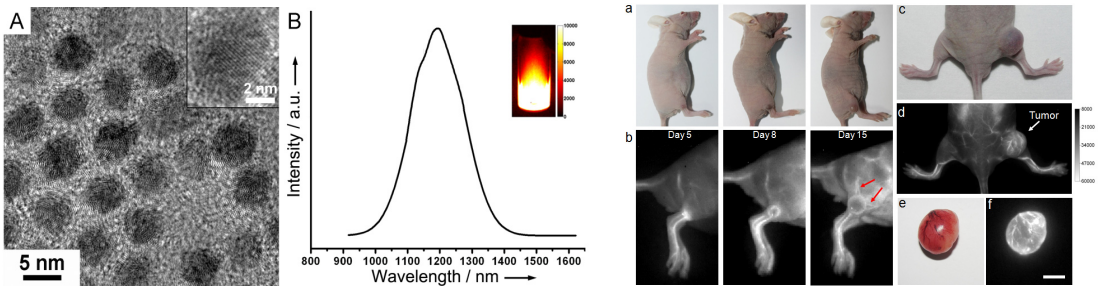

Figure. Characterization of Ag_2S QDs and their in vivo real-time visualization of angiogenesis mediated by a subcutaneous xenograft 4T1 mammary tumor.

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Memo:

Nanoparticles for multi-modal bio-imaging

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Imaging techniques such as magnetic resonance imaging (MRI), X-ray computed tomography (XCT) or positron emission tomography (PET) are clinical standard methods to detect and locate tumour tissue. However, none of these techniques offer a universal solution. For instance, they do not allow for visualisation of malignant tissue under surgery. Similarly, available contrast agents are very different in terms of specificity (targeting), toxicity, clearance and signal. There is therefore a need for the design of contrast agents that can be precisely engineered to offer optimal properties for the targeted cells (and disease) independently to the imaging technology.

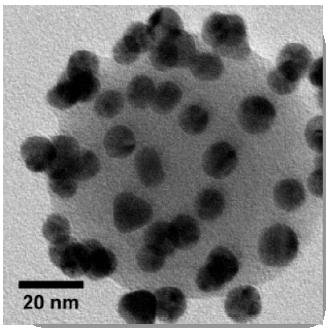

Figure 1: TEM micrograph of multi-modal contrast agent.

Multi-modal contrast agents can be synthesised by combining individual nanoparticles to more sophisticated nano-architectures as seen in the example of Figure 1. However, even the basic building blocks of complex nano-architectures (for example hetero-dimers) are difficult to fabricate. Nanoparticle hetero-dimers made out of separate and individual particles represent the first level of sophistication. Despite the fact that high-quality nanocrystals of almost any inorganic material can be synthesised since the beginning of this millennium, the preparation of simple hetero-dimers, consisting of two dissimilar nanoparticles and linked by at least one covalent bond, has not been achieved yet. Unlike the seeded-growth method, where one type of nanocrystal is grown on top of another, the method presented here is generic and does not require any fundamental compatibility between the two types of nanoparticles.

Our method is based on a two-step approach: in the first step, the two types of nanoparticles are mono-functionalised, which means they bear functionality in just one spot of their surface. The hetero-dimerisation is then being undertaken in a second step. Particles have been mono-functionalised by attaching them covalently to a solid support (cf. Figure 1), passivating their surface and subsequent cleavage of the linker between particles and solid support. Then, two types of nanoparticles having been functionalised with different functional groups were finally dimerised. In this presentation, we will show the new synthesis method and examples for the hetero-dimerisation of dissimilar nanocrystals, as well as some examples for using this type of particles for bio-imaging.

Memo:

Advanced Science -Top Science with Maximum Accessibility

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Imagine you've just made an exciting breakthrough and you need to get it published fast, but you don't want to publish it just anywhere. This is an important discovery – it demands to be published alongside the best research, and it deserves to be shared with the world, not just with those paying for a journal subscription. More than that, you want the paper to be handled by independent, experienced editors, in a reputable publishing house that offers not only the highest quality production and professional and high-profile promotion of its papers. Then here's your new journal: *Advanced Science*.

Memo:

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Ratiometric Zn^{2+} Fluorescence Imaging in Living Systems

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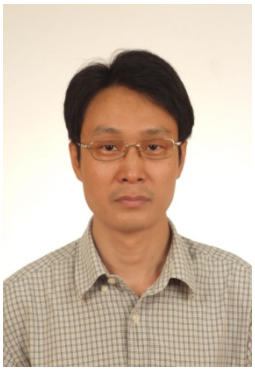

Zinc plays essential roles in many physiological processes such as neuron transmission and gene transcription, and is also associated with the pathologies of many diseases. The tracking of Zn^{2+} homeostasis is essential to clarify all these physiology and pathology, and fluorescence imaging has been adopted as one of the most reliable technique to monitor the quick fluctuation of labile Zn^{2+} of low level in living systems. In our study, Zn^{2+} sensor of specific subcellular distribution patterns have been developed for subcellular Zn^{2+} tracking. Among these sensors, Naph-BPEA displays the nuclear envelope penetrability and can be utilized for the nuclear Zn^{2+} tracking due to its DNA-targeting 1,8-naphthalimide moiety, while Mito-ST shows the distinct mitochondria-targetability and the ratiometric sensing ability for Zn^{2+}. These specifically distributed sensors should be helpful to clarify the Zn^{2+}-associated cell biology. In addition, the intracellular Zn^{2+} deviation upon cisplatin treatment has also been effectively tracked by ratiometric Zn^{2+} sensor CPBT, and the different cisplatin-induced labile Zn^{2+} profiles were observed for the cisplatin- sensitive and insensitive cell lines. On the other hand, we have developed several Zn^{2+} sensors of visible or NIR excitation/emission with the purpose to explore the in vivo Zn^{2+} imaging in live animals. In this case, a visible light excitable sensor SBD-TPEA, which displays the turn-on Zn^{2+} sensing ability has been successfully utilized to realize the first in vivo turn-on imaging of Zn^{2+} in zebrafish larva. The more accurate in vivo Zn^{2+} imaging in zebrafish larva was realized with ratiometric Zn^{2+} sensor SBD-TPEA. Recently, the vivo ratiometric Zn^{2+} imaging in live mice was realized in our lab by using a NIR ratiometric sensor for Zn^{2+}, BODIPY-TPEA.

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Memo:

Synthesis and Characterization of Water-Soluble Polythiophene Derivatives for Cell Imaging

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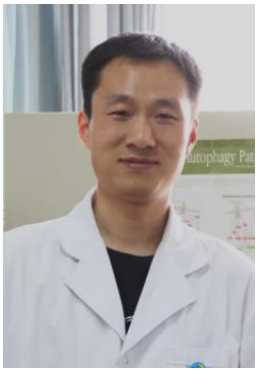

Four water-soluble polythiophene derivatives (PT, PT-DDA, PT-ADA, and PT-ADA-PPR) with different pendant moieties were synthesized via oxidative copolymerization by FeCl3. By increasing the hydrophobic ability of side chain moieties, there is a gradually blue shift for the maximum absorption wavelength and red shift for the maximum emission wavelength, a reducing trend for fluorescence quantum yields, a growing trend for Stokes shift, and an increasing trend for the mean sizes in the order of PT, PT-ADA, and PT-DDA. All the synthesized polymers show low toxicity and good photostability and accumulate in the lysosomes of A549 cells. Furthermore, the introduction of porphyrin group to PT-ADA side chain (PT-ADA-PPR) broadens the absorption and emission ranges of PT-ADA. PT-ADA-PPR could be excited at two different excitation wavelengths (488 nm and 559 nm) and exhibits two emission pathways, and dual-color fluorescence images (orange and red) of PT-ADA-PPR accumulated in A549 cells are observed. Thus, PT-ADA-PPR could be used as an excellent dual-color fluorescent and lysosome-specific imaging material.

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Memo:

Fabrication of Multi-functional Nanoparticles through Self-assembly Methods and Their Applications as Molecular Imaging Probes

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Self-assembly is an important strategy for fabrication of multifunction nanostructures. Here we show two examples of fabrication of multi-function nanoparticles through self-assembly strategies. Firstly, a facile method for one-pot synthesis of hollow gold nanoshell was developed by direct reduction of gold (III) salt on the surface of emulsion template. The emulsion was formed by the self-assembly of 3-aminopropyltriethoxysilane (APTES) in water. The size of the gold nanoshells could be tuned in a range of 37-96 nm by changing the molar ratio of APTES/$HAuCl_4$ in the reaction solutions. Correspondingly, the surface plasmon resonance of the nanoshells can be varied in the wavelength from the visible to the near-infrared region. The as-prepared gold nanoshells showed high photothermal conversion efficiency up to 45% and had excellent thermal stability, making them have great potentials in the fields of biomedicine and cancer therapy. Secondly, multi-function nanoparticles combining magnetic, fluorescence and photodynamic therapy functions were prepared by self-assembly of iron oxide, quantum dots and photosensitive molecules. The assembly process was driven by hydrophobic interaction between nanoparticles and molecules. The aggregation of photosensitive molecules inside the particles could be tuned by adjusting the assembly process, which in turn control the photodynamic therapy efficiency. This simple strategy makes the prepared multifunctional nanoparticles promising for cancer diagnosis and therapy.

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Memo:

Innovative magnetic vortex nanoring platform for biomedical application

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Superparamangetic iron oxide (SPIO) formulations have been demonstrated the great potential for various biomedical applications such as protein/cell separation, biosensor, drug delivery, magnetic resonance imaging (MRI) and magnetic hyperthermia treatment. However, the application of these nanoparticles for cancer diagnostics and therapy has been largely hindered by low MR detection sensitivity and low thermal conversion efficiency. Here, we show an innovative ferrimagnetic vortex-domain iron oxide nanorings (FVIO) platform which may overcome these drawbacks facing to SPIO. FVIO possesses a ferrimagnetic vortex domain structure, in which magnetization is circumferential to the ring without stray fields. This unique magnetic structure endows these FVIOs with negligible remanance and coercivity that can reduce greatly dipole-dipole interactions and enable a good colloidal stability, but much high saturation magnetization and susceptibility in comparison with SPIOs. Under the external field, FVIOs will subject to a transition from vortex state to onion state, and move along the field direction rapidly. Benefits from their unique magnetic properties, FVIO formulations have exhibited both high MR r_2* relativity and high specific absorption rate (SAR). Combined with the enhanced permeability and retention effect arising from the relatively large particle size, the highly biocompatible FVIOs allows us to design high sensitively MRI contrast agent and high efficient hyperthermia agent for early-diagnostics and efficacious treatment of various types of cancers in the future.

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Memo:

Preparation of biocompatible dual characteristic magnetic and fluorescence carbon coated iron nanoparticles for bioimaging applications

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Single step a novel method was introduced to synthesize biocompatible water soluble carbon-encapsulated magnetic iron nanoparticles（Fe@c）. In this work water soluble highly fluorescent Fe@c was prepared through reactions between citric acid and ethylenediamine at ~150°C in presence of ortho-H_3PO_4 to facilitate the carbonization and iron source from $FeCl_2$. In which citric acids both functioned as precursor and as stabilizer for iron nanoparticles. While the involvement of ethylenediamine in the pyrolysis of citric acid greatly enhances fluorescence。The structure, size distribution, magnetic properties were investigated. Results showed that the carbon-coated iron nanoparticles are spherical particles with a diameter of 20-50 nm feature well-constructed core/shell structures with an iron core inside and a skin carbon layer outside, carbon layers can protect inner iron core from being oxidized and gave strong paramagnetic character at room temperature. Fe@c is more sophisticated than conventional bioimaging because it is small molecules or signaling moieties, such as fluorophores or paramagnetic. This procedure provides easy to reproducible strategy to sufficiently produce water soluble Fe@c nanoparticles for their emerging biomedical applications.

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Memo:

In Situ ^{111}In-doping for Achieving Biocompatible and Non-leachable ^{111}In-labeled Fe_3O_4 Nanoparticles

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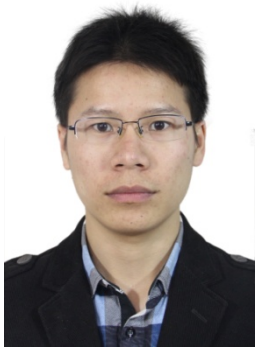

Superparamagnetic iron oxide nanoparticles as contrast agents for magnetic resonance imaging (MRI) and platforms for constructing novel molecular imaging probes have been intensively investigated.[1-6] Nonetheless, the pharmacokinetics of iron oxide nanoparticles are rather complex and remain in lack of in-depth studies. The primary obstacle is how to accurately trace the iron oxide particles in the high iron background of tissues. Since radioactive labeling is widely used for evaluating the pharmacokinetics of drugs, labeling iron oxide nanoparticles with radioactive tracers can in principle be adopted for disclosing their pharmacokinetics. However, due to the defects of the conventional radioactive labeling method, the dissociation of radiolabels will result in inaccurate pharmacokinetic information for the labeled nanoparticles. Herein, following on from our previous studies on "one-pot" synthesis of biocompatible Fe_3O_4 nanoparticles,[7,8] we report a reliable approach for achieving non-leachable and biocompatible Fe_3O_4 nanoparticles labeled by ^{111}In. By pyrolyzing $Fe(acac)_3$ in the presences of carboxylated PEG, oleylamine, and radioactive $^{111}InCl_3$ in diphenyl ether, radiolabeled biocompatible Fe_3O_4 nanoparticles can be obtained. Further investigations demonstrated that the resulting ^{111}In-doped Fe_3O_4 nanoparticles possess excellent anti-leaching properties in water solutions with $2 < pH < 7$ and physiological conditions. Based on the excellent radiolabeling stability, ^{111}In-doped Fe_3O_4 nanoparticles were further used for revealing the biodistribution of the PEGylated Fe_3O_4 nanoparticles in mice. In addition, the leaching behavior of the radioactive dopant is found to be dependent on the solubility product values of the corresponding dopant hydroxides.

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Memo:

A Protease-activated Ratiometric Fluorescent Probe for pH-mapping of Malignant Tumor

Yi Hou[†], Jin Zhou[†], Zhenyu Gao[†,‡], Xiaoyu Sun[†], Chunyan Liu[†], Dihua Shangguan[†], Wensheng Yang[‡], and Mingyuan Gao[†,*]

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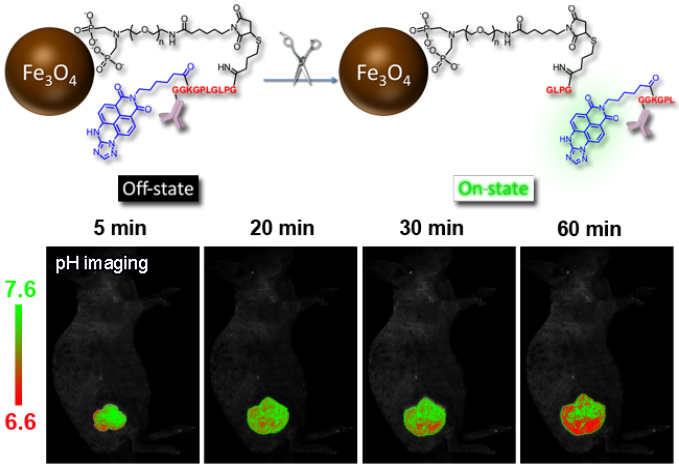
Tumor microenvironment is strongly correlated with prognostic factors relating to growth, invasion, and metastasis of malignant tumors.[1] Furthermore, there is increasing awareness of the impact of spatiotemporal heterogeneity in tumor properties that impact therapeutic administration. Therefore, developing noninvasive methods for visualizing tumor microenvironment is critical not only for tumor diagnostics, but also for predicting the metastasis potential, determining therapeutic efficacy, therapy development, and prognostics. In a clinical scenario, this information could also direct personalized care specified by the tumor response.



Schematic drawing of the protease-activatable fluorescence probe and its application for pH-imaging of malignant tumor.

Herein, a protease-activated ratiometric fluorescence probe based on fluorescence resonance energy transfer (FRET) between a pH-sensitive fluorescence dye and biocompatible Fe_3O_4 nanocrystals was constructed. A peptide substrate of MMP-9 served as a linker between the particle quencher and the chromophore that was covalently attached to anti-tumor antibody. The optical response of the probe to activated MMP-9 and gastric cell line SGC7901 tumor cells was investigated, followed by in vivo tumor imaging. Based on the ratiometric pH response to tumor microenvironment, the resulting probe was successfully used to image the pH of subcutaneous tumor xenografts.[2]

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Memo:

Noninvasive Visualization of Ras Proteins Based on Monomolecular Luminescence Complementation

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Objective**:** Ras proteins, an important small GTPase proteins family, which function as nucleotide-dependent switches,and participate in various biological processes[1]. It is necessary to measure the activity of Ras proteins. However, traditional methods, such as “pull-down” and two-hybrid procedures, are complex, time-wasting and poorly suited to dynamically evaluate the activity of Ras proteins. To provide an alternative approach to analyzing the activity of Ras proteins in vitro and in vivo, we developed a novel monomolecular bioluminescent biosensors based on the genetically engineered firefly luciferase[2]. **Methods：** The firefly luciferase was spilt into two non-functional fragments:N-FLuc（1aa-416aa）and C-FLuc（398aa-550aa）, and then inserted the two non-functional fragments, Raf-1 sequence IRES sequence and Gaussia luciferase (GLuc) into the bone plasmid pcDNA3.1(+) and finally construct the complete plasmid, Nfluc-Raf-1-Cfluc-IRES-GLuc probe（Raf-1 probe）.The CRC cell sw1116 were Transfected with Raf-1 probe and stimulated with EGF and Gefitinib. The sw1116 were co-transfected with Raf-1 probe and different H-Ras plasmids separately and stimulated with EGF and Gefitinib. The sw1116 cells transfected Raf-1 probe were implanted in null mice subcutaneously, after 24h, EGF and Gefitinib were used to activate or inhibit the activity of Ras in vivo. The activity of Ras proteins was reflected by the luminescence intensity after adding substrates. **Results：** The Raf-1 probe is sensitive to the activity change of Ras proteins induced by EGF and Gefitinib in vitro. The Raf-1 probe is sensitive to different mutations of H-Ras. The Raf-1 probe can measure the real-time activity of Ras proteins in living cells. The Raf-1 probe can measure the activity of Ras proteins in vivo. **Conclusion:** By virtue of the properties and advantages of bioluminescence imaging, this biosensor can be directly applied to living mammalian cells and in vivo and makes it possible to carry out high-throughput screening assay for identifying therapeutic agents targeted to Ras signal pathways.

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Memo:

The Establishment and Immunohistochemical Analysis of Primary Colorectal Carcinoma Mice Model

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Xenograft model, which is mostly used to investigate the in vivo progression of cancer, can not mimic the tumorigenesis and metastasis of tumor in the natural state. There is an urgent need to establishment of a primary tumor model to study the microenvironment of tumors and migration shift. Our present study constructed a mice primary colorectal carcinoma model by treated with DMH. As the induction times goes on, the different degree of gland disorder, lymphocyte proliferation and invasion were appeared in process of colorectal carcinoma. During the progress, the expression of Nodal, which is overexpressed in embryology and cancer, was increaesd in the tumor. The tumor can be observed by use of upconversion luminescent imaging. After treated with DMH for 25 weeks, the adenoma formation rate was about 100%, and of which the malignant conversion to carcinoma rate was about 40%. These results suggested that primary colorectal carcinoma mice model was sucessfully establised.

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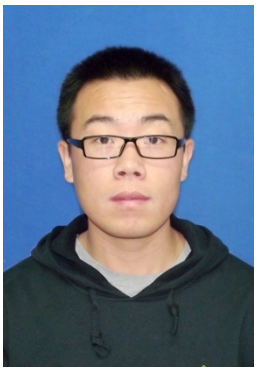
Memo:

Size Cnotrolled Synthesis of Highly Water-Dispersible and Stable Fe_3O_4 Nanocrystal Clusters



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Superparamagnetic and nearly monodispersed Fe_3O_4 aggregated spheres with controllable size have been successfully prepared by a simple one-pot route. The preparation was completed by injecting solution of NaOH into the diethylene glycol (DEG) solution of $FeCl_3$ and poly (acrylic acid) (PAA) at an elevated temperature. Fe_3O_4 clusters with different average grain sizes were obtained by adjust the amounts of NaOH, PAA and DEG, respectively. The morphology and stability of the Fe_3O_4 clusters were characterized by transmission electron microscopy (TEM) and dynamic light scattering (DLS). The spherical aggregates are formed by the assembling among the Fe_3O_4 primary nanoparticles (~10 nm). The superior water solubility and stability is achieved by using PAA as the capping agent, which could improve the space resistance and electrostatic repulsion of the clusters. Besides, the abundant carboxylate groups on the cluster surface make it possible for further biological surface functionalization. These excellent properties make prepared Fe_3O_4 clusters promising candidates for applications in various biorelated fields, such as cell imaging and cell sorting, and for sample pre-enrichment to analyze trace peptides or proteins in proteomics, and in particular those related with diseases,and to find biomarkers.

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Memo:

Near-Infrared Fluorescent image-guided resection of colorectal cancer in orthotopic colorectal cancer mouse model

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Dextran Sodium(DSS)-Azoxymethane(AOM) was used to induce colorectal cancer mouse model. After 9 weeks, orthotopic colorectal cancer mouse mode was successfully established. During the near-infrared fluorescence (NIRF) image-guided colorectal cancer surgery indocyanine green （ICG） was used to delineate tumor margin. And with its help the tumor could be completely resected while the surrounding healthy could be preserved as much as possible.

Keywords: colorectal cancer, orthotopic colorectal cancer mouse model, ICG, NIRF image-guided surgery.

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Memo:

The Biological Application of Upconversion Luminescence Core-Shell Nanoparticles

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Due to the unique magnetic and optical properties associated with f-electrons, rare-earth elements emerge enormous potential of creating functional materials for biological applications. As a typical optical material, upconversion luminescence (UCL) nanomaterials have been widely used in biological detection and medical diagnose owning to the intrinsic attractive optical properties, such as large effective Stokes shift, sharp emissions, long fluorescence lifetimes, and high resistance to photobleaching[1-2]. Especially the near-infrared light excitation falls in the optical window of the body, deeper tissue penetration of the excitation and lower background noise benefit the biological application of upconversion luminescence nanoparticles[2,3].

Herein, $NaGdF_4$:Yb,Er@$NaGdF_4$ core-shell nanoparticles were prepared through a replacement reaction at high temperature. The core-shell architecture significantly improved the upconversion luminescence and more effectively retained the luminescence during the following phase transfer process by ligand exchange. Then the water-soluble nanoparticles were introduced to biological detection and the in vivo imaging. On one hand, the nanoparticles were coupled with anti-cephalexin monoclonal antibody, and then the resultant probe was used in a lateral flow immunochromatographic assay (LFIA) to detect the antibiotic residue of cephalexin. Under optimized conditions, the detection limit of UCL nanoparticles-based LFIA was considerably comparable with gold nanoparticles based LFIA. The results reveal that the UCL nanoparticles-based LFIA becomes an alternative approach for Au nanoparticles based LFIA, and may become useful for actual sample detection due to low UCL background. On the other hand, the UCL nanoparticles are also favorable for excluding the interference of autofluorescence of strong background signal caused by the ingested foods in in vivo imaging. Therefore, the UCL nanoparticles were conjugated with folic acid to prepare optical imaging probe for the early detection of primary colorectal tumor induced by 1,2-dimethylhydrazine (DMH) in rodents. The Kunming mice were sacrificed 6 h after intravenous injection of the probe, and the obvious UCL signal could be observed on the part of the rectum. Further histopathological analysis the excised rectum tissue reveal that the DMH has been succeeded in inducing the primary colorectal tumor, and the probe based on UCL nanoparticles achieves the early detection of colorectal cancer. In brief, the excellent properties of UCL nanoparticles benefit of the biological detection and diagnose, which pave a novel strategy to improve the sensitivity of biological application.

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Memo:

Study of ICG-DOX Loaded Albumin nanoparticles for Diagnosis and Therapy of Breast Cancer

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To build a nanoparticulate drug-delivery system which could smartly integrate diagnostic and therapeutic functions is an urgent need for the clinical applications. Indocyanine green (ICG) is a noninvasive near-infrared (NIR) fluorescence imaging dye approved by FDA for ophthalmic rmangiography to deteine cardiac output and liver blood flow and function. Its optimized emission wavelength (around 800nm) and low toxicity make it highly suitable for bio-imaging applications. It also can be used for photothermal and photodynamic therapies. However, the application of ICG is limited by its numerous disadvantages, including poor aqueous stability, short half-life in vivo and lack of tumor target specificity. In this work, we have produced an albumin-based nanoparticulate system which encapsulated both ICG and DOX (ICG-DOX NPs) via a modified nanoprecipitaion method. The resulting nanoparticles exhibited good biocompatibility, enhanced photostability and high drug-loading rate and entrapment efficiency. The size of ICG-DOX NPs was controlled at around 120nm. The intracellular uptake experiment proved that the ICG-DOX NPs can be easily internalized into human breast cancer cells and distributed in lysosome. Furthermore, the in vivo experiments showed that ICG-DOX NPs was preferentially accumulated in tumor via EPR effect, and its circulation time was much longer than free ICG. Such biocompatible and biodegradable nanoparticulate system proves a potential application in diagnosis and therapy of breast cancer.

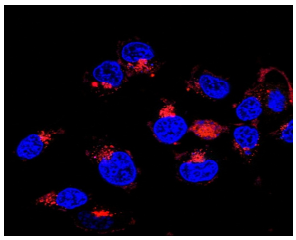

Figure 1. In vitro experiment

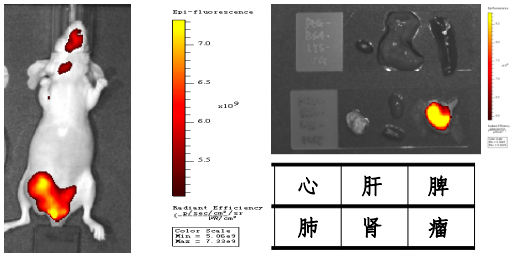

Figure 2. In vivo experiment

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Memo:

Chemical Spacer Design for Engineering Relaxometric Properties of Rare Earth Nanoparticles

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T_1/T_2 dual mode contrast agents for magnetic resonance imaging (MRI) not only show great potential to improve the image contrast between normal and diseased tissues, but also can efficiently eliminate artifacts. Various strategies have been employed to construct T_1/T_2 dual mode contrast agents but their T_1 or T_2 contrast effects have been evaluated only based on the concentration of T_1 or T_2 contrast agents, not the total concentration of T_1 and T_2 contrast agents.[1] It is more reasonable to take them both into account to compare their contrast effects with single mode T_1 or T_2 contrast agents and to calculate the injection dose of contrast agents in clinical application.

In this work, core-shell-shell structured $NaDyF_4$@$NaLnF_4$@$NaGdF_4$:Yb,Er (Ln = Gd, Er, Y) nanoparticles have been prepared via seed-growth method to integrate Dy and Gd elements into single particles and serve as T_1/T_2 dual mode contrast agents. The total concentration of magnetic lanthanide ions has been included when calculating the relaxivity. Noticing that tuning the components of the separating layer (the middle layer) can bring different T_1 contrast effects (longitudinal relaxivity), the interaction of $NaDyF_4$ and $NaGdF_4$ as well as the role of the separating layer have been studied employing the theory of longitudinal relaxivity and polarization. Then a series of experiments have been designed to verify the theory.

Reference:

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Memo:

Star-shaped polycation containing zwitterionic sulfobetaine grafted onβ-cyclodextrin core as non-viral gene vector

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Gene therapy shows much promise in the treatment of various genetic diseases, cancers, viral infection, and cardiovascular disorders[1]. Development of gene delivery vectors with low cytotoxicity and high transfection is the key challenge in gene therapy. As non-viral gene vectors, cationic polymers such as polyethylenimine, poly(L-lysine), polyamidoamine and cyclodextrin (CD)-based polycation have attracted considerable attentions. However, these positively charged polymers suffer from colloidal aggregation when administered intravenously, which may cause severe serum inhibition and are rapidly cleared from the bloodstream. In the previous study, polyethylene glycol (PEG) was commonly used to shield the positive charges. However, the PEGylation has been reported to have a negative effect on transfection efficiency of polyplexes, which limits its application in gene delivery. Zwitterionic polymers such as polyphosphorylcholine, polysulfobetaine and polycarboxybetaine exhibit ultra-high resistance to non-specific protein adsorption, which offer promising alternatives to conventional PEG. In the present study, well-defined star-shaped polymer CD-*g*-(PDMAEMA-*b*-PSBMA) (named as CDPDS) is prepared by the subsequent atom transfer radical polymerization (ATRP) of a hydrophilic cationic monomer (2-(dimethylamino)ethyl methacrylate) (DMAEMA) and a zwitterionic monomer (sulfobetaine methacrylate) (SBMA) from bromoisobutyryl-terminated β-CD (CD-Br) with multi-initiator sites. The CD-*g*-(PDMAEMA) star polymer (CDPD) was used as the control. The DNA binding capabilities of the star polymers were evaluated by electrophoresis retardation assay, dynamic laser light scattering and atomic force microscope. The results showed that CDPDS could completely inhibit pDNA migration when the N/P ratio is larger than 1.5/1 and were able to condense pDNA into 100-200 nm size nanoparticles at N/P ratios above 10, which indicated that incorporation of polysulfobetaine into cationic polymers retained a good DNA condensation capability. BSA absorption assays showed that CDPDS had much higher resistance to protein absorption than CDPD, which was probably attributed to the shielding effects of the zwitterionic polysulfobetaine. Moreover, the cytotoxicities of the star polymers were evaluated in COS-7 cells by CCK-8 assay. CDPD exhibit significant dose-dependent cytotoxicity due to the great quantity of positive amino groups on PDMAEMA. However, after polymerization of SBMA on CDPD, no significant cytotoxicity is observed up to the polymers concentration of 160 μg mL^{-1}. These results provide that the CDPDS star polymers have good DNA binding ability and biocompatibility, which can be good candidates for potential applications in gene therapy.

Reference

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Memo:

A multifunctional nanomicelle system for combining sonodynamic therapy and chemotherapy in the treatment of hepatocellular carcinoma

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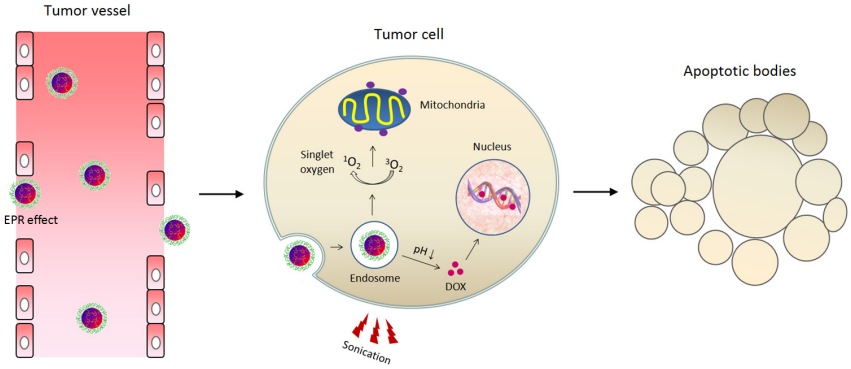
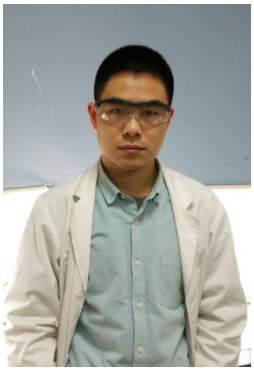
Some investigations have reported that sonodynamic therapy (SDT) has inhibitory effect on hepatocellular carcinoma (HCC) through multi-mechanisms and can markedly enhance the chemosensitivity of cancer cells to chemotherapeutic drugs. In this study, we designed a simple nanomicelle system containing haematoporphyrin (HP) and doxorubicin (DOX) for combining SDT and chemotherapy in the treatment of HCC. The HP/DOX nanocomplex (HPD) was firstly prepared by π-π conjugation. Pluronic F68, as a polymeric surfactant, was then coated on the surface of HPD using drying-hydration method to form HPDF nanomicelles. Subsequently, the efficiency of HPDF nanomicelles on HCC was evaluated by the cell and animal experiments. The results showed that HPDF nanomicelles had a spherical core-shell structure and their mean size was about 90 nm. In HPDF nanomicelles, the contents of HP and DOX were 2.7% and 13.0%, respectively. After ultrasound irradiation (1.4 MHz, 1.5 W/cm^2) for 30 s, HPDF nanomicelles significantly increased the cytotoxicities of DOX in human hepatoma HepG2 and PLC/PRF/5 cells in comparison to both free DOX and HPDF nanomicelles without ultrasound irradiation, and the IC_{50} values were respectively about 4 and 10 times lower than that of free DOX. At the same time, the levels of reactive oxygen species (ROS) in the cells were also extremely enhanced by the treatment of HPDF nanomicelles with ultrasound irradiation. After intravenous injection into nude mice bearing HepG2 hepatoma, Cy5.5-labeled HPDF nanomicelles could be highly and consistently accumulated in the tumor during 4–10 h and the red fluorescence of Cy5.5 was only observed in the tumor after 24 h, which indicated that HPDF nanomicelles had a good HCC targeting property. Moreover, the growth of HepG2 cell-transplanted tumors in nude mice was evidently inhibited by the treatment of ultrasound irradiation at 6 h after intravenous injection of HPDF nanomicelles at DOX dose of 3 mg/kg. Altogether, the multifunctional nanomicelle system prepared in this study realized the effective combination of SDT with chemotherapy and exerted significant synergistic effects on HCC at both cell and animal levels.



Memo:

Lactosylated PLGA nanoparticles containing ε-polylysine for the sustained release and liver-targeted delivery of the negatively charged proteins



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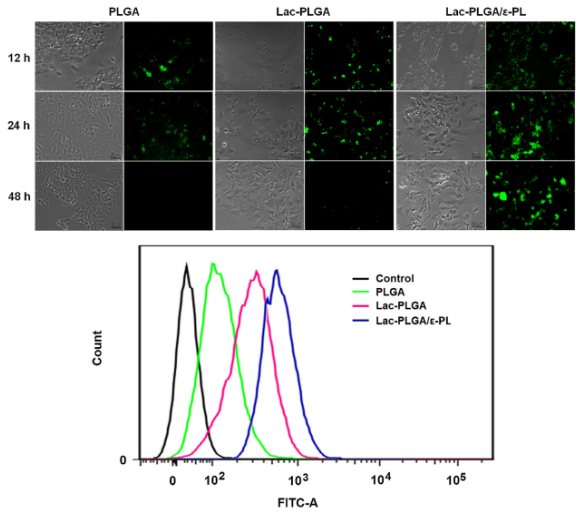
The acidic internal pH environment, initial burst release and lack of targeting property are main limitations of poly(lactide-co-glycolide) (PLGA) nanoparticles for carrying proteins. In this study, ε-polylysine (ε-PL) was used as an anti-acidic agent and a protein protectant to prepare PLGA nanoparticles for the protein delivery. To obtain the liver-targeting capability, lactosylated PLGA (Lac-PLGA) was synthesized by conjugation of lactose acid to PLGA at both ends, and then used to prepare nanoparticles containing ε-PL by the nanoprecipitation method. Bovine serumal bumin (BSA), a negatively charged protein, was efficiently loaded into Lac-PLGA/ε-PL nanoparticles and exhibited significant decreased burst release in vitro, sustained release in the blood and increased liver distribution in mice after intravenous injections. The enhanced stability of BSA was due to its electrical interaction with ε-PL and the neutralized internal environment of nanoparticles. Due to the presence of galatose residues at both ends of Lac-PLGA, Lac-PLGA and Lac-PLGA/ε-PL nanoparticles possessed the liver-targeting capability. Moreover, Lac-PLGA/ε-PL nanoparticles exhibited significantly higher cellular uptake than Lac-PLGA nanoparticles, and green fluorescence of FITC-BSA was clearly detectable in HepG2 cells even after 48 h. We believed this was due to the following two reasons. First, Lac-PLGA/ε-PL nanoparticles with positive charges could be internalized in mammalian cells more efficiently than PLGA and Lac-PLGA nanoparticles with negative charges due to the negatively charged character of cell membrane. Second, FITC-BSA loaded by Lac-PLGA/ε-PL nanoparticles maintained the structural and biological integrality due to the avoidance of acidic environment that caused by the degradation of Lac-PLGA. In conclusion, Lac-PLGA/ε-PL nanoparticle system can be used as a promising carrier for the negatively charged proteins.



Memo:

Insight into Strain Effects on Band Alignment Shifts, Carrier Localization and Recombination Kinetics in CdTe/CdS Core/Shell Quantum Dots

Lihong Jing, Stephen V. Kershaw, Tobias Kipp, Sergii Kalytchuk, Ke Ding, Jianfeng Zeng, Mingxia Jiao, Xiaoyu Sun, Alf Mews, Andrey L. Rogach, and Mingyuan Gao*

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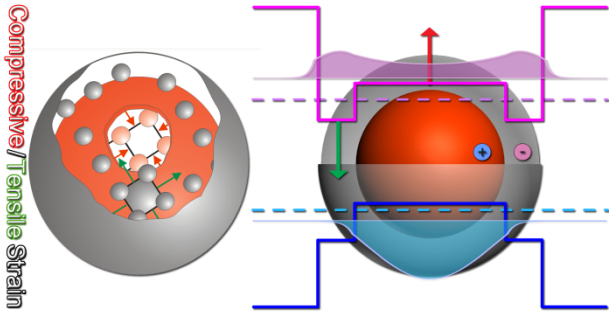
The impact of strain on the optical properties of semiconductor quantum dots (QDs) is fundamentally important while still awaiting detailed investigation. CdTe/CdS core/shell QDs represent a typical strained system due to the substantial lattice mismatch between CdTe and CdS. To probe the strain-related effects, aqueous CdTe/CdS QDs were synthesized by coating different sized CdTe QD cores with CdS shells upon the thermal decomposition of glutathione as a sulfur source under reflux. The shell growth was carefully monitored by both steady-state absorption and fluorescence spectroscopy and transient fluorescence spectroscopy. In combination with structural analysis, the band alignments as a consequence of the strain were modified based on band deformation potential theory. By further taking account of these straininduced band shifts, the effective mass approximation (EMA) model was modified to simulate the electronic structure, carrier spatial localization, and electron−hole wave function overlap for comparing with experimentally derived results. In particular, the electron/hole eigen energies were predicted for a range of structures with different CdTe core sizes and different CdS shell thicknesses. The overlap of electron and hole wave functions was further simulated to reveal the impact of strain on the electron−hole recombination kinetics as the electron wave function progressively shifts into the CdS shell region while the hole wave function remains heavily localized in CdTe core upon the shell growth. The excellent agreement between the strainmodified EMA model with the experimental data suggests that strain exhibits remarkable effects on the optical properties of mismatched core/shell QDs by altering the electronic structure of the system.



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Memo:

A novel radiolabeled cyclic arginine-glycine-aspartic (cRGD) conjugated ultrasmall superparamagnetic iron oxide nanoparticles for dual-modality imaging for breast cancer

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Email: zbnuclmd@126.com

Objective**:** To describe the radiosynthesis of ^{125}I-radiolabeled ultrasmall superparamagnetic iron oxide nanoparticles (USPIOs) modified with a novel cyclic arginine-glycine-aspartate (RGD) peptide and demonstrate the applicability of these radioiodinated nanoprobes for dual SPECT and MRI of tumor integrin $\alpha_v\beta_3$ expression in vivo using a small-animal model.

Methods**:** RGD peptides, CC-16: c(Cys-Arg-Gly-Asp-dSer-Cys)-Tyr-dSer-Lys-Tyr-c(Cys-Arg-Gly -Asp-dSer-Cys) (MW:1798.98), were designed by our lab and synthesized. cRGD peptide was conjugated to the carboxyl group on the surface of CMD-USPIO through the actions of dehydration reagents DCC and NHS. cRGD-USPIO was radiolabelled with ^{125}I using Chloramine-T method. Transmission Electron Microscope (TEM) imaging of CMD-USPIO and ^{125}-cRGD-USPIO were obtained. The average hydrodynamic diameter of the samples was determined by dynamic light scattering (DLS). Cells were incubated with nanoparticle solution for 4 h and then harvested. Subsequently, the cells were transferred to agar gelatin in 2-mL Eppendorf tubes and measurements were taken at room temperature. The relaxivity of ^{125}I-cRGD-USPIO and CMD-USPIO was measured. The uptake of ^{125}I-cRGD-USPIO and CMD-USPIO was also assessed histologically using Prussian blue staining. An MRI scan was performed using a 3.0-T whole-body clinical scanner at various time points after injection. Tumor tissues were also studied by TEM images. To compare cell uptake of ^{125}I-CMD-USPIO and ^{125}I-cRGD-USPIO in human breast cancer cell line Bcap37. The SPECT scans were carried out at various time points using ^{125}I-CMD-USPIO or ^{125}I-cRGD-USPIO. Female Bcap37-bearing nude mice were given an i.v. injection of ^{125}I-CMD-USPIO or ^{125}I-cRGD-USPIO via the tail vein. Tissues, including blood, liver, kidneys, tumor, small intestine, etc., were obtained at intervals, weighed, and counted for radioactivity. The percentage of injected dose per gram of wet tissue (% ID/g tissue) was calculated.

Results: The average hydrodynamic size of CMD-USPIO dispersed in cell culture media was 32.61 nm, and the hydrodynamic size of ^{125}I-RGD-USPIO was 53.67 nm. The result of paper chromatography showed that (99.49±0.24)% of ^{125}I was bound to cRGD-USPIO. High radiochemical stability was found in fresh human serum and in phosphate-buffered saline. The results of Prussian blue staining demonstrated a strong uptake of ^{125}I-cRGD-USPIO but a weak uptake of CMD-USPIO in the Bcap37 cells post incubation. Blocking the $\alpha_v\beta_3$ integrin receptor with free cRGD effectively reduced the amount of blue staining in the Bcap37 cells. MRI signal intensity of Bcap37 cells in gelatin incubated with ^{125}I-cRGD-USPIO decreased significantly compared with cells incubated with CMD-USPIO. The tumor presented high signal intensity on MRI T2WI before the administration of radiolabeled conjugates. A

negative contrast enhancement was observed in the tumor after intravenous administration. Four hours after the administration of ^{125}I-cRGD-USPIO, the Bcap37 tumor exhibited a low-intensity signal in various areas of the tumor on T2WI. TEM images showed a certain amount of ^{125}I-RGD-USPIO probe accumulated in lysosome. The uptake of ^{125}I-cRGD-USPIO in Bcap37 cells increased in the first 4 h and then decreased. The uptake of ^{125}I-CMD-USPIO was lower than that of ^{125}I-cRGD-USPIO at various time point ($P<0.01$). The radioactivity of ^{125}I-CMD-USPIO mainly accumulated in liver and spleen on SPECT images. Tumors were clearly visualized almost from the start of SPECT imaging after injection of ^{125}I-cRGD-USPIO. There was no accumulation of ^{125}I-cRGD-USPIO in the opposite forelimb. In later static images, the background radioactivity decreased, while radioactivity in tumor increased. The use of ^{125}I-cRGD-USPIO provided good contrast in the images. The biodistribution study showed that the radioactivity levels in tumor increased during the first 4 h following injection, whereas those in tissues, including liver, spleen, lung, kidney, and stomach, decreased with blood levels. Accumulation of radioactivity in tumor reached a maximum of (8.08 ± 0.3) %ID/g after 4 h. Tumor/muscle ratios increased over time and the ratio reached 9.45 ± 4.03 at 96 h after injection.

Conclusion：^{125}I-cRGD-USPIO showed a long circulation half-life, high tumor uptake, and high initial blood retention with moderate liver uptake, making it an attractive SPECT/MRI dual-modality agent for the detection of breast cancer.

Memo:

Near-Infrared Fluorescent Theranostic Reduction-sensitive Polymeric Prodrug for Pancreatic Cancer

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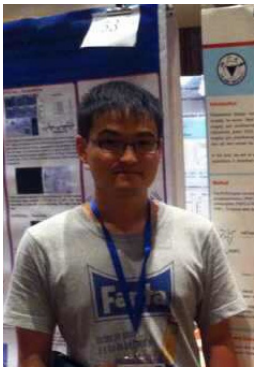

Pancreatic cancer is one of the most lethal malignancies. Five-year survival rate for pancreatic cancer is only less than 5%. 85% of patients have tumors which cannot be surgically resected, so chemotherapy is usually the only choice for these patients. In the process of chemotherapy, gemcitabine(dFdC) is frequently used as first-line treatment. However, its use is limited by high resistance towards tumor tissue. Meanwhile, in the clinical management of pancreatic cancer patients, timely assessment of therapeutic response to a given therapy is critical for making treatment decisions[1].

To overcome these limits, reduction-sensitive gemcitabine prodrugs were synthesized by using poly(ethylene glycol)-co-polycolactide-co-polycarbonate-graft-(SS-gemcitabine-co-IR820) as polymeric carriers. This novel disulfide-linked conjugates were able to release the drug in an intracellular-mimicking reductive environment[2]. At the same time, poly-(isobutylene-alt-maleic anhyride)-functionalized near-infrared (NIR) IR-820 dye was used as fluorescent probe for detection of gemcitabine activity.

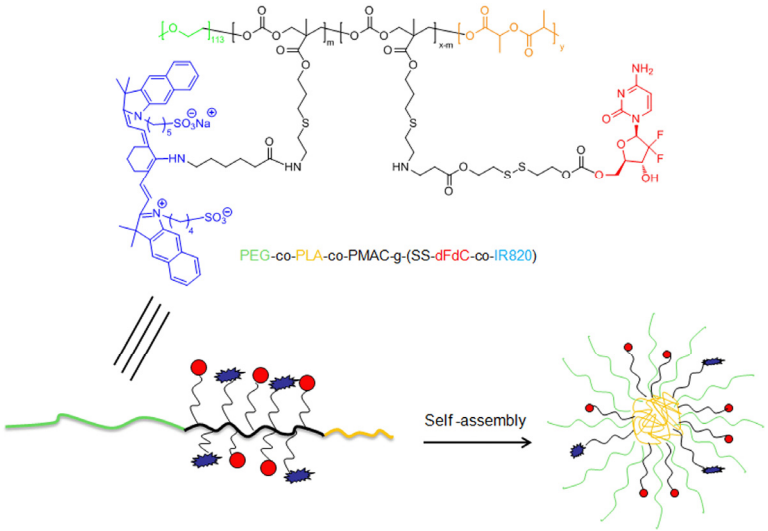

Figure 1. Schematic illustration of preparation of reduction-sensitive prodrug micelles.

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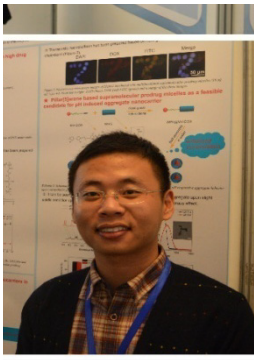
Memo:

Pillar[5]arene based supramolecular prodrug micelles with pH induced aggregate behavior for intracellular drug delivery



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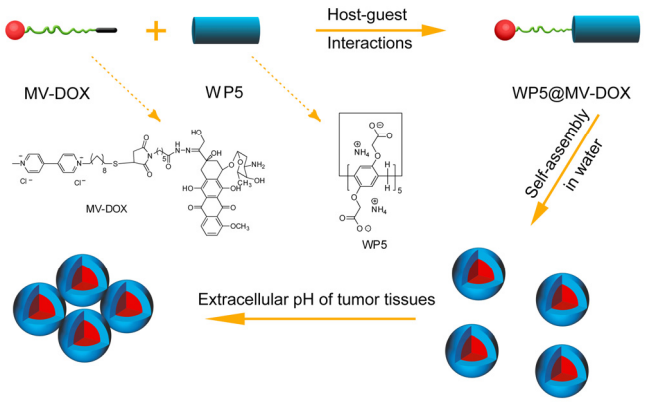
Cancer has been considered as the leading cause to people's death in the past decades. Various kinds of nanocarriers have been developed to deliver drug to tumor site. However, they could not realize functions until being effectively accumulated at malignant tumor sites, which is not an easy task due to the complexity of biological systems. Up to now, accumulation is generally mediated by EPR effect which is highly relied on the physicochemical characteristics of nanocarriers such as size. It is well proved that the size of the nanocarriers play an important role in accumulation. Specifically, on one hand, small sized nanocarriers can penetrate more effectively inside tumor tissues whereas have a possibility of re-entering the bloodstream. On the other hand, relatively large ones favor being trapped for a long time due to the lack of functional lymphatic drainage in tumor tissue. Therefore, how to balance these two processes and achieve maximum accumulation in tumor site is a challenging task.

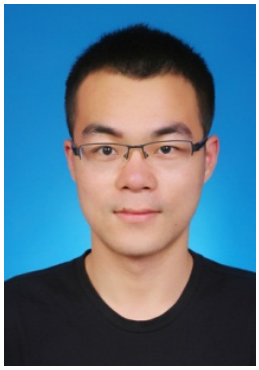
Herein, we report preparation of dual pH responsive supramolecular prodrug micelles by host-guest interactions between water soluble pillar[5]arene (WP5) and methyl viologen functioned doxorubicin (MV-DOX) (Scheme 1). The resultant supraassemblies could aggregate upon extracellular pH of tumor tissues but still could be internalized into cancer cells. The aggregation would lead to the enhanced accumulation and better therapy effect. Moreover, following cell uptake, DOX could be cleaved from the backbone at endo-/lysosomal pH, further inhibit the proliferation of cancer cells. These properties implied their promising future in cancer therapy. Moreover, since pillar[5]arenes are easily to be functionalized with different groups such as target ligands, it provides us an opportunity to integrate different functional groups into complex which holds potentials for different applications.



Scheme 1 Schematic illustration of preparation of supramolecular prodrug micelles and their pH responsive aggregate behavior upon extracellular pH stimulus of tumor tissues.

Memo:

A multi-modality probe constructed by bio-orthogonal chemistry for imaging of fibroblast activation protein-alpha



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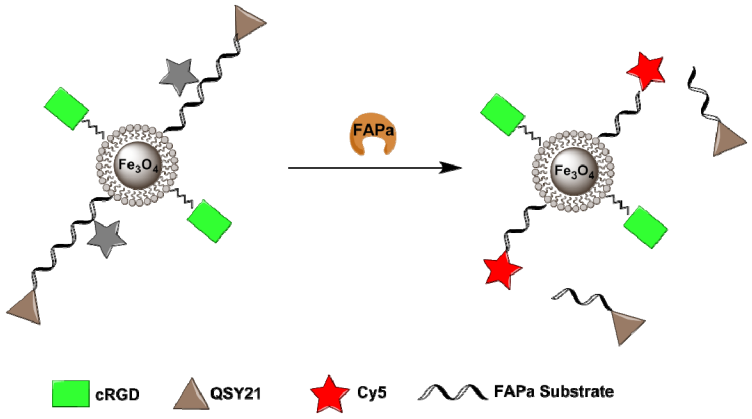
Multi-modality probes that enable complementary multi-modal imaging have emerged as powerful tools for visualizing diverse biomolecules in living systems. Construction of these multi-modality probes usually relies on the application of various chemical strategies. The orthogonality of these chemical methods is thus critical for integrating different functionalities into one probe. Here, we report the application of bio-orthogonal chemistry including click and photo-click reactions for construction of a multi-modality probe, which can be used for simultaneous fluorescent imaging and magnetic resonance imaging. Targeting ligand, cyclic RGD, was modified onto iron oxide nanoparticles (IONP) through click reaction and activatable fluorescent probes that respond to fibroblast activation protein-alpha[1] (FAPα) was conjugated with IONP via photo-click reaction. *In vitro* evidence suggests the multi-modality probe is highly selective and sensitive toward FAPα. Cellular imaging results also demonstrate the fluorescence of multi-modality probe was activated in FAPα positive cell lines in comparison with that in FAPα negative cell lines. The multi-modal imaging of such probe in living mice is now underway in our group.



Scheme1 Design strategy of dual-modality probe for FAPα

Reference:

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Memo:

Cysteine-Mediated Intracellular Building of Luciferin to Enhance Probe Retention and Fluorescence Turn-On

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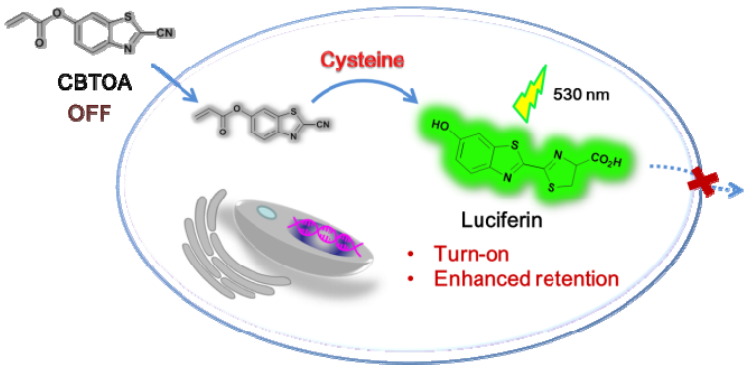
Sensitive and selective small molecular probes that enable real-time detection of endogenous cysteine (Cys) has become an attractive topic due to its essential roles in controlling cellular nitrogen balance and maintaining biological redox homeostasis. Herein, we report a Cys-specific probe **CBTOA** that showed not only fluorescence turn-on for sensitive detection of endogenous Cys but also enhanced probe retention inside cells for the real-time monitoring of Cys levels upon external stimulation. Using **CBTOA** as a real-time probe, we were able to monitor the change on Cys levels in living HeLa cells under ROS-induced oxidative stress as well as in human mesenchymal stem cells during adipogenic differentiation.



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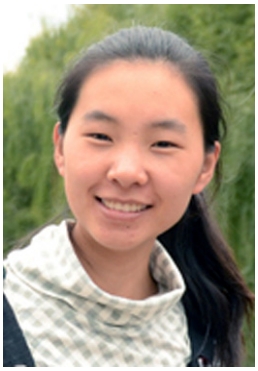
Memo:

Flow Synthesis of Biocompatible Fe_3O_4 Nanoparticles: Insight into the Effects of Residence Time, Fluid Velocity, and Tube Reactor Dimension on Particle Size Distribution



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PEGylated Fe_3O_4 nanoparticles were prepared through flow synthesis upon the pyrolysis of ferric acetylacetonate ($Fe(acac)_3$) in anisole at 250°C under pressure of 33 bar, in the presence of α,ω-dicarboxyl-terminated polyethylene glycol (HOOC–PEG–COOH) and oleylamine. In combination with theoretical analysis, the effects of linear velocity, residence time, and reactor dimension on particle size distribution were systematically investigated. In addition, the impact of Ostwald ripening on particle size distribution was also revealed. In particular, the impacts of monomer concentration distributions along both axial and radial directions of the tube reactor on the particle size distribution were carefully investigated. Under optimized conditions, PEGylated Fe_3O_4 nanoparticles with the relative standard deviation of particle size down to 10.6% were thus obtained. The resulting 4.6 nm particles exhibited excellent colloidal stability and high longitudinal relaxivity (r_1) up to 11.1 $mM^{-1}\cdot s^{-1}$, which manifested the reliability of flow synthesis in preparing PEGylated Fe_3O_4 nanoparticles as contrast agents for magnetic resonance imaging applications.

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Memo:

Near-infrared Light Activated Bioluminescent Probe On the Basis of Photocaged Upconversion Nanoparticles Conjugate

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Cell structures exhibit dynamic and complex spatial and temporal organization properties. The precise tracking of the dynamic properties of cellular functions at a desired time or location in intact cells or organism will be crucial for many biomedical applications. One appealing approach of providing such information is the photolysis of photoactivable or "caged"molecules, by which the activation process can be readily modulated by a beam of light with high spatial and temporal precision. However, most of the existing photocaged systems have to heavily rely on high-intensity UV or visible light to initiate the photoactivation. The inevitable cellular damage and less tissue-penetration from the short wavelength light irradiations will be the potential limitation for their applications in biological systems.

Herein, we demonstrated a novel method by combining versatile photocaged compounds with the upconversion nanoparticles (UCNPs) for *in vitro* and in *vivo* uncaging and bioluminescence imaging studies. Upon bioconjugation of photoreleasable bioluminescent probes with silica UCNPs and followed by near-infrared light (NIR) irradiation, the sharp emission converted from the UCNPs complex can effectively photorelease the imaging probe and thus significantly produce the fluorescence and bioluminescence signals. The non-autofluorescence and high tissue-penetration depth offered by this complex provide a platform for their biomedical applications in real-time imaging and targeted drug delivery in living system with less photo-damage. We anticipate that this UCNPs based photolysis with effective NIR uncaging activity would offer new possibilities for monitoring the dynamic functions of cells and selectively delivering the drug molecules at targeted areas *in vitro* and *in vivo*.

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Memo:

Long-Circulating Iodinated Albumin–Gadolinium Nanoparticles as Enhanced Magnetic Resonance and Computed Tomography Imaging Probes for Osteosarcoma Visualization

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Multimodal imaging probes represent an extraordinary tool for accurate diagnosis of diseases due to the complementary advantages of multiple imaging modalities.[1] The purpose of the work was to fabricate a simple dual-modality MR/CT probe for osteosarcoma visualization in vivo. Protein-directed synthesis methods offer a suitable alternative to MR/CT probe produced by synthetic chemistry.[2-4] Bovine serum albumin stabilized gadolinium nanoparticles (BSA-GdNPs) was first prepared via a biomimetic synthesis method and was subsequently iodinated by chloramine-T method. The final iodinated BSA-GdNPs (I-BSA-GdNPs) showed excellent chemical stability and biocompatibility, intense X-ray attenuation coefficient, and good MR imaging ability. However, an iodinated protein nanoparticles synthesis for MR/CT imaging, as well as its useful application, has not been reported yet. Intravenous injection of I-BSA-GdNPs into orthotopic osteosarcoma-bearing rats led to its accumulation and retention by the tumor, allowing for a noninvasive tumor dual-modality imaging through the intact thigh (Figure 1). Our study is therefore highlighting the properties of albumin in this field combined with its useful use in dual-model MR/CT osteosarcoma visualization, underlining its potential use as a drug carrier for a future therapy on cancer.

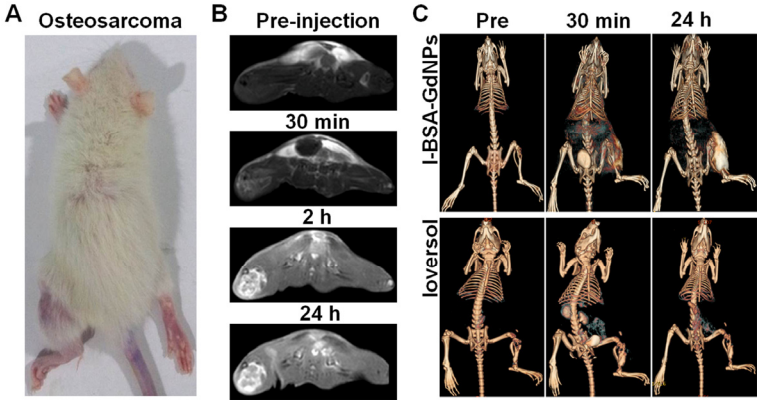

Figure 1. (A) Orthotopic osteosarcoma animal models. (B) In vivo T1-weighted MRI images of orthotopic osteosarcoma rats before and at 30 min, 2 h, and 24 h after I-BSA-GdNPs injection. (C) CT 3Dimages of orthotopic osteosarcoma rats after Ioversol and I-BSA-GdNPs injection.

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Memo:

Rapid 3D-Sodium MRI of Knee Joint In-vivo at 7T

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Synopsis: The main purpose of this work was to demonstrate the feasibility of acquiring high resolution, isotropic 3D-sodium knee images of healthy and OA patients in vivo at 7T with clinically acceptable scan times via 3D-radial acquisition. The preliminary results suggest that the sodium imaging at 7T may be a viable potential alternative for OA imaging.

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Memo:

Sensitive Detection of Metallo β-lactamases (MBLs)-expressing Bacteria using A Bioluminogenic Probe

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Antibiotic resistance among Gram-negative bacteria such as *Escherichia coli*, *Klebsiella species*, and other *Enterobacteriaceae* is emerging worldwide at an alarming rate because of the misuse and overuse of antibiotics.[1] Particularly, the resistance against broad-spectrum β-lactam antibiotics has become a major public health concern. Of the many antibiotics, carbapenems have the broadest spectrum of activity and greatest potency against different types of bacteria, and have become the last resort in the treatment of serious bacterial infections.[2] However, carbapenem-resistant *Enterobacteriaceae* (CRE) are now frequently being observed and the number of cases is steadily growing, mostly as a consequence of acquired carbapenemases which have been increasingly reported as the cause of therapeutic failures both in hospital- and community-acquired infections, especially for MBLs.[3] Therefore, rapid and accurate detection of MBLs producers is critically important for appropriate antibacterial chemotherapies and rigorous infection control. Herein, we have synthesized a novel bioluminogenic probe **(*s*)-CL-6** by conjugation of D-luciferin to the 3' position of the 6,7-trans cephalosporin.[4] The results show **(*s*)-CL-6** has good specificity and high sensitivity for detection of MBLs in pathogenic bacteria.

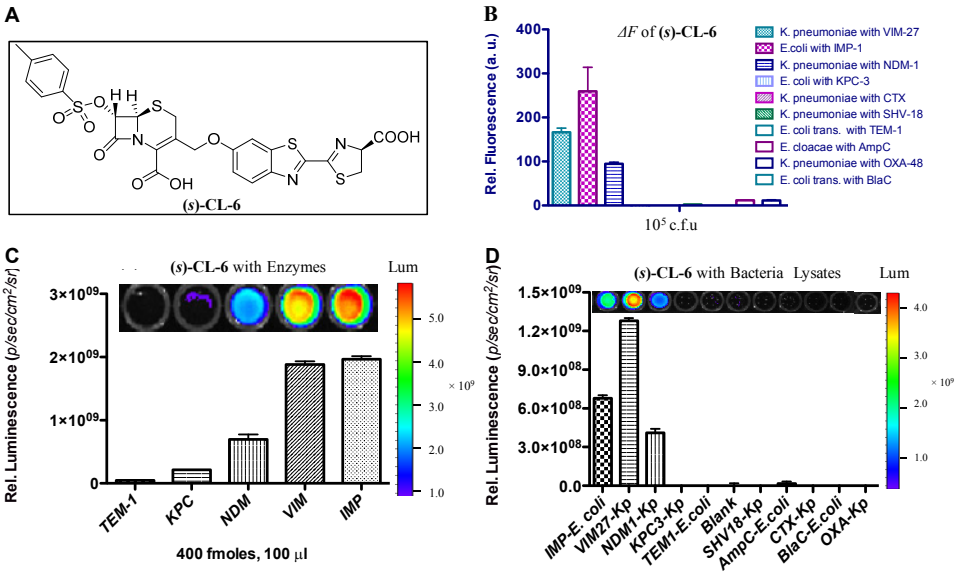

Figure 1. (A) Structure of (s)-CL-6; (B) Relative fluorescence of various β-lactamase-expressing bacteria after incubation with (s)-CL-6 (1 μM); (C) Relative bioluminescence and photographs of various β-lactamases after incubation with (s)-CL-6 (1 μM) and fluc; (D) Relative bioluminescence and photographs of various β-lactamase-expressing bacteria lysates (105 c.f.u bacteria) after incubation with (s)-CL-6 (1 μM) and fluc

Memo:

Phenoxazinium based near-infrared fluorescent probe for the selective detection of potassium ions

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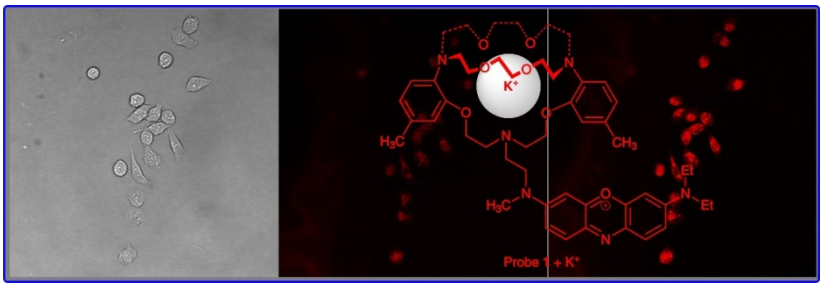
Abstract: the near-infrared fluorescent probe (1) with a cryptand ligand and phenoxazinium fluorophore for potassium ion was designed and synthesized. Based on photoinduced electron transfer mechanism, the fluorescence at 672 nm is increased after binding with potassium ions. This probe had an affinity for potassium ions in the mM range, and good selectivity for potassium ion over sodium ion and the other physiological cations in the physiological condition. The long-wavelength emission and water solubility of this probe are further suitable for potassium ions imaging in living cells such as vascular endothelial cell, cardiac muscle cell and cancer cell.



Keywords: *Biosensor, Chemosensor, Potassium, Phenoxazinium, Long-wavelength excitation, Near-infrared emission.*

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Memo:

^{99m}Tc labled Zoledronic for colorectal cancer nuclear medicine molecular imaging

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The targeting to aim organic or pathologic tissues is an important index to judge the value of the nuclear medicine imaging agent. Zoledronic acid (ZOL) has been widely used to inhibit skeletal fractures in patients with cancers such as multiple myeloma and prostate cancer, as well as for treating osteoporosis. In this work, we label ZOL with 99mT for SPECT imaging, obtaining ^{99m} Tc- ZOL complex. In vivo SPECT imaging exhibit high tumor uptake of 99mTc- ZOL via enhance the penetration and retention. Our results further improve the biomedical applications in colon tumor therapeutics.

The labeled rate of ^{99m}Tc-ZOL was 87.6% and the radiochemical purity was 99%. So the specific activity of the labeled compound was 1.38 MBq / mg by calculation (118.4 MBq*87.6%/74.8mg). The stability of ^{99m}Tc-ZOL was assessed by incubating in fresh human plasma or normal saline at 37^{o}C, the remained ^{99m}Tc -ZOL were still greater than 95% either in saline or in fresh human plasma. Scatchard plot showed that two different affinity carriers involved ^{99m}Tc -ZOL transmembrane transportation. The higher affinity carrier Kd was 3.33μmol/L (n=3), and the maximum binding capacity, Bmax, was 93667pmol/mg (n=3); the lower affinity carrier Kd was 116.28pmol/L (n=3), and the maximum binding capacity, Bmax, was 107.73pmol/mg (n=3).

In the group treated with ^{99m}Tc -ZOL at 1.5 μmol/L, the proportion of cells at G_2/M were increased from 18.26% ± 1.59 to 34.28%±0.16 and simultaneously accompanied by a significant decrease in the proportion of cells in S phase, which was decreased from 29.65% ± 0.83 to 0 %. The result indicated that treatment of lovo cells with ^{99m}Tc -ZOL could induce the occurrence of the retardation of cells at G2/M phases and displayed a significant dose-dependent relationships. At the same time with the cell cycle retardation, the proportion of cells at the SubG1 displayed a significantly increasing treatment with ^{99m}Tc -ZOL, indicating that ZOL could induce lovo cells apoptosis.

Lovo cells were cultured in medium containing 1.5μmol/L for 48 hours, respectively. After being cultured, the red fluorescent light intensities within Lovo cells were gradually reduced, indicating that the stability of mitochondrial membrane potential is reduced, leads to the reduction of the capacity of mitochondrial membrane to gather JC-1.

Detection with Western blot revealed that ^{99m}Tc -ZOL caused significant effects on the expression of apoptosis-related proteins. As shown, the expression of pro-apoptosis protein Caspase-3 was basically unchanged whereas the expression of the activated Caspase-3 was significantly increased, indicating that ZOL induced apoptosis is mediated via controlling the activation degree of Caspase-3.

The SPECT scan imaging showed that nude mice bearing tumors injected with $Na^{99m}TcO_4$ exhibited the same radioactive of the tumors as the background levels. In contrast, tumors in the lower flank of the mice treated with ^{99m}Tc -ZOL could be clear imaged, and the radioactivity in tumor place was notably higher than the background level. In ^{99m}Tc -ZOL plus ZOL group, the tumor uptake of ^{99m}Tc -ZOL were blocked by overdose unlabeled ZOL, and exhibited no obvious radioactivity from SPECT imaging.

In a summary, we indicated that there was two transmembrane transport systems with higher or lower affinity to carry ZOL or $^{\mathbf{99m}}$Tc -ZOL against the electrochemical gradient. Our SPECT data also testified that ZOL or $^{\mathbf{99m}}$Tc -ZOL can be engulfed by colon tumor xerography in vivo. It implied that $^{\mathbf{99m}}$Tc -ZOL or its derivatives have potential as a new SPECT imaging agent for cancer diagnosis.

Memo:

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Notes:

*Please pay attention to the weather, especially in the morning and the evening.

*Please give your powerpoint files to Mr. Tiancong Ma before your report.

*Check out time is at 14:00 on the day of departure.

附：入住敬斋酒店的与会代表注意事项

往返敬斋-独墅湖的巴士接送安排		
2015-4-25	17:00-21:00，发车间隔：30 min	往返敬斋酒店-独墅湖酒店
2015-4-26	7:40	敬斋前往独墅湖酒店
	21:00	前往敬斋酒店
2015-4-27	7:40	敬斋前往独墅湖酒店
	20:00	独墅湖前往敬斋酒店
2015-4-28	7:40	敬斋前往独墅湖酒店
	13:30	独墅湖前往敬斋酒店
	21:00	前往敬斋酒店

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